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Flame Retardants Used in Flexible Polyurethane Foam: An Alternatives Assessment Update

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List of Acronyms and Abbreviations

ACR	Acute to chronic ratio
APP	Ammonium polyphosphate
ASTM	American Society for Testing and Materials
BAF	Bioaccumulation factor
BCF	Bioconcentration factor
BEARFTI	Bureau of Electronic and Appliance Repair, Home Furnishings and Thermal Insulation
CASRN	Chemical Abstracts Service Registry Number
CDC	Centers for Disease Control and Prevention
CDR	Chemical Data Reporting
CFR	Code of Federal Regulations
CHO	Chinese hamster ovary cells
ChV	Chronic value
CPSC	Consumer Product Safety Commission
DecaBDE	Decabromodiphenyl ether
DfE	Design for the Environment
DMSO	Dimethyl sulfoxide
E_bC_{50}	Concentration at which 50% reduction of biomass is observed
EC_{50}	Half maximal effective concentration
ECHA	European Chemicals Agency
ECOSAR	Ecological Structure Activity Relationships
EDSP	Endocrine Disruptor Screening Program
EEC	European Economic Community
EPA	U.S. Environmental Protection Agency
EPI	Estimation Program Interface
E_rC_{50}	Concentration at which a 50% inhibition of growth rate is observed
EU	European Union
FFRP	Furniture Flame Retardancy Partnership
FPUF	Flexible polyurethane foam
GD	Gestation day
GHS	Globally Harmonized System of Classification and Labeling of Chemicals
GLP	Good laboratory practice
HPLC	High performance liquid chromatography
HPV	High Production Volume
HPVIS	High Production Volume Information System
HSDB	Hazardous Substances Data Bank
IARC	International Agency for Research on Cancer
ID_{50}	Median ineffective dose
IFR	Inherently flame retardant
IPTPP	Isopropylated triphenyl phosphate
IRIS	Integrated Risk Information System
IUCLID	International Uniform Chemical Information Database
K_{oc}	Sediment/soil adsorption/desorption coefficient

K_{ow}	Octanol/water partition coefficient
LbL	Layer-by-layer
LC_{50}	Median lethal concentration
LC_{100}	Absolute lethal concentration
LCA	Life cycle assessment
LD	Lactation day
LD_{50}	Median lethal dose
LD_{Lo}	Lethal dose low
LFL	Lower limit of flammability
LOAEL	Lowest observed adverse effect level
LOEC	Lowest observed effect concentration
MF	Molecular formula
MITI	Japanese Ministry of International Trade and Industry
MSDS	Material Safety Datasheet
MW	Molecular weight
NAS	National Academy of Sciences
NCI	National Cancer Institute
NCP	New Chemicals Program
NES	No effects at saturation
NFPA	National Fire Protection Association
NGO	Non-governmental organization
NICNAS	National Industrial Chemicals Notification and Assessment Scheme
NOAEC	No observed adverse effect concentration
NOAEL	No observed adverse effect level
NOEC	No observed effect concentration
NTP	National Toxicology Program
OECD	Organisation of Economic Cooperation and Development
OEHHA	California Office of Environmental Health Hazard Assessment
OPFR	Organophosphate flame retardant
OPP	Office of Pesticide Programs
OPPT	Office of Pollution Prevention and Toxics
PBDE	Polybrominated diphenyl ether
PBT Profiler	Persistent, Bioaccumulative, and Toxic Chemical Profiler
PentaBDE	Pentabromodiphenyl ether
PINFA	Phosphorus, Inorganic & Nitrogen Flame Retardants Association
PMN	Premanufacture Notification
ppm	parts per million
QSAR	Quantitative Structure Activity Relationship
REACH	**R**egistration, **E**valuation, **A**uthorisation and Restriction of **Ch**emicals
SAR	Structure Activity Relationship
SF	Sustainable Futures
SIDS	Screening Information Data Set
SMILES	Simplified Molecular-Input Line-Entry System
SNUR	Significant New Use Rule
TB	Technical Bulletin
TBB	Benzoic acid, 2,3,4,5-tetrabromo-, 2-ethylhexyl ester

TBPH	Di(2-ethylhexyl) tetrabromophthalate
TBPP	Tris (p-t-butylphenyl) phosphate
TCEP	Tris (2-chloroethyl) phosphate
TCP	Tricresyl phosphate
TCPP	Tris (2-chloro-1-methylethyl) phosphate
TDCPP	Tris (1,3-dichloro-2-propyl) phosphate
TG	Test guidelines
TPP	Triphenyl phosphate
TSCA	Toxic Substances Control Act
UFAC	Upholstered Furniture Action Council
UFL	Upper limit of flammability
V6	Phosphoric acid, P,P'-[2,2-bis(chloromethyl)-1,3-propanediyl] P,P,P',P'-tetrakis(2-chloroethyl) ester
WAF	Water accommodated fraction

1 Introduction

1.1 The Furniture Flame Retardancy Partnership

The flame retardant pentabromodiphenyl ether (pentaBDE) was widely used as an additive in furniture foam and in other products to meet flammability requirements in the late 20th century. In the early 2000s, growing concerns over the possible environmental and public health impacts of pentaBDE led to a voluntary phase-out of the chemical by the sole U.S. manufacturer. At the end of 2004, industry voluntarily ceased production of pentaBDE, and U.S. Environmental Protection Agency (EPA) issued a regulation that prohibited further manufacture of the chemical without notification of EPA under the Toxic Substances Control Act (TSCA). The substitution likely to result from the move to alternatives to pentaBDE resulted in the need for evaluating flame retardants.

In 2003, EPA's Design for the Environment Program (DfE) convened a multi-stakeholder group to undertake an assessment of viable alternatives to pentaBDE. The Furniture Flame Retardancy Partnership (FFRP) included chemical manufacturers, furniture manufacturers, governmental representatives and environmental non-governmental organizations (NGOs). In 2005, EPA issued a report[1] based on the partnership's work assessing the human health and environmental profiles of alternatives to pentaBDE, indicating that a number of alternatives were available that appeared to pose a lower level of concern than was associated with pentaBDE. This DfE Alternatives Assessment update report identifies and evaluates flame retardants that may be used in flexible polyurethane foam (FPUF) products (as of 2013) and updates hazard profiles from the previous report.

Additional actions regarding pentaBDE were outlined in the EPA 2009 Action Plan for polybrominated diphenyl ethers (PBDEs) (U.S. EPA 2009).

1.2 Updating the 2005 Furniture Flame Retardancy Report

Purpose and Scope of the Updated Report

The goal of the FFRP, as stated in its 2005 report, was to "identify and assess environmentally safer chemical alternatives to pentaBDE, and to investigate other technologies for improving furniture fire safety" (U.S. EPA 2005a). Since the publication of the 2005 FFRP report, the marketplace for flame retardants used in FPUF has changed significantly, with some flame retardant chemicals being withdrawn from the market, and others being introduced. This update is intended to identify all flame retardants either known to be used, or marketed to be used, in meeting fire safety requirements for upholstered consumer products containing FPUF. Also, DfE published updated hazard criteria in 2011 (see "Alternatives Assessment Criteria for Hazard Evaluation"), and data from the 2005 FFRP report were re-evaluated using the current criteria, and included in this report. The resulting hazard profiles allow a direct comparison among

[1] Available at: http://www2.epa.gov/saferchoice/environmental-profiles-chemical-flame-retardant-alternatives-low-density-polyurethane.

substances found in the two DfE alternative assessment reports. It should be noted that, as in all DfE Alternatives Assessments, the term "alternative" is used to designate any chemical that can be used in the functional category, and does not designate preferability for environmental or health endpoints.

DfE is publishing the current update for several reasons, in addition to the marketplace changes and data developments described above. Public and media attention to flame retardants in recent years has led to new scrutiny of flame retardant chemistry. Also, both the State of California and the Consumer Product Safety Commission (CPSC) have established or are planning to establish updated flame retardancy standards for upholstered furniture (see Section 3 below). The impact of these changes in terms of flame retardant selection and use is as yet unknown; therefore, it is important that the most current information be available to decision makers, which requires an update of the chemicals and hazard data contained in the 2005 report. In addition, several chemicals in this category (notably benzoic acid, 2,3,4,5-tetrabromo-, 2-ethylhexyl ester (TBB), di(2-ethylhexyl) tetrabromophthalate (TBPH), and tris (2-chloroethyl) phosphate (TCEP)) were identified by EPA as TSCA Work Plan chemicals for assessment beginning in 2013 (U.S. EPA 2013b). The full list of chemicals for assessment can be found here: http://www.epa.gov/oppt/existingchemicals/pubs/assessment_chemicals_list.html. Updating the hazard and use information for these and related chemicals complements other assessment projects underway at EPA.

As mentioned above, this report by EPA's DfE Program updates and supplements the previous alternatives assessment report developed by the FFRP (U.S. EPA 2005a). DfE identified 16 flame retardant chemicals, one non-proprietary mixture, and 2 proprietary mixtures to be evaluated in the update report. Additional information on polyurethane foam is available in the 2005 FFRP report (U.S. EPA 2005a).

The scope of this report was expanded to include all upholstered consumer products containing FPUF (i.e., not just furniture), including a number of flame retardants that have been identified in products such as car seats and nursing pillows (Stapleton, Klosterhaus et al. 2011). These products, like the furniture that was the subject of the 2005 report, are made from FPUF with a covering fabric, and, when flame retarded, are expected to rely on the same set of flame retardants. (Some upholstered FPUF products, particularly for babies and children, are exempt from flame retardancy requirements, but may still contain flame retarded foam.)

The 2005 report describes alternative methods of improving furniture fire safety; for example, the use of IFR upholstery, or the use of fire barriers between upholstery and foam. Since the 2005 report was published, one additional technology, known as layer-by-layer (LbL) assembled flame retardancy, has been in development, but is not yet commercialized. The hazards associated with this technology are not addressed in this update because it is nanoscale and not commercially available, and the DfE criteria have not been evaluated for suitability to assess nano-sized substances. The current update addresses the hazards associated with one alternative technology--expandable graphite (used in graphite impregnated foam), which may be commercially viable as a replacement for flame retardant chemicals in FPUF for some applications. All other alternatives are briefly described in Section 4. Because the DfE hazard criteria are developed for chemical-to-chemical comparison under a specific functional use,

rather than material-to-material comparison, a life cycle assessment (LCA) might be a better tool for evaluating and comparing alternative materials (see Section 1.3).

How to Use This Report

Audiences for this report include stakeholders interested in chemical hazards and safer alternatives, including but not limited to chemical manufacturers, component manufacturers, product manufacturers, retailers, consumers, NGOs, consultants, and state and federal regulators. Three potential uses of this report include:

Identification of potential substitutes. This report allows stakeholders interested in chemical substitution to identify functional alternatives for flame retardants used in flexible polyurethane foam, which is commonly found in furniture. The two lists of potential alternatives includes chemicals identified by stakeholders as viable, functional alternatives, as well as chemicals that are not considered functional alternatives, and information on inherently flame retardant (IFR) polymers. The inclusion of a chemical in this assessment does not indicate environmental- or health-based preferability. By identifying potential functional alternatives, this report assists manufacturers in selecting chemicals for additional performance testing, and can identify a need for alternative approaches to fire safety such as barrier materials, as studied by the CPSC (CPSC 2013b). Although the alternatives identified in this report are additive flame retardants that can be used in barrier materials, an evaluation of the use of the identified chemicals in these technologies is outside of the scope of this report.

Selection of alternative chemicals based on comparative chemical hazard assessment. This report helps decision-makers understand and compare the hazards associated with potential alternatives to which they can supplement information on performance and cost. Some alternatives may be associated with hazard concerns similar to those of pentaBDE; others may be associated with different hazard concerns. Use of the hazard information in Section 2 may help businesses avoid the cost of repeated substitution. Section 7 contains a robust human health and environmental profile for each chemical that is based on empirical data when available, and enhanced with modeling and expert judgment to fill data gaps. The profiles can help decision-makers understand which potential alternatives may come under scrutiny in the future, and choose the safest possible alternative now to reduce future costs. In addition to reading the hazard comparison table, decision-makers should review the full hazard assessments for each chemical available in Section 7. The hazard assessments provide more information on hazard criteria, data interpretation, and information used to assign hazard values in each category, and ensure a complete understanding of the hazard profiles of each alternative.

Use of hazard information for further analysis and decision-making. The information in this report can be used to inform further analyses on preferred alternative chemicals, such as risk assessments or LCA. For example, a decision-maker could identify several functional alternatives with preferable hazard profiles, and conduct product-specific risk assessments based on exposure expectations along the product's life-cycle. A decision-maker could also conduct an assessment of the (non-hazard) environmental impacts associated with the life cycles of the alternatives (or any differences in environmental impacts of the product that may result from choosing one alternative over another). This type of supplementary information may be helpful

in guiding product-specific decision-making. In addition, information in this report can be used to identify the Very Persistent Very Bioaccumulative chemicals, PBT chemicals, and those with an "equivalent level of concern" targeted under European Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) policy. This report does not evaluate the relative hazards of alternatives, but GreenScreen® (www.cleanproduction.org/Greenscreen.php) is one tool that can be used for this purpose. The criteria used to develop the hazard assessments in this report can also be used to inform Green Chemistry design.

1.3 Alternatives Assessment as a Risk Management Tool

The DfE Alternatives Assessment process was one of a suite of actions EPA chose to pursue to manage the potential risks associated with pentaBDE. The Agency chose this tool to inform the chemical substitution that may occur as an outcome of other risk management activities.

Chemical alternatives assessment compares chemicals within the same functional use group, and evaluates alternatives across a consistent and comprehensive set of hazard endpoints and environmental fate parameters. Information about chemical hazards derived from this type of comparative chemical hazard assessment, in combination with analyses of cost, performance, and other factors, can be used by industry and other decision-makers to select safer alternative chemicals for a particular use. (For details on DfE's Hazard Assessment criteria, see "Alternatives Assessment Criteria for Hazard Evaluation," available at http://www2.epa.gov/saferchoice/design-environment-alternatives-assessments.)

Alternatives assessment is most useful in identifying safer substitutes when available alternatives meet performance requirements and are expected to present lower hazards for human health and the environment. Alternatives assessments may identify scenarios in which there do not appear to be any preferable alternatives to the chemical being considered for replacement. In this case, the resulting information can be used to guide innovation, and the development of safer chemicals and products.

Functional Use Approach and Chemical Fate

DfE's "functional use" approach to alternatives assessment orients chemical evaluations within a given product type and functionality. Under this approach, factors related to exposure scenarios, such as physical form and route of exposure, can be similar within a given functional use analysis and will fall out of the comparison, so that a reduction in hazard is equivalent to a reduction of risk. When less hazardous alternatives have different physical-chemical profiles or require different use levels, it may be appropriate to also conduct an exposure or risk assessment.

DfE Alternatives Assessments consider intrinsic properties of chemical substitutes that affect exposure potential, including absorption potential, persistence, and bioaccumulation. Under this approach, the health and environmental hazard profiles in the alternatives assessments become the key variable and source of distinguishing characteristics. Information on key properties that can be used to evaluate significant differences in environmental fate and transport, including persistence, bioaccumulation, and physical properties, are included in the hazard assessment.

Under conditions where fire or incineration occurs, a halogenated substance may contribute to halogenated dibenzodioxin and dibenzofuran formation, increase the generation of PAHs, and impact fire parameters such as smoke and carbon monoxide (Sidhu, Morgan et al. 2013). However, combustion reactions are complex and variable, and make inclusion of combustion byproducts in hazard assessment challenging. Both halogenated and non-halogenated flame retardants may yield other toxic by-products that would need to be compared, not only halogenated dioxins and furans. For these reasons, the pyrolysis transformation products are not assessed in this report.

DfE Alternatives Assessments Scope and Data Sources

As described above, the DfE Alternatives Assessment process is intended to provide useful hazard and fate data on chemicals within a given functional class; it is not intended to describe exposure or risk, nor do alternatives assessments provide quantitative information on chemical performance in the product or cost, which are most appropriately conducted by manufacturers who have hands-on expertise in product cost and performance. DfE Alternatives Assessments provide complete hazard data according to a uniform set of criteria, in a format amenable to comparison among chemicals, and in a relatively quick timeframe. This information can contribute important information for decision makers, whether chemical manufacturers, product manufacturers, consumers, or NGOs.

As with other DfE Alternatives Assessments, this report summarizes available data from many sources, including information from experts on uses of flame retardants, and hazard and fate information from the scientific literature. Because EPA oversees the TSCA Premanufacture Notification (PMN) process, DfE also has access to hazard and fate information from confidential and non-confidential studies submitted to the Agency as part of a PMN chemical review. Furthermore, when little data are available on a chemical of interest, hazard and fate information may be derived from data on analog molecules, which may be confidential. Experts from DfE, from other groups within EPA's Office of Chemical Safety and Pollution Prevention (OCSPP), and from DfE's contractors, provide expert judgment on chemical hazard and fate for those chemicals. This report compiles existing data and does not include results of new research on chemical hazards; EPA did not undertake any testing for this report.

When reporting hazard data on available alternatives, DfE does not recommend specific flame retardants. It is the role of manufacturers to use the data provided, along with their own expert knowledge, to choose the safest chemicals possible, while also meeting their requirements for efficacy, price, and other criteria.

Green Chemistry Principles

The DfE Alternatives Assessment approach is aligned with established green chemistry principles. Two of these principles are particularly relevant to the DfE approach:

- Principle 4: Design of safer chemicals – "Chemical products should be designed to affect their desired function, while minimizing their toxicity;" and

- Principle 10: Design for degradability – "Chemical products should be designed so that at the end of their function they break down into innocuous degradation products and do not persist in the environment" (Anastas and Warner 1998).

DfE incorporates these two green chemistry principles in its criteria, and applies them in its assessment of chemical hazard and fate in the environment. This approach enables identification of safer substitutes that emphasize greener chemistry, and points the way to innovation in safer chemical design, where hazard becomes a part of a performance evaluation.

Alternatives, Life-Cycle, and Risk Assessments

Alternatives assessment, life-cycle assessment (LCA), and risk assessment are tools that can be used to evaluate and improve the sustainability profiles of chemicals, products, and services. These tools, which can be complementary to one another, should be selected according to the ultimate decisions needing to be made, and other regulatory and policy considerations. DfE Alternatives Assessments establish a foundation that other tools, such as risk assessment and LCA, can build upon.

Risk assessment and alternatives assessment are both based on the premise that risk is a function of hazard and exposure. Risk assessment characterizes the nature and magnitude of hazard and exposure from chemical contaminants and other stressors. A DfE Alternatives Assessment evaluates and compares the nature of the chemical hazards, and reflects a view that when exposure is comparable, risk is reduced through the use of less hazardous chemicals. Alternatives assessment strives to decrease the reliance on exposure controls, thus reducing risk when exposure controls fail.

An LCA can create a robust picture of a variety of environmental impacts associated with the material and energy inputs and outputs throughout the life cycle (or part of a life cycle) of a product or service, and by doing so can identify opportunities for reducing those impacts. However, an LCA may not assess the inherent hazards of the chemical inputs and outputs for each life cycle stage. During decision-making, risk assessment or LCA can be applied to the lower-hazard or potentially preferable alternatives, to further distinguish between preferable substitutes, or to identify unintended consequences.

1.4 DfE Alternatives Assessment and the Toxic Substances Control Act

EPA's DfE Program is administered by the Office of Pollution Prevention and Toxics (OPPT), which is charged with the implementation of the Toxic Substances Control Act (TSCA) and the Pollution Prevention Act (PPA).

Central to the administration of TSCA is the management of the TSCA Inventory. Section 8 (b) of TSCA requires EPA to compile, keep current, and publish a list of each chemical substance that is manufactured or processed in the United States. Companies are required to verify the TSCA status of any substance they wish to manufacture or import for a TSCA-related purpose. For more information, please refer to the TSCA Chemical Substance Inventory website: http://www.epa.gov/opptintr/existingchemicals/pubs/tscainventory/basic.html.

Substances selected for evaluation in a DfE Alternatives Assessment generally are subject to TSCA regulations, and therefore must be listed on the TSCA Inventory, or be exempt or excluded from reporting before being manufactured in or imported to, or otherwise introduced in commerce in, the United States. For more information see http://www.epa.gov/oppt/newchems/pubs/whofiles.htm.

To be as inclusive as possible, DfE Alternatives Assessments may consider substances that may not have been reviewed yet as new chemicals under TSCA, and therefore may not be listed on the TSCA Inventory. DfE has worked with stakeholders to identify and include chemicals that are of interest and likely to be functional alternatives, regardless of their TSCA status. Chemical identities are gathered from the scientific literature and from stakeholders and, for non-confidential substances, appropriate TSCA identities are provided.

Persons are advised that substances, including DfE-identified functional alternatives, may not be introduced into U.S. commerce unless they are in compliance with TSCA. Introducing such substances without adhering to the TSCA provisions may be a violation of applicable law. Those who are considering using a substance discussed in this report should check with the manufacturer or importer about the substance's TSCA status. If you have questions about the reportability of substances under TSCA, please contact the OPPT Industrial Chemistry Branch at 202-564-8740.

2 Hazard Evaluation Results for Flame Retardants Used in Flexible Polyurethane Foam

2.1 Hazard Comparison Table

The hazard comparison table is shown below, followed by the results described both by the chemical groupings found in the hazard comparison table and by type of hazard endpoint.

Other approaches to improving fire safety of upholstered FPUF products exist, including flame resistant cover fabrics and fire barriers, which could be comprised of chemically treated materials (e.g., treated cotton-based materials) or inherently flame retardant materials (e.g., wool, Kevlar), and nanoclay technologies (See Section 4). These alternative technologies are not assessed for hazard in this report. The DfE Hazard Evaluation Criteria (described in Section 5.1.2) are not amenable to assessing the hazard from the flame resistant cover fabrics and fire barriers. Additionally, the DfE Hazard Evaluation Criteria have not been evaluated for suitability to assess nano-sized substances. Further, layer-by-layer nanoclay technologies are currently in research and development and are not commercially available for use in upholstered FPUF products.

Table 2-1. Screening Level Toxicity Hazard Summary

This table contains hazard information for each chemical; evaluation of risk considers both hazard and exposure. Variations in end-of-life processes or degradation and combustion by-products are discussed in the report but not addressed directly in the hazard profiles. The caveats listed below must be taken into account when interpreting the information in the table.

VL = Very Low hazard L = Low hazard M = Moderate hazard H = High hazard VH = Very High hazard — Endpoints in colored text (VL, L, M, H, and VH) were assigned based on empirical data. Endpoints in black italics *(VL, L, M, H,* and *VH*) were assigned using values from predictive models and/or professional judgment.

* Each hazard designation for a mixture is based upon the component with the highest hazard, whether it is an experimental or estimated value. For Firemaster® mixtures there is no corresponding profile in Section 7.

^ This component of Firemaster® 550 may be used alone or in other mixtures as an alternative.

¥ Aquatic toxicity: EPA/DfE criteria are based in large part upon water column exposures, which may not be adequate for poorly soluble substances such as many flame retardants that may partition to sediment and particulates.

Chemical (for full chemical name and relevant trade names see the individual profiles in Section 7)	CASRN	Human Health Effects											Aquatic Toxicity		Environmental Fate	
		Acute Toxicity	Carcinogenicity	Genotoxicity	Reproductive	Developmental	Neurological	Repeated Dose	Skin Sensitization	Respiratory Sensitization	Eye Irritation	Dermal Irritation	Acute	Chronic	Persistence	Bioaccumulation
Halogenated Flame Retardant Alternatives																
Firemaster® 550 Components																
Firemaster® 550*	Mixture	L	*M*	M	H	*H*	*H*	H	*M*		L	L	VH	VH	*H*	*H*
Benzoic acid, 2,3,4,5-tetrabromo-, 2-ethylhexyl ester (TBB)¥	183658-27-7	*L*	*M*	*L*	*M*	*M*	*M*	*M*	*M*		*M*	*L*	*L*	*L*	*H*	*H*
Di(2-ethylhexyl) tetrabromophthalate (TBPH)^¥	26040-51-7	*L*	*M*	M	*M*	*M*	*M*	M	L		L	L	*L*	*L*	*H*	*H*
Isopropylated triphenyl phosphate (IPTPP)^	68937-41-7	L	*M*	L	H	*H*	*H*	H	L		L	L	VH	VH	M	*H*
Triphenyl phosphate (TPP)^	115-86-6	L	*M*	L	L	L	L	H	L		L	VL	VH	VH	L	M
Firemaster® 600																
Firemaster® 600*	Mixture; Proprietary	L	*M*	M	M	*M*	M	H	*M*		L	M	VH	VH	*H*	H
Chlorinated Phosphorus Alternatives																
Tris (2-chloroethyl) phosphate (TCEP)	115-96-8	H	H	M	M	H	M	M	L		L	L	H	*H*	M	L
Tris (2-chloro-1-methylethyl) phosphate (TCPP)	13674-84-5; 6145-73-9	L	*M*	L	H	H	*M*	M	L		L	L	M	*M*	H	L
Tris (1,3-dichloro-2-propyl) phosphate (TDCPP)	13674-87-8	L	H	M	H	M	L	H	L		L	L	H	H	H	L
Phosphoric acid, P,P'-[2,2-bis(chloromethyl)-1,3-propanediyl] P,P,P',P'-tetrakis(2-chloroethyl) ester	38051-10-4	L	*M*	L	M	H	L	M	L		L	L	M	*M*	H	*L*

Table 2-2. Screening Level Toxicity Hazard Summary

This table contains hazard information for each chemical; evaluation of risk considers both hazard and exposure. Variations in end-of-life processes or degradation and combustion by-products are discussed in the report but not addressed directly in the hazard profiles. The caveats listed below must be taken into account when interpreting the information in the table.

VL = Very Low hazard L = Low hazard M = Moderate hazard H = High hazard VH = Very High hazard — Endpoints in colored text (VL, L, M, H, and VH) were assigned based on empirical data. Endpoints in black italics *(VL, L, M, H,* and *VH*) were assigned using values from predictive models and/or professional judgment.

♦ Expandable graphite commercial formulations are prepared using chemical washes that may be present in the final product as residues. The associated hazards vary depending on the specific wash chemicals used, and as a result, the hazards may change by manufacturer. One confidential wash has additional hazard concern as follows, based on experimental data: HIGH-Acute Toxicity, Eye Irritation, Dermal irritation. Other manufacturers may use a wash that contains chromic acid (CASRN 7738-94-5) with additional hazard concerns as follows, based on experimental data: HIGH-Acute Toxicity, Carcinogenicity, Genotoxicity, Reproductive, Repeated dose, Skin sensitization, Respiratory sensitization, Eye Irritation, Dermal irritation.

[d] This hazard designation would be assigned MODERATE for a potential for lung overloading if >5% of the particles are in the respirable range as a result of dust forming operations.

¥ Aquatic toxicity: EPA/DfE criteria are based in large part upon water column exposures, which may not be adequate for poorly soluble substances such as many flame retardants that may partition to sediment and particulates.

Chemical (for full chemical name and relevant trade names see the individual profiles in Section 7)	CASRN	Human Health Effects											Aquatic Toxicity		Environmental Fate	
		Acute Toxicity	Carcinogenicity	Genotoxicity	Reproductive	Developmental	Neurological	Repeated Dose	Skin Sensitization	Respiratory Sensitization	Eye Irritation	Dermal Irritation	Acute	Chronic	Persistence	Bioaccumulation
Non-Halogenated Flame Retardant Alternatives																
Inorganic/Other Alternatives																
Ammonium polyphosphate (APP) ¥	68333-79-9	L	*L*	*L*	*L*	*L*	*L*	*L*[d]	L		VL	L	*L*	*L*	*VH*	*L*
Expandable graphite ¥	12777-87-6	L♦	*M*♦	L♦	*L*♦	*L*	*L*	*M*♦	*L*♦	♦	M♦	M♦	L♦	*M*♦	*H*	*L*
Melamine	108-78-1	M	M	M	H	*M*	*L*	M	L		L	VL	L	L	H	L

Table 2-2. Screening Level Toxicity Hazard Summary (Continued)

This table contains hazard information for each chemical; evaluation of risk considers both hazard and exposure. Variations in end-of-life processes or degradation and combustion by-products are discussed in the report but not addressed directly in the hazard profiles. The caveats listed below must be taken into account when interpreting the information in the table.

VL = Very Low hazard L = Low hazard M = Moderate hazard H = High hazard VH = Very High hazard — Endpoints in colored text (VL, L, M, H, and VH) were assigned based on empirical data. Endpoints in black italics *(VL, L, M, H,* and *VH*) were assigned using values from predictive models and/or professional judgment.

[§] Based on analogy to experimental data for a structurally similar compound.

[d] This hazard designation would be assigned MODERATE if >5% of the particles are in the respirable range as a result of dust forming operations.

[†] This component of Firemaster® 550 may be used alone or in other mixtures as an alternative. It can also be found in Table 2-1 of this report.

[‡] The highest hazard designation of any of the oligomers with MW <1,000.

*Each hazard designation for a mixture is based upon the component with the highest hazard, whether it is an experimental or estimated value.

[∞] Based on experimental test data for a residual impurity reported to be present in this substance at levels up to 5% by weight.

Chemical (for full chemical name and relevant trade names see the individual profiles in Section 7)	CASRN	Human Health Effects											Aquatic Toxicity		Environmental Fate	
		Acute Toxicity	Carcinogenicity	Genotoxicity	Reproductive	Developmental	Neurological	Repeated Dose	Skin Sensitization	Respiratory Sensitization	Eye Irritation	Dermal Irritation	Acute	Chronic	Persistence	Bioaccumulation
Non-Halogenated Flame Retardant Alternatives continued																
Phosphate Alternatives																
Triphenyl phosphate (TPP)[†]	115-86-6	L	*M*	L	L	L	L	H	L		L	VL	VH	VH	L	M
Tricresyl phosphate (TCP)[1]	1330-78-5	M	L	L	H	M	M	H	*M*		L	L	VH	*H*	M	H
Isopropylated triphenyl phosphate (IPTPP)[†]	68937-41-7	L	*M*	L	H	*H*	*H*	H	L		L	L	VH	VH	M	*H*
Tris (p-t-butylphenyl) phosphate (TBPP)	78-33-1	L	*M*	L	M	L	M	H	*M*		L	M	VH	VH	M	H
Diethyl bis(2-hydroxyethyl)aminomethylphosphonate	2781-11-5	L	*M*	M	L	L	*M*	*M*	*M*		L	VL	M	*L*	H	*L*
Oligomeric ethyl ethylene phosphate	184538-58-7	L	*L*	*M*	*L*	*M*	*M*	*L*[d]	*L*		M	L	*L*	*L*	*VH*	*L*
Oligomeric phosphonate polyol	363626-50-0	L	*M*	*M*	*L*	*M*	*M*	*L*	*L*		L	VL	*L*	*M*	*M*	*L*
New-to-Market Proprietary Mixtures																
Emerald Innovation™ NH-1*	Proprietary	H	*M*	L	*M*	L	M	H	M		M	M	VH	VH	*M*	*H*
Confidential C	Confidential	H	*M*	L	*M*	VL	M	L	M		M	M	H	H	L	L
Confidential D	Confidential	L	*M*	L	L	L	L	H	L		L	VL	VH	VH	L	M
Confidential E	Confidential	L	*M*	L	L	L	M	M	M		VL	M	VH	VH[∞]	*M*	*H*
Fyrol™ HF-5*	Proprietary	L	*M*[§]	*M*	L	M	M[§]	M[d]	*L*		M	L	VH	VH	*VH*	*H*[‡]
Confidential A	Confidential	L	*L*	*M*	*L*	*L*	*M*	*L*[d]	*L*		M	L	*L*	*L*	*VH*	*L*
Confidential B	Confidential	L	*M*[§]	L	L	M	M[§]	M	*L*		L	VL	VH	VH[∞]	M	*H*[‡]

[1]This assessment also includes information for other methylated triphenyl phosphate isomers (phosphoric acid, bis(methylphenyl) phenyl ester (CASRN 26446-73-1) and phosphoric acid, methylphenyl diphenyl ester (CASRN 26444-49-5)).

2.2 Hazard and Fate Results by Chemical Group

The **components of Firemaster® 550**, thought to be one of the primary alternatives used since pentaBDE was phased out, are predicted to have Moderate to High hazards for reproductive, developmental, neurological and repeated dose toxicities. The phosphate components have inherently Very High hazard for aquatic toxicity, due to the phosphate ester structure and molecular weight (MW); all the components have Moderate or High potential to bioaccumulate, based on parent compound or degradation products. Similar to several of the alternatives evaluated, the components TBB and TBPH lack full data characterization necessary to adequately describe hazard and risk.

Firemaster® 600 is currently marketed for use in flexible polyurethane foams and other applications as a mixture of phosphorus and bromine based flame retardants (Great Lakes Solutions, 2010; Chemtura, 2014). Although the identity and composition of some of the ingredients in Firemaster® 600 are proprietary and cannot be disclosed in this report, the summary hazard designation profile is provided, based upon the mixture component with the highest hazard. The hazard designations for Firemaster® 600 are similar to Firemaster® 550.

The **chlorinated phosphorus alternatives** are tris (2-chloroethyl) phosphate (TCEP), tris (2-chloro-1-methylethyl) phosphate (TCPP), tris (1,3-dichloro-2-propyl) phosphate (TDCPP), and phosphoric acid, P,P'-[2,2-bis(chloromethyl)-1,3-propanediyl] P,P,P',P'-tetrakis(2-chloroethyl) ester (V6), which are fairly well characterized with empirical test data. In addition to Firemaster® 550, TDCPP is also thought to be one of the primary alternatives used to replace pentaBDE in FPUF. The four chlorinated phosphate substances exhibit several distinguishing characteristics. They have Moderate to High hazard designations for at least four of the following human health endpoints: carcinogenicity, genotoxicity, reproductive toxicity, developmental/ neurodevelopmental toxicity, neurological toxicity, and repeated dose toxicity. TCEP is also acutely toxic. These four substances also have aquatic toxicity hazards in the Moderate to High range, but lack adequate characterization of chronic aquatic toxicity. Due to the structure and size of these substances they are not expected to bioaccumulate, but there is a potential for 'pseudo persistence.' Pseudo persistence is a term for chemicals that are observed to be continually present in the environment because they are released at a rate greater than or equal to their rate of removal.

The non-halogenated alternatives include two inorganics, the nitrogen substance melamine, and a collection of non-halogenated phosphate esters.

The hazard profiles for the **inorganics** ammonium polyphosphate (APP) and expandable graphite indicate lower levels of concern than the other profiles in this report. APP is a high MW polymer. Although APP is not well characterized with test data, it is predicted to be Low hazard based on its structure and very high MW. While it is not expected to be readily absorbed due to its MW, it is predicted to be highly persistent. Expandable graphite is not likely to bioaccumulate and has potentially Low to Moderate human health and aquatic toxicity, but there is low confidence in the hazard profile due to the lack of empirical data, and there is potential for the use of hazardous chemical washes in the production process.

The profile for **melamine** identifies key hazards in human health endpoints including acute toxicity, carcinogenicity, genotoxicity, reproductive and repeated dose toxicity. Bioaccumulation potential is low, aquatic toxicity is Low, and persistence is High, but with potential for degradation.

The **phosphorus-based non-halogenated alternatives** have varied designations for human health toxicity; several have Moderate to High hazard for reproductive, developmental, neurological, and repeated dose toxicity, in addition to insufficient data to characterize the potential for carcinogenicity. These human health hazards are compounded by the Very High aquatic toxicity associated with the phosphate esters of this size and structure. Trade-offs can be seen within this group: the more degradable (Low to Moderate persistence) phosphate esters triphenyl phosphate (TPP), tricresyl phosphate (TCP), isopropylated triphenyl phosphate (IPTPP) and tris (p-t-butylphenyl) phosphate (TBPP) have High to Very High aquatic toxicity and Moderate to High bioaccumulation potential, whereas the more persistent substances diethyl bis(2-hydroxyethyl)aminomethylphosphonate and oligomeric ethyl ethylene phosphate have Moderate to Low aquatic toxicity and bioaccumulation designations.

While there is uncertainty associated with the hazard profiles of diethyl bis(2-hydroxyethyl)-aminomethylphosphonate, the oligomeric ethyl ethylene phosphate, and the oligomeric phosphonate polyol, due to heavy reliance on analog or modeled data (especially for the two oligomers)--yielding conservative Moderate designations for several human health endpoints, they may be the most preferable out of all the chemicals assessed in this report. Of these three chemicals, the most preferable may be the oligomeric phosphonate polyol, which has Low to Moderate aquatic toxicity, Moderate persistence, and Low bioaccumulation potential. Human health and aquatic toxicity designations are Low or Moderate for this chemical. Also, the oligomeric phosphonate polyol is a component of the polyurethane foam, and as such may have no potential for release from the foam during product use. The combination of Low to Moderate hazard designations and its reaction into the polyurethane foam make oligomeric phosphonate polyol an alternative anticipated to be safer for use in upholstered polyurethane foam, when flame retardants are added to make the end-use product meet flammability standards.

Two proprietary mixtures that are new to the market were also reviewed. EPA knows the chemical identification, but cannot reveal it in this report due to regulations regarding confidential business information. The two mixtures have one or more components with highest hazards for aquatic toxicity, and the potential to bioaccumulate.

2.3 Hazard and Fate Results by Endpoint

The following text describes results by class of endpoint: human health, aquatic toxicity, persistence, and bioaccumulation potential.

The human health endpoints evaluated in DfE Alternatives Assessments include acute toxicity, carcinogenicity, genotoxicity, reproductive toxicity, developmental toxicity, neurotoxicity, repeated dose toxicity, skin sensitization, respiratory sensitization, eye irritation, and dermal irritation. Acute mammalian toxicity was Low for all but four of the alternatives: tricresyl phosphate, melamine, TCEP, and Emerald Innovation NH-1. Carcinogenicity and genotoxicity hazards varied among the alternatives, with many Low or Moderate designations. Two of the

chemicals had High concerns for carcinogenicity: TCEP and TDCPP. Reproductive, developmental, neurological, and repeated dose toxicity varied from Low to High across the chemicals. Irritation and sensitization endpoints were generally not distinguishing, with many Low or Very Low designations, although a few substances had Moderate designations.

Aquatic toxicity hazards varied significantly, due to the diverse chemistries of the alternatives. The endpoints evaluated in DfE Alternatives Assessments include acute and chronic aquatic toxicity based on water column exposures, which may not be suitable tests for some of the poorly soluble substances.

Most flame retardants have High or Very High persistence designations, because they are expected to be stable by design in order to maintain their flame retardant properties throughout the lifetime of the product. Several of the flame retardant alternatives in this report were not designated as highly persistent, including TPP, which is readily biodegradable (low persistence). Also, TCP, IPTPP, TBPP, and TCEP are inherently biodegradable chemicals that degrade slowly (Moderate persistence); however, these substances have aquatic toxicity hazards, including deformities in fish and eutrophication from degradation to inorganic phosphates. There is an apparent trade-off between persistence and toxicity for diethyl bis(2-hydroxyethyl)-aminomethylphosphonate and the oligomeric ethyl ethylene phosphate that have High and Very High persistence but Low to Moderate toxicity. The oligomeric phosphonate polyol appears to remove this trade-off with only estimated Moderate persistence and estimated Low – Moderate toxicity. Predicting long-term fate in the environment is challenging, so there is an uncertainty as to how substances will eventually degrade, and whether some substances that are degradable in standard tests may be 'pseudo persistent.'

The ability of a chemical to accumulate in living organisms is described by bioconcentration, bioaccumulation, biomagnification, and/or trophic magnification factors. Some of the alternatives assessed in this report also have a High potential for bioaccumulation, including the New-to-Market mixtures, the brominated alternatives, and some of the phosphate alternatives: TCP, IPTPP, and TBPP.

3 Flexible Polyurethane Foam Flame Retardants and Flammability Standards

This section provides an overview of flexible polyurethane foam (FPUF), discusses which flame retardants are used in FPUF, and summarizes the standards that drive their use. For more details about FPUF, and its manufacture and exposure potential during the manufacturing processes, see Chapter 3 of the 2005 FFRP report[2].

3.1 Flexible Polyurethane Foam

Numerous types of furniture and other products incorporate FPUF. Rigid polyurethane foams, by contrast, are used in insulation, construction, and other applications (ISOPA 2005), and are not assessed in this report update.

Flexible foam is made either in large slabs ("slabstock") that are cut to shape, or in molds that have the shape of the finished product. The basic ingredients include polyols, isocyanates, blowing agents, and other additives (including flame retardants). In manufacturing slabstock, the ingredients are blended in a mixing head and deposited on a conveyor belt, where the polymerization reactions occur, and the foam is expanded by blowing agents into a large (e.g., 60 foot) "bun." The buns are cured before being cut into shapes for a finished product. In molded foam, the polymerization reactions occur within the mold, and are heated to accelerate curing.

Furniture and other foam product manufacturers typically receive cured foam and do not directly handle flame retardant chemicals. Because slabstock is made in very large buns, uses requiring smaller pieces of foam may consist of off-cuts from larger buns. This may be why smaller polyurethane foam products may contain flame retardants, even when they are not required to do so by regulation.

3.2 Flame Retardant Classification and Exposure Considerations

Flame retardants used in FPUF are typically classified as "additive." Additive flame retardants are blended evenly into the foam, but remain unbound. Additive flame retardants are expected to be more mobile during the consumer use phase, for example, by volatilizing from the foam, by being washed from the foam or from the foam surface, or in dust as the foam itself is mechanically abraded. Reactive flame retardants are chemically bound to the polymer in the finished product and are used in rigid PUF; they are not typically used in FPUF.

Additive flame retardants have been widely identified in air, house dust, and handwipe samples (Stapleton, Allen et al. 2008; Dodson, Perovich et al. 2012; Stapleton, Eagle et al. 2012; van der Veen and de Boer 2012; Carignan, Heiger-Bernays et al. 2013), supporting the idea that additive flame retardants can mobilize from a plastic or foam into the local microenvironment. Furthermore, detection of additive flame retardants in blood and urine samples (Stapleton, Eagle

[2] Available at: http://www2.epa.gov/saferchoice/environmental-profiles-chemical-flame-retardant-alternatives-low-density-polyurethane.

et al. 2012; Carignan, McClean et al. 2013) and *in vivo* studies (Patisaul, Roberts et al. 2012) demonstrate the bioavailability and absorption of several additive flame retardants.

Reactive flame retardants, because they are chemically bound to the foam polymer itself, are expected to have lower mobility, volatility, and bioavailability than additive flame retardants, especially in the consumer use phase of product life. However, reactive flame retardants may still be released from furniture, either because they are liberated from the polymer, or the original polymerization was incomplete (U.S. EPA 2005a). As such, exposure to reactive flame retardants could occur at all points in the life cycle, including manufacture, use, and disposal.

Under conditions where fire or incineration occurs, a halogenated substance may contribute to halogenated dibenzodioxin and dibenzofuran formation, increase the generation of PAHs, and impact fire parameters such as smoke and carbon monoxide (Sidhu, Morgan et al. 2013). However, combustion reactions are complex and variable, and make inclusion of combustion byproducts in hazard assessment challenging. Both halogenated and non-halogenated flame retardants may yield other toxic by-products that would need to be compared, not only halogenated dioxins and furans. For these reasons, the pyrolysis transformation products are not assessed in this report.

3.3 Sources of Data for Identifying Foam Flame Retardants

Published Data

Publication of the 2005 FFRP report was one of a set of actions undertaken by EPA and other stakeholders in response to growing concerns about pentaBDE. After a voluntary phase-out of pentaBDE by the sole U.S. manufacturer in 2004, EPA issued a Significant New Use Rule (SNUR), effective August 14, 2006, to ensure that production could not re-commence in the United States without prior notice to EPA.

Recent data suggest that the pentaBDE phase-out has had the desired effect of decreasing the environmental prevalence of the flame retardant. A study of house dust in 16 California homes found an overall reduction in median values of pentaBDE components between 2006 and 2011; the declines in pentaBDE component concentrations were significantly associated with new (purchased between 2006 and 2011) furniture, electronics, and flooring (Dodson, Perovich et al. 2012). However, the changes were not uniform; two homes showed marked increases in pentaBDE congeners. In another study of 102 FPUF samples from residential couches purchased across the United States, including 24 percent from California, pentaBDE was identified in 16 of 41 samples purchased between 1985 and 2004, but in only one of the 61 samples dating from 2005 or later (Stapleton, Sharma et al. 2012).

These same studies, along with others, helped confirm the major flame retardants used to replace pentaBDE. In the study of residential couches, TDCPP was detected in 52 percent of foam samples dating from 2005 or later (Stapleton, Sharma et al. 2012). Firemaster® 550, identified by its brominated components, TBB and TBPH, was identified in 18 percent of post-phase-out samples, while alkylated triphenyl phosphates were identified in another 16 percent of samples. In only 2 of the 61 post-phase-out samples were flame retardants not identified. The high detection rate of flame retardants, even in couches purchased outside of California, suggested to

the authors that California's furniture flammability standard 1975 Technical Bulletin (TB) 117 (TB117; see Section 3.5 for more details on the recent update to this standard) "is becoming a de facto standard across the United States" (Stapleton, Sharma et al. 2012).

Several other flame retardants were identified in these studies. In a study of foam baby products, Stapleton et al. (2011) identified a chlorinated organophosphate flame retardant (OPFR) sold commercially as V6, previously thought to be used in automobiles; TCPP, a major flame retardant in FPUF in the United Kingdom, but expected to have limited use in the United States; and TCEP. All of these chemicals are included in the current report.

Stakeholder Information

In the course of developing this report, DfE had conversations with several stakeholders from the 2005 FFRP, other stakeholders in the chemical and furniture industries, and academic researchers with expertise on flame retardancy. DfE developed a candidate list of chemicals known to be used in FPUF, including a number of flame retardants for which there was the possibility of use, but that were ultimately excluded from the report. Discussion of these lists with various stakeholders provided critical information about flame retardant use, including valuable information about the limitations of some flame retardants (e.g., that discolor or "scorch" the foam) that likely limit their use in the marketplace.

Process of Identifying Chemicals for Assessment

Flame retardant chemicals assessed in this update were identified through the following approach:

1. ***Reviewed all chemicals from the 2005 report***. Many of the chemicals were identified in the original report by proprietary placeholders (i.e., generic names). In some of these cases, the chemicals have since been publicly identified either by the manufacturer or by another party; for example, the brominated components of Firemaster® 550 were identified publicly by Stapleton et al. (2008). In these cases, the publicly available chemical names were used. Many of the compounds assessed in the 2005 report are no longer sold; manufacturer information as well as direct conversations with manufacturers was used to ascertain the current market status of these products.

2. ***Identified products advertised for use in FPUF***. Website and promotional materials from the major U.S. manufacturers, as well as from the trade organization Phosphorus, Inorganic & Nitrogen Flame Retardants Association (PINFA), were reviewed. Manufacturers of proprietary formulations were also consulted to ensure that the candidate list included all chemical components.

3. ***Examined all PMN chemicals associated with FPUF that were identified by PMN submitters as being suitable for flame retardancy***. New chemicals are required by TSCA to be submitted by the manufacturer through the PMN process before being produced in or imported into the United States. In some cases it was possible for these PMNs to be

associated with trade names, to ascertain whether they were sold for possible use in FPUF or limited to other markets (e.g., rigid polyurethane foam).

4. ***Added flame retardants identified in furniture and other FPUF applications by external researchers.*** In particular, all flame retardants recently identified in FPUF baby products by Stapleton et al. were included.

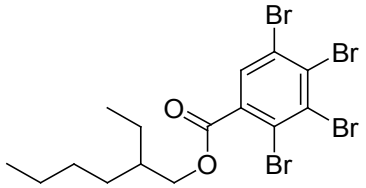
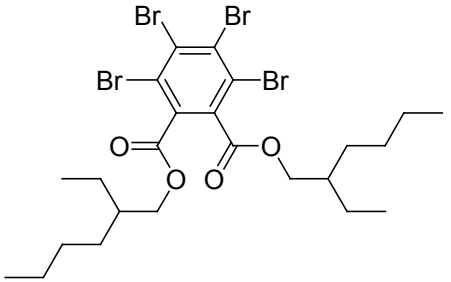
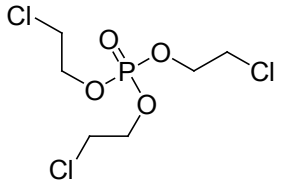
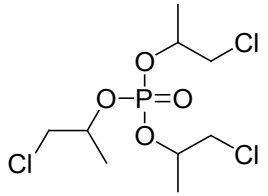
Chemicals identified through these sources were then grouped into two lists: chemicals known to be currently used in FPUF, which would therefore be assessed; and chemicals thought not to be used in FPUF (see Table 3-1 and Table 3-2, respectively). Stakeholders from the 2005 partnership and other experts were then contacted, and provided with the proposed lists of chemicals to be included and excluded. In some cases, each chemical on the lists was discussed to receive feedback on whether it was actually in use, or specific reasons its use had been halted.

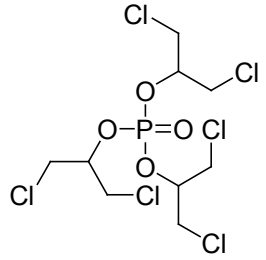
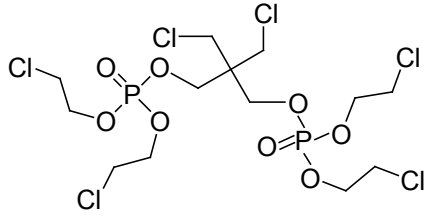
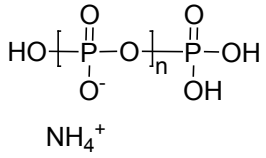
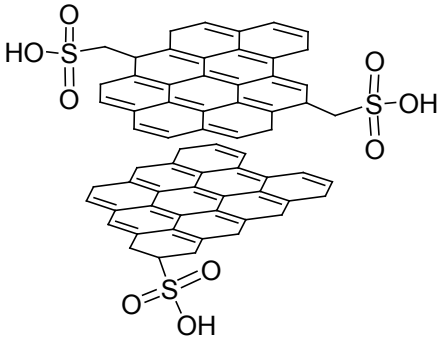
When chemicals were excluded from the assessment, the reason for exclusion is given on that list. For example, some flame retardants were identified by manufacturers' promotional materials as being suitable for polyurethane foam, but were described by experts as suitable only for rigid polyurethane, lacking the appropriate characteristics for FPUF (e.g., unsuitable viscosity). Other chemicals had previously been identified as suitable for FPUF, but are no longer sold for that market.

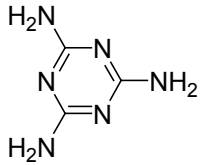
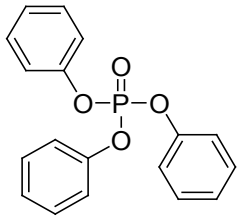
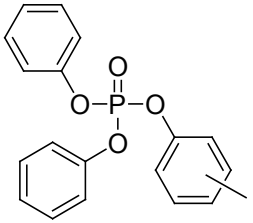
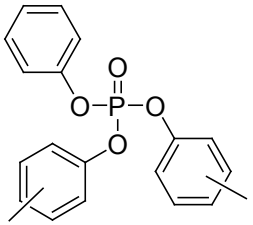
It is difficult to assess the precise number and volume of flame retardants used in furniture and other products. Although chemical manufacturers are required to periodically report the amount of raw chemicals manufactured in or imported into the United States, there is no general requirement for disclosure of the amount of chemicals contained in manufactured or imported articles.

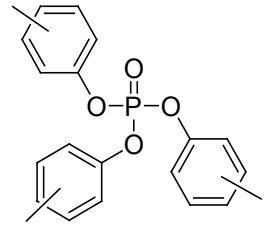
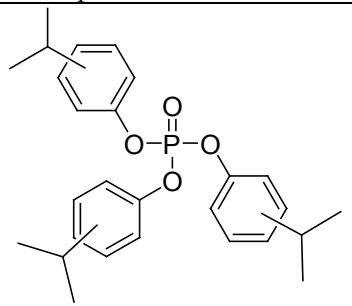
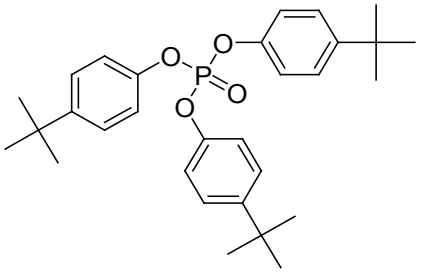
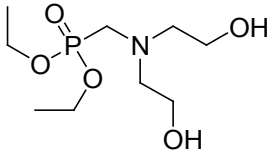
As mentioned above, chemical and FPUF manufacturers consulted for this report identified issues such as odor and scorch with particular flame retardant chemicals, and suggested that they are unlikely to be in use in the United States. Flame retardant chemicals phased out by U.S. manufacturers with odor or scorch issues are unlikely to be used in overseas manufacture as well.

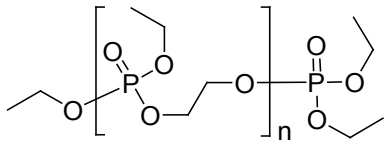
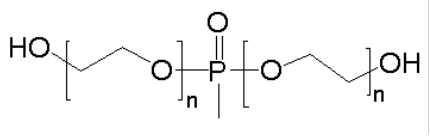
Table 3-1. Flame Retardants Evaluated in the DfE Furniture Flame Retardancy Update

CASRN	Preferred Chemical Abstract Index Name	Common Names and Acronyms[b]	Molecular Formula (MF)	Structure
Brominated Alternatives				
183658-27-7	Benzoic acid, 2,3,4,5-tetrabromo-, 2-ethylhexyl ester	TBB; EH-TBB	$C_{15}H_{18}Br_4O_2$	
26040-51-7	1,2-Benzenedicarboxylic acid, 3,4,5, 6-tetrabromo-, 1,2-bis(2-ethylhexyl) ester	TBPH; BEH-TEBP	$C_{24}H_{34}Br_4O_4$	
Halogenated Phosphorus Alternatives				
115-96-8	Ethanol, 2-chloro-, phosphate (3:1)	TCEP; Tris(2-chloroethyl) phosphate	$C_6H_{12}Cl_3O_4P$	
13674-84-5; 6145-73-9	2-Propanol, 1-chloro-, 2,2',2"-phosphate; 1-Propanol, 2-chloro-, 1,1',1"-phosphate	TCPP; Tris(2-chloro-1-methylethyl)phosphate; TCIPP	$C_9H_{18}Cl_3O_4P$	 Representative structure

CASRN	Preferred Chemical Abstract Index Name	Common Names and Acronyms[b]	Molecular Formula (MF)	Structure
13674-87-8	2-Propanol, 1,3-dichloro-, phosphate (3:1)	TDCPP; Tris-(1,3-dichloro-2-propyl)phosphate; TDCIPP	$C_9H_{15}Cl_6O_4P$	
38051-10-4	Phosphoric acid, P,P'-[2,2-bis(chloromethyl)-1,3-propanediyl] P,P,P',P'-tetrakis(2-chloroethyl) ester	V6; BCMP-BCEP	$C_{13}H_{24}Cl_6O_8P_2$	
Inorganic/Other Alternatives				
68333-79-9	Polyphosphoric acids, ammonium salts	APP; Ammonium polyphosphate	$[NH_4PO_3]_n$	 Representative structure
12777-87-6	Sulfuric acid, compd. with graphite (1:?)	Expandable graphite	$[C]_n[SO3H]_x$	 Representative structure

CASRN	Preferred Chemical Abstract Index Name	Common Names and Acronyms[b]	Molecular Formula (MF)	Structure
108-78-1	1,3,5-Triazine-2,4,6-triamine	Melamine	$C_3H_6N_6$	
Phosphate Alternatives				
115-86-6	Phosphoric acid, triphenyl ester	TPP; Triphenyl phosphate; TPHP	$C_{18}H_{15}O_4P$	
26444-49-5	Phosphoric acid, methylphenyl diphenyl ester	Cresyl diphenyl phosphate; Methylphenyl diphenyl phosphate; Disflamoll DPK; MPHDPHP	$C_{19}H_{17}O_4P$	 Representative structure
26446-73-1	Phosphoric acid, bis(methylphenyl) phenyl ester	Methylated triphenyl phosphates; Bis(methylphenyl) phenyl phosphate; MPHP	$C_{20}H_{19}O_4P$	 Representative structure

CASRN	Preferred Chemical Abstract Index Name	Common Names and Acronyms[b]	Molecular Formula (MF)	Structure
1330-78-5	Phosphoric acid, tris(methylphenyl) ester	Tricresyl phosphate; Disflamoll TKP; TMPHP	$C_{21}H_{21}O_4P$	 Representative structure
68937-41-7	Phenol, isopropylated, phosphate (3:1) Commercial product may include mono-, di-, tri- and higher substitutions with appropriate CASRNs.	IPPP; ITP; IPTPP; Isopropylated triphenyl phosphate; Isopropylated phenol phosphate; TIPPP	$C_{27}H_{33}O_4P$ Formula for tri-propyl substitution	 Representative structure
78-33-1	Phenol, 4-(1,1-dimethylethyl)-, 1,1',1''-phosphate Includes mono-, di-, tri-, and higher substitutions with appropriate CASRNs.	TBPP; tris(4-(tert-butyl)phenyl phosphate; tert-butylphenyl diphenyl phosphate; bis(4-(tert-butyl)phenyl) phenyl phosphate; TTBPHP	$C_{30}H_{39}O_4P$ Formula for tri-butylated substitution	 Representative structure
2781-11-5	Phosphonic acid, P-[[bis(2-hydroxyethyl)amino]methyl]-, diethyl ester	N,N-(bis)-hydroxyethyl-aminomethane phosphonic acid diethyl ester; BHEAMP-DE	$C_9H_{22}NO_5P$	

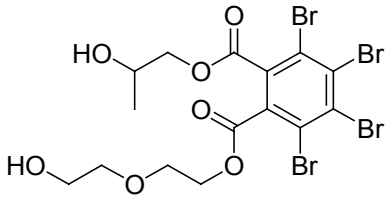
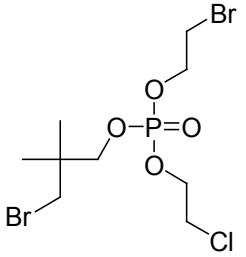
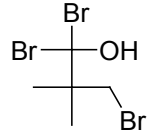
CASRN	Preferred Chemical Abstract Index Name	Common Names and Acronyms[b]	Molecular Formula (MF)	Structure
184538-58-7	Phosphoric acid, triethyl ester, polymer with oxirane and phosphorus oxide (P_2O_5)	Oligomeric ethyl ethylene phosphate; Alkylphosphate oligomer	$(C_6H_{15}O_4P \cdot C_2H_4O \cdot O_5P_2)_n$	 Representative structure
363626-50-0	Poly(oxy-1,2-ethanediyl), α,α`-(methylphosphinylidene)bis[ω-hydroxy-	Oligomeric phosphonate polyol; Bis(polyoxyethylene) methylphosphonate; Polyethylene glycol methylphosphonate (2:1)	$CH_5O_3P \cdot (C_2H_4O)_n \cdot (C_2H_4O)_n$	
New-to-Market Proprietary Mixtures				
Proprietary	Halogen-free flame retardant	Emerald Innovation NH-1		--
Proprietary	Halogen-free phosphorus-based	Fyrol HF-5		--

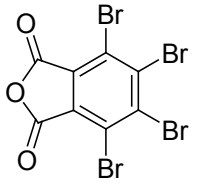
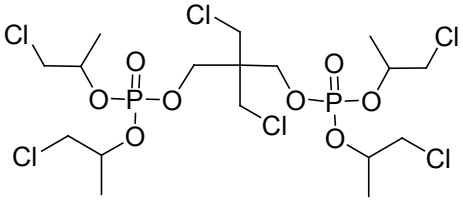
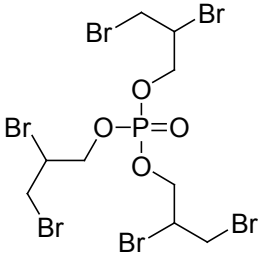
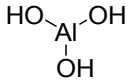
[a] The list of flame retardants evaluated in the Furniture Flame Retardancy update is based on publicly available information on product availability, public and confidential information on chemical production, and DfE's conversations with stakeholders. The inclusion of these chemicals in the DfE Alternatives Assessment does not denote environmental preference.

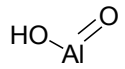
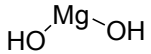
[b] The last acronym listed for each substance is the "practical abbreviation" according to Bergman et al. (2012)'s proposed standard approach for making acronyms for organic flame retardants. Bergman et al. 2012. *Environment International* 49: 57-82.

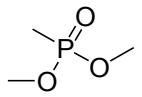
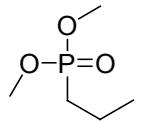
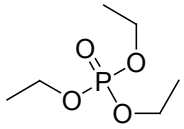
Table 3-2. Flame Retardants That Were Not Evaluated in the DfE Furniture Flame Retardancy Update

Flame retardants listed here have been identified as being used in polyurethane or other plastics, but are not thought to be used in flexible polyurethane foam (FPUF), or are not candidates for DfE's hazard assessment process.

CASRN	Preferred Chemical Abstract Index Name	Common Names and Acronyms[a]	MF	Structure	Reason for Exclusion[b]
Brominated Alternatives					
77098-07-8; 20566-35-2	1,2-Benzenedicarboxylic acid, 3,4,5,6-tetrabromo-, mixed esters with diethylene glycol and propylene glycol; 1,2-Benzenedicarboxylic acid, 3,4,5,6-tetrabromo-, 1-[2-(2-hydroxyethoxy)ethyl] 2-(2-hydroxypropyl) ester	Diester/ether diol of tetrabromophthalicanhydride; 2-(2-Hydroxyethoxy)ethyl 2-hydroxypropyl 3,4,5,6-tetrabromophthalate; HEEHP-TEBP	$C_{15}H_{20}Br_4O_9$; $C_{15}H_{16}Br_4O_7$	 Representative Structure	Appears to be used in rigid polyurethane foams only.
125997-20-8	Phosphoric acid, mixed 3-bromo-2,2-dimethylpropyl and 2-bromoethyl and 2-chloroethyl esters	BBDMP-CDMP-P	$C_9H_{18}Br_2ClO_4P$	 Representative Structure	Historical FR for polystyrene boards; no current production. Not reported in Chemical Data Reporting (CDR)[c].
36483-57-5	1-Propanol, 2,2-dimethyl-, tribromo deriv.	Tribromoneopentyl alcohol; TBNPA	$C_5H_9Br_3O$	 Representative Structure	Appears to have been an unsuccessful product.

CASRN	Preferred Chemical Abstract Index Name	Common Names and Acronyms[a]	MF	Structure	Reason for Exclusion[b]
632-79-1	1,3-Isobenzofurandione, 4,5,6,7-tetrabromo-	Tetrabromophthalic anhydride; TEBP-Anh			Advertised for use in rigid foams.
1047637-37-5	Phosphoric acid, P,P'-[2,2-bis(chloromethyl)-1,3-propanediyl] P,P,P',P'-tetrakis(2-chloro-1-methylethyl) ester	U-OPFR; BCMP-BCMEP			Although identified in consumer products, there is no evidence of commercial production.
Halogenated Phosphorus Alternatives					
126-72-7	1-Propanol, 2,3-dibromo-, 1,1',1''-phosphate	TDBPP; Tris-(2,3-dibromopropyl)phosphate	$C_9H_{15}Br_6O_4P$		Historical FR identified in house dust, but no evidence of use in FPUF. Not reported listed in CDR[c].
Inorganic/Other Alternatives					
21645-51-2	Aluminum hydroxide ($Al(OH)_3$)	ATH; Aluminum trihydrate	$Al(OH)_3$		Inefficient, requiring very high loadings. Probably not used in FPUF[d].

CASRN	Preferred Chemical Abstract Index Name	Common Names and Acronyms[a]	MF	Structure	Reason for Exclusion[b]
1318-23-6	Boehmite (Al(OH)O)	Aluminum oxide hydroxide	Al(OH)O		Inefficient, requiring very high loadings. Possible use in some niche applications.
1309-42-8	Magnesium hydroxide ($Mg(OH)_2$)	Milk of magnesia	$Mg(OH)_2$		Inefficient, requiring very high loadings. Probably not used in flexible polyurethane foam[d].
	Nano: layers, clays, mesoporous silicate	Nano: layers, clays, mesoporous silicate	--	--	Research product; not yet commercially available.
68953-58-2	Quaternary ammonium compounds, bis(hydrogenated tallow alkyl)dimethyl, salts with bentonite	Surface treated, Inorganic, mineral based FR synergist	--	--	Vendor described use in thermoplastic polyurethane; no other use data available.

CASRN	Preferred Chemical Abstract Index Name	Common Names and Acronyms[a]	MF	Structure	Reason for Exclusion[b]
Phosphate Alternatives					
756-79-6	Phosphonic acid, P-methyl-, dimethyl ester	DMMP; Dimethyl methyl phosphonate	$C_3H_9O_3P$		Used in rigid polyurethane foams. PINFA website lists as appropriate for FPUF; however, no evidence of such use is available.
18755-43-6	Phosphonic acid, P-propyl-, dimethyl ester	Dimethyl propane phosphonate DMPP; Levaguard DMPP	$C_5H_{13}O_3P$		Thought to be used in rigid but not flexible polyurethane foam; however, not reported on listed on CDR[c].
78-40-0	Phosphoric acid, triethyl ester	Triethyl phosphate; Levaguard TEP-Z	$C_6H_{15}O_4P$		Used in rigid but not flexible polyurethane foam. Could be an impurity from other flame retardants.

CASRN	Preferred Chemical Abstract Index Name	Common Names and Acronyms[a]	MF	Structure	Reason for Exclusion[b]
Proprietary Alternatives					
--		Antiblaze PR82			For use in rigid foams.

[a] The last acronym listed for each substance is the "practical abbreviation" according to Bergman et al. (2012)'s proposed standard approach for making acronyms for organic flame retardants. Bergman et al. 2012. *Environment International* 49: 57-82.

[b] Flame retardants and use information were identified based on publicly available information on product availability, public and confidential information on chemical production, and DfE's conversations with stakeholders.

[c] The CDR Rule requires manufacturers, including importers, to submit information on the chemical they produce domestically or import into the United States during the principal reporting year, subject to reporting requirements. http://epa.gov/cdr/ The last two reporting years were 2005 and 2011.

[d] This substance was assessed in the Alternatives Assessment for Decabromodiphenyl Ether (DecaBDE) Report, available at: http://www2.epa.gov/saferchoice/partnership-evaluate-flame-retardant-alternatives-decabde.

3.4 Notes on Specific Foam Flame Retardants

Notes on selected foam flame retardant chemicals included in the report follow.

- **TDCPP**, known to be a major flame retardant in FPUF and produced in a volume between 10 and 50 million pounds per year in 2011, was listed by California as a Proposition 65 chemical[3] in late 2011 for concerns about carcinogenicity (OEHHA 2011; U.S. EPA 2013a). The Proposition 65 listing may impact the TDCPP market because it requires relabeling products that contain TDCPP for sale in California, though labeling of TDCPP products for sale outside of California is not required. TDCPP was identified by Stapleton, Sharma et al. (2012) in more than half of couch samples tested since 2005. In 2012, the major U.S. manufacturer of TDCPP announced a voluntary phase-out of TDCPP production by 2015 (ICL Industrial Products 2012). New York State has banned TDCPP from use in children's products, including baby products, toys, car seats, nursing pillows, crib mattresses, strollers and other items intended for use by children under three years of age, effective December 1, 2015 (New York State Governor's Office 2014). Maryland has also prohibited importing, selling, or offering for sale any child care product containing more than one-tenth of 1% (by mass) of TDCPP intended for use by children under the age of three including baby products, toys, car seats, nursing pillows, crib mattresses, and strollers (State of Maryland 2014). The ban became effective on October 1, 2014, and does not contain a provision for phasing out existing stock.

- There has been recent opposition from consumer and environmental groups to the use of **halogenated flame retardants**, and this opposition may shape the market suitability of these flame retardants, regardless of hazard data. Some shift away from halogenated flame retardants appears to have already occurred. While the 2005 FFRP report assessed a number of brominated flame retardants, the two brominated components of Firemaster® 550 (TBB and TBPH) are the only **brominated flame retardants** included in the current update report.

- Although **TCEP** was previously not thought to be used in foam, it has been identified in upholstered FPUF products (Stapleton, Klosterhaus et al. 2011). TCEP was a TSCA work plan chemical for 2013-14, so the DfE Alternatives Assessment process is a useful contribution to other EPA activities on this compound (U.S. EPA 2013b). New York State banned the sale or offer for sale of children's products containing TCEP, effective December, 1, 2013 (State of New York 2011). Maryland also passed a law prohibiting the import, sale, or offer for sale of child care products containing more than one-tenth of 1% (by mass) of TCEP intended for use by children under the age of three, including baby products, toys, car seats, nursing pillows, crib mattresses, and strollers (State of Maryland 2014). The ban became effective on October 1, 2014, and does not contain a provision for phasing out existing stock.

[3] A chemical known to the State of California to cause cancer or reproductive toxicity; businesses are required to provide a warning (e.g., label consumer products, distribute notices to residents) when exposure to a Proposition 65 chemical may occur.

- **TCPP and melamine** are the major flame retardants used in the United Kingdom to meet the stringent "Crib 5" standard (BS-5852; UK Parliament 1988), but use of this mixture is not known to be common in the United States. However, because TCPP was identified in FPUF products by Stapleton et al. (2011), it is included in this report.

- The larger molecule "**V6**" (CASRN 38051-10-4) has been used in automobile foam, due to its lower volatility, but was also identified by Stapleton et al. (2011) in baby products. V6 is a dimer of TCEP, and contains TCEP as an impurity.

- Researchers first experimented with the use of **expandable graphite** in FPUF in the 1980s, but performance limitations restricted its commercial adoption (Bhagat 2001). These limitations have been overcome (Wolska, Goździkiewicz et al. 2012; Wang, Ge et al. 2013), and expandable graphite is now considered viable in FPUF (PINFA 2012).

- A new molecule, "**U-OPFR**" ("unknown organophosphate flame retardant," BCMP-BCMEP), a dimer of TCPP, was identified by Stapleton et al. (2011). This molecule is not in EPA's CDR data on the manufacturing, processing, and use of commercial chemical substances and mixtures; however, it is possible that whole products with this molecule have been imported. Experts consulted by DfE were unfamiliar with this molecule, and no references to it beyond the Stapleton paper have been identified. U-OPFR was not assessed in this update, because there is no evidence of commercial production of this chemical.

Flame Retardants as Mixtures

The assessment of flame retardant hazard properties is complicated by the fact that many flame retardant products are sold as mixtures. This may be the result of a deliberate mixing of diverse flame retardant chemicals for performance reasons, or as a natural result of the synthesis of the flame retardant molecules. For example, a number of flame retardant products now contain alkylated triphenyl phosphates with a number of different side chains in use (e.g., methyl, isopropyl, tert-butyl). As a natural result of the synthesis process, these mixtures are likely to contain the unalkylated TPP itself, along with mixtures of mono-, di-, tri-, and possibly higher alkyl substitutions. Each of these substitutions can also occur in numerous isomers (e.g., the substitution might occur on the *meta*, *ortho*, or *para* positions). A single product identified as IPTPP, therefore, may in fact consist of a large number of molecules of differing properties, making evaluation more difficult.

Deliberate mixtures of different molecules are also common. Most notably, Firemaster® 550 has been identified as a mixture of TBB, TBPH, TPP, and IPTPP (Stapleton, Allen et al. 2008); approximately 50% of the mixture is TBB and TBPH at a ratio of 4:1 by mass, while the remainder is comprised of the other two molecules. This constitutes a challenge to the DfE assessment process. Some of the toxicity studies available are of the Firemaster® 550 mixture itself; others are of the mixture of only the two brominated components (also sold as Firemaster® BZ-54), while some data exist for each component individually. Therefore, it is not always possible to attribute effects seen in toxicologic studies to an individual component. (Effects

resulting from additive, synergistic, or antagonistic interactions of a combination could complicate the analysis further.) It is likely that the composition of some commercial products varies from batch to batch. In addition, differential volatilization, degradation, or absorption may lead to different exposure patterns to the individual components at various points along the life cycle of the product.

DfE attempted to assess hazard profiles of the commercial products, where possible. For example, since mono- and tri-substituted cresyl triphenyl phosphate are sold as different products, DfE listed them separately in the list of substances for assessment, but for efficiency assessed the variety of substitutions of the cresyl phosphate in one profile "tricresyl phosphate." Similarly, since IPTPP appears to be sold as a mixture of mono/di/tri-substitutions, that mixture was evaluated as a whole. In practical terms, little data are available for each component, and most available data are associated with a mixture. Where data on individual components do exist, DfE takes a conservative approach by using the highest hazard designation for any one component of the mixture as the hazard designation for the whole mixture.

In the case of mixtures of dissimilar molecules, DfE evaluated, as far as possible, both the components and the complete mixture. Here, again, DfE's criteria were followed in assigning to each endpoint for the mixture the highest hazard call for a mixture component. (No attempt was made to assess synergistic or other interactions between component chemicals.) For example, Firemaster® 600 is a mixture of phosphorus and bromine-based flame retardants marketed for use in flexible polyurethane foams and other applications. Although the identity and composition of some of the ingredients in Firemaster® 600 are proprietary and cannot be described in this report, the summary hazard designations based upon the mixture component with the highest hazard are provided.

3.5 Standards that Influence the Use of Flame Retardants

Several regulations currently drive the use of flame retardants in FPUF. As described below, changes to some of the standards have been proposed or passed. As these changes are implemented, this report will provide valuable information on available alternatives to enable informed substitution, should there be a continuing need for flame retardants in FPUF or upholstery fabric.

California TB117

In 1975, California's Bureau of Electronic and Appliance Repair, Home Furnishings and Thermal Insulation (BEARHFTI) (then the Bureau of Home Furnishings and Thermal Insulation) promulgated TB117. Meeting TB117 required a small, candle-sized flame to be applied directly to the uncovered foam for 12 seconds without igniting a fire (Cal/DCA 2000). Passing such a test required either an IFR foam or the use of flame retardants. The most common solution was the addition of flame retardants to FPUF (NRDC 2013). Since manufacturers generally prefer to make a single product for the U.S. market, the TB117 standard had to some extent become a national *de facto* standard. TB117 required labeling of compliant furniture in California, but labels did not always appear in other states.

In 2010, California amended TB117 to specifically exempt "juvenile furniture": "strollers, infant carriers, and nursing pillows" (Cal/DCA 2010). However, as described above, FPUF is manufactured in large (60-foot) "buns," which are then cut to shape. It is likely that most buns are made with flame retardants, in anticipation of being used in a mixture of TB117-compliant and -exempt products. Similarly, the flame retardants in FPUF "pit cubes" identified by Carignan, Heiger-Bernays, et al. (2013) in a study of gymnast exposure to flame retardants may have been the result of a manufacturing process that incorporates flame retardants to meet TB117 standards.

In 2013, California enacted changes to the TB117 standard. In contrast to the 1975 standard, the new TB117-2013 does not require open flame testing for filling materials used in upholstered furniture. TB117-2013 tests for smolder resistance by applying a lit cigarette to a miniature assembly of the cover fabrics, barrier materials, and filling materials that represents the finished piece of furniture (Cal/DCA 2013b). Fabric materials failing the smolder test can still be used if a fire blocker (inter-liner) layer is added. The new test is based on the voluntary American Society for Testing and Materials (ASTM) E1353 standard (Cal/DCA 2013b). Manufacturers were able to use the new testing requirements as of January 1, 2014, and required to be fully compliant by January 1, 2015 (California Governor's Office 2013).

Although TB117-2013 does not regulate or mandate the use of flame retardant chemicals, BEARHFTI anticipates that the new standard will significantly reduce or eliminate manufacturers' use of flame retardant chemicals in upholstered furniture, because these products may meet the new standards without the use of flame retardant chemicals (Cal/DCA 2013a). Many of the more common thermoplastic fabrics are likely to pass the smolder test, although some fabrics, primarily cellulosic, are likely to need modification before passing the test (CPSC 2008). Although not assessed for possible hazards in this report, Section 4 provides information on flame retardant technologies that may provide increased fire safety, with and without the use of flame retardant chemicals.

A number of other localities have passed flammability standards, which are often based on California standards; for example, the Boston Fire Code incorporates TB133 (Boston Fire Department 1995). How local standards will change as a result of revisions to TB117 remains an open question.

California TB133

The more stringent TB133 standard, promulgated in 1991, was designed to increase fire safety in public spaces. Meeting TB133 requires a large open flame, provided by a gas burner, to be applied to the assembled piece of furniture for about 80 seconds without igniting a fire. TB133 has been used as the basis for legislation in other localities (TB133 compliance is often voluntary for sprinklered buildings, in which case TB117 still applies in California (PFA 1992)).

Detailed data on how products meet TB133 are not available, but two general approaches are possible: the use of flame-retardant fabrics and foams that together provide suitable flame resistance; alternatively, an intrinsically flame-retardant fire blocker or "inter-liner" layer can be used between the foam and the cover fabric (PFA 1992). Anecdotal evidence gathered from

manufacturers suggests that the foam components are typically TB117 compliant, and that a cover fabric back-coated with flame retardant is commonly used. No public data exist on which flame retardants are used in back-coatings.

Consumer Product Safety Commission

In a March 4, 2008, notice of proposed rulemaking (NPR) published in the *Federal Register*, CPSC proposed a national standard addressing the risk of deaths and injuries associated with residential upholstered furniture fires[4] (CPSC 2008). The proposed rule focused primarily on fires ignited by smoldering cigarettes. The standard could be met by either using cover materials that are sufficiently smolder-resistant to meet a cigarette ignition performance test, or by using fire barriers (inter-liners) that meet smoldering and open flame resistance tests placed between the cover fabric and interior filling materials. In order to reduce reliance on additive flame retardants, the proposed rule did not contain performance requirements for filling materials. As such, CPSC specified a standard foam that did not include any flame retardant chemicals when testing cover materials, thereby removing additive flame retardants in the foam from consideration in order to meet the requirements of the flame resistance test. Technical challenges with the test methods in this approach prompted CPSC staff to investigate other approaches. Validation of the test methodology proposed in the NPR showed that furniture constructed with fire barriers and exposed to a small open flame produced a significantly less intense fire than furniture constructed without fire barriers. CPSC staff believes the fire barrier approach may have the potential to address nearly all of the upholstered furniture-related fires and save more lives each year than the 2008 proposed standard. Subsequently, in 2013, CPSC requested comments on a standard that would cover a wider range of ignition sources found in the home (CPSC 2013a).

It should be noted that other open flame standards, including the more stringent Crib 5 standard in the United Kingdom, which tests PUF covered with a standard fire-retarded polyester fabric but does not allow for the use of fire barriers, are typically met with a combination of additive flame retardants (NRDC 2013).

Other Standards and Laws

The Upholstered Furniture Action Council (UFAC) has developed a voluntary industry standard for cigarette ignition, which is embodied in the ASTM E-1353 method. The revised California TB117-2013 follows this method, with modifications. CPSC estimates that 90% of currently produced furniture meets the voluntary UFAC standard, which does not address open flame ignitions (CPSC 2008).

In 2013, the New York State Assembly (the lower house of the Legislature) passed a bill (A06557 in the Assembly, introduced as S04780 in the Senate) that would establish an as-yet-undefined open flame standard for furniture (NY State Assembly 2013). The bill also prohibits the use of halogenated flame retardants in furniture. Also, as noted in Section 3.4, New York

[4] This standard would apply to cushioned, upholstered seating products available for residential, home office, and/or dormitory use.

State has also passed a law (A4741/S3703-B) banning TDCPP from consumer products intended for use by children under three years of age, such as baby products, toys, car seats, nursing pillows, crib mattresses, and strollers, effective December 1, 2015 (New York State Governor's Office 2014). New York State banned the sale of children's products containing TCEP in 2011, effective December 1, 2013 (State of New York 2011).

As also noted in Section 3.4, Maryland passed a law prohibiting the importing, selling, or offering for sale any child care product containing more than one-tenth of 1% (by mass) of TDCPP and TCEP. Under the law, child care products are those intended for use by children under the age of three, including baby products, toys, car seats, nursing pillows, crib mattresses, and strollers (State of Maryland 2014). The ban became effective on October 1, 2014, and does not contain a provision for phasing out existing stock.

During its July 2013 meeting, the National Fire Protection Association (NFPA) Standards Council reviewed a request to consider establishing an open flame standard for upholstered furniture. In 2014, NFPA was accepting public comments on the need for a new standard, available resources on the issue, individuals who may be interested in participating in the development of a new standard, and organizations involved in furniture flame retardant standards (Durso 2013; NFPA 2013).

Other Product Sectors

In addition to furniture, other products contain upholstered FPUF. Automobile and aircraft seating is constructed in a manner similar to furniture, with a need for stringent fire protection, as well as other requirements. For example, the flame retardant known as "V6" (Phosphoric acid, P,P'-[2,2-bis(chloromethyl)-1,3-propanediyl] P,P,P',P'-tetrakis(2-chloroethyl) ester) has a higher molecular weight (MW) and lower volatility, and has been identified in automobile applications, where window fogging is an important problem. Aircraft seating is less cost-sensitive than most consumer products, and has relied on more expensive flame barriers as well as additive flame retardants, including expandable graphite. This report includes all flame retardants that DfE identified as being used in these other sectors; this update does not address the flammability standards for these sectors.

Impacts of Changing Standards

It is difficult to predict the impact of changes to these standards on the use of flame retardants. The recent changes to TB117, moving from an open flame to a smolder test, may lessen the need for flame retardant additives in foam; however, for some fabrics, TB117-2013 will still require flame retardant coatings or other modifications. The Consumer Product Safety Commission and New York State have indicated that they may issue a performance-based standard that is more difficult to meet than TB117 (e.g., an open flame test); if they do, it may need to be met either with flame retardant inter-liners or with higher loads of flame retardants in foam, a choice made by individual manufacturers and likely to be driven in many cases by costs.

4 Alternative Flame Retardant Solutions not Addressed in This Report

While the focus of recent public attention has been on additive flame retardant chemicals in FPUF, other methods can be used to provide increased fire safety. These methods are described briefly here; however, this update does not attempt to fully characterize these methods. A rigorous comparison of costs and benefits, particularly over the product life cycle, would require analysis beyond the scope of this report. More information on alternative methods is available in the 2005 FFRP report. Additionally, with the advent of changes to flammability standards, manufacturers may also consider whether the standards can be met without incorporating flame retardants to FPUF. In fact, several major furniture manufacturers have announced plans to produce furniture that does not contain flame retardants (Chicago Tribune 2015).

Flame Resistant Cover Fabrics

In its 2008 proposal for a national furniture flame retardancy standard, CPSC estimated that about 14% of fabrics used at that time would fail the proposed smolder test (CPSC 2008); these fabrics could be coated with a flame retardant to meet a smolder test. Coating fabrics raises the issue of chemical safety in the coatings used; flame retardant chemicals used for coatings tend to differ from the flame retardant chemicals used in FPUF. Anecdotal information indicates that decaBDE, tetrabromobisphenol A, and hexabromocyclododecane – each one the subject of a DfE Alternatives Assessment (see http://www2.epa.gov/saferchoice/design-environment-alternatives-assessments) – have been used as fabric coatings (Stapleton July 2013, personal communication). The current report does not attempt to identify or assess flame retardants used in fabric coatings.

Fire Barriers

To meet a more stringent test (e.g., an open flame test), a fire barrier may be used between the foam and the upholstery fabric. A fire barrier may be IFR (e.g., Kevlar or Nomex), or may be coated with a flame retardant chemical, possibly including the chemicals identified as alternatives in this report. Fire barriers have proven highly effective in aircraft seating, even in extreme fire situations (CPSC 2013b). A suitable fire barrier is likely to be able to achieve almost any flame retardancy standard; however, costs of such products are likely to be higher. Mattresses meeting the CPSC 1633 open flame standard most commonly use fire barriers, although designs of these barriers vary widely (Nazare, Davis et al. 2012).

Polymers and Reactive Flame Retardants

The current report includes only one polymeric flame retardant (excluding expandable graphite). While polymers would be expected to have lower mobility, reducing exposures during the consumer use phase, they are difficult to use in the manufacture of FPUF. Polymeric and reactive flame retardants typically have high viscosities incompatible with flexible polyurethane, are not compatible with the extremely small pores used in the blending nozzle, and have difficulty blending with the polyol. Reactive products are available in other product sectors (e.g., in printed

circuit boards), and there is great interest in the manufacturing industry in finding reactive flame retardants for FPUF.

Nanoclays

There has been recent interest in nanoclay flame retardants, which may slow or prevent the breakdown of materials and decrease the temperature of the flame, and have been shown to improve the mechanical properties of polyurethane foam (Betts 2008; Nayani, Gunashekar et al. 2013). Nanoclays can also be combined with other classes of flame retardants to improve their performance. These materials are currently in the research and development stage, but may become viable products in the near future. Layer-by-layer (LbL) coatings are nanocomposite structures assembled by an alternate deposition of anionic and cationic monolayers onto a substrate (Li, Schulz et al. 2009; Kim, Harris et al. 2012). The LbL deposition technique was discovered in 1966, and flame retardant LbL coatings have recently gained attention beyond the areas of academic research and development, with some industrial companies pursuing internal studies on the effectiveness of LbL coatings as flame retardants in commercial products (Apaydin, Laachachi et al. 2013). Research has shown that LbL coatings can be effective flame retardants for a number of different substrates including polyurethane foam (Kim, Harris et al. 2012; Laufer, Kirkland et al. 2012a) and cotton fabric (Li, Schulz et al. 2009; Laufer, Kirkland et al. 2012b).

5 Hazard Evaluation Methodology

This section summarizes the toxicological and environmental hazards of furniture flame retardants (FFRs) and each alternative chemical or proprietary mixture that was identified as a potential functional substitute for them. Evaluations of chemical formulations may also include associated substances (e.g., starting materials, byproducts, and impurities) if their presence is specifically required to allow that alternative to fully function in the assigned role. Otherwise, pure substances were analyzed in this assessment. Users of this DfE alternatives assessment should be aware of the purity of the trade product they purchase, as the presence of impurities may alter the assessment of the alternative. This report is a hazard assessment, not a risk assessment. Hazard assessment as a risk management tool is discussed in more detail in Section 1.3.

Toxicological and environmental endpoints included in the hazard profiles are discussed in Section 5.1, along with the criteria used to evaluate each hazard endpoint. Data sources and the review methodology are described in Section 5.2. The report then offers a detailed description of the utility of physical-chemical properties in understanding hazard in Section 5.3, and the process of evaluating human health and environmental endpoints in Sections 5.4 and 5.5, respectively. A discussion of the evaluation of endocrine activity is included in Section 5.6. The characteristics of each chemical included in the alternatives assessment are summarized in the comparative hazard summary table in Section 2. Lastly, the collected data and hazard profile of each chemical are presented in Section 7.

5.1 Toxicological and Environmental Endpoints

The assessment of endpoints with the intent to create hazard profiles for a DfE alternatives assessment follows the guidance of the *DfE Alternatives Assessment Criteria for Hazard Evaluation* (U.S. EPA 2011b). The definitions for each endpoint evaluated following these criteria are outlined in Section 5.1.1, and the criteria by which these endpoints are evaluated are outlined in Section 5.1.2. Lastly, there are endpoints that DfE characterizes but to which it does not assign criteria; these are summarized in Section 5.1.3.

5.1.1 Definitions of Each Endpoint Evaluated Against Criteria

Hazard designations for each chemical discussed in this report were made by direct comparison of the experimental or estimated data to the *DfE Alternatives Assessment Criteria for Hazard Evaluation* (U.S. EPA 2011b). Table 5-1 provides brief definitions of human health toxicity, environmental toxicity, and environmental fate endpoints.

Table 5-1: Definitions of Toxicological and Environmental Endpoints for Hazard Assessment

Endpoint Category	Endpoint	Definition
Human Health Effects	**Acute Mammalian Toxicity**	Adverse effects occurring following oral or dermal administration of a single dose of a substance, or multiple doses given within 24 hours, or an inhalation exposure of 4 hours.

Endpoint Category	Endpoint	Definition
	Carcinogenicity	Capability of a substance to increase the incidence of malignant neoplasms, reduce their latency, or increase their severity or multiplicity.
	Mutagenicity/Genotoxicity	*Mutagenicity* - The ability of an agent to induce permanent, transmissible changes in the amount, chemical properties or structure of the genetic material. These changes may involve a single gene or gene segment, a block of genes, parts of chromosomes, or whole chromosomes. Mutagenicity differs from genotoxicity in that the change in the former case is transmissible to subsequent cell generations. *Genotoxicity* – The ability of an agent or process to alter the structure, information content, or segregation of DNA, including those which cause DNA damage by interfering with normal replication process, or which in a non-physiological manner (temporarily) alter its replication.
	Reproductive Toxicity	The occurrence of biologically adverse effects on the reproductive systems of females or males that may result from exposure to environmental agents. The toxicity may be expressed as alterations to the female or male reproductive organs, the related endocrine system, or pregnancy outcomes. The manifestation of such toxicity may include, but is not limited to: adverse effects on onset of puberty, gamete production and transport, reproductive cycle normality, sexual behavior, fertility, gestation, parturition, lactation, developmental toxicity, premature reproductive senescence or modifications in other functions that were dependent on the integrity of the reproductive systems.
	Developmental Toxicity	Adverse effects in the developing organism that may result from exposure prior to conception (either parent), during prenatal development, or postnatally to the time of sexual maturation. Adverse developmental effects may be detected at any point in the lifespan of the organism. The major manifestations of developmental toxicity include: (1) death of the developing organism, (2) structural abnormality, (3) altered growth, and (4) functional deficiency.
	Neurotoxicity	An adverse change in the structure or function of the central and/or peripheral nervous system following exposure to a chemical, physical or biological agent.

Endpoint Category	Endpoint	Definition
	Repeated Dose Toxicity	Adverse effects (immediate or delayed) that impair normal physiological function (reversible and irreversible) of specific target organs or biological systems following repeated exposure to a chemical substance by any route relevant to humans. Adverse effects include biologically significant changes in body and organ weights, changes that affect the function or morphology of tissues and organs (gross and microscopic), mortality, and changes in biochemistry, urinalysis, and hematology parameters that are relevant for human health; may also include immunological and neurological effects.
	Respiratory Sensitization	Hypersensitivity of the airways following inhalation of a substance.
	Skin Sensitization	A cell-mediated or antibody-mediated allergic response characterized by the presence of inflammation that may result in cell death, following an initial induction exposure to the same chemical substance (i.e., skin allergy).
	Eye Irritation/Corrosivity	Irritation or corrosion to the eye following the application of a test substance.
	Skin Irritation/Corrosion	Skin irritation- reversible damage to the skin following the application of a test substance for up to 4 hours. Skin corrosion- irreversible damage to the skin namely, visible necrosis through the epidermis and into the dermis following the application of a test substance for up to 4 hours.
Environmental Toxicity	**Environmental toxicity refers to adverse effects observed in living organisms that typically inhabit the wild; the assessment is focused on effects in three groups of surrogate aquatic organisms (freshwater fish, invertebrates, and algae).**	
	Aquatic Toxicity (Acute)	The property of a substance to be injurious to an organism in a short-term, aquatic exposure to that substance.
	Aquatic Toxicity (Chronic)	The property of a substance to cause adverse effects to aquatic organisms during aquatic exposures which were determined in relation to the life-cycle of the organism.
Environmental Fate	**Environmental Persistence**	The length of time the chemical exists in the environment, expressed as a half-life, before it is destroyed (i.e., transformed) by natural or chemical processes. For alternatives assessments, the amount of time for complete assimilation (ultimate removal) is preferred over the initial step in the transformation (primary removal).
	Bioaccumulation	The process in which a chemical substance is absorbed in an organism by all routes of exposure as occurs in the natural environment (e.g., dietary and ambient environment sources). Bioaccumulation is the net result of competing processes of chemical uptake into the organism at the respiratory surface and from the diet and chemical elimination from the organism, including respiratory exchange, fecal egestion, and metabolic biotransformation of the parent compound and growth dilution.

The hazard profile for each chemical contains endpoint specific summary statements (see Section 7). For each of the endpoints listed in Table 5-1, these summary statements provide the hazard designation, the type of data (experimental or estimated) and the rationale. The endpoint summaries may also include explanatory comments, a discussion of confounding factors, or an indication of the confidence in the data to help put the results in perspective.

5.1.2 Criteria

Table 5-2 summarizes the criteria that were used by DfE to interpret the data presented in the hazard evaluations. The *DfE Alternatives Assessment Criteria for Hazard Evaluation* underwent internal and public comment, and were finalized in 2011 (U.S. EPA 2011b). A hazard designation for each human health endpoint was not given for each route of exposure, but rather was based on the exposure route with the highest hazard designation. Data may have been available for some or all relevant routes of exposure.

The details as to how each endpoint was evaluated are described below and in the DfE full criteria document, *DfE Alternatives Assessment Criteria for Hazard Evaluation*, available at: http://www2.epa.gov/saferchoice/alternatives-assessment-criteria-hazard-evaluation.

Table 5-2: Criteria Used to Assign Hazard Designations

Endpoint	Very High	High	Moderate	Low	Very Low
Human Health Effects					
Acute mammalian toxicity					
Oral median lethal dose (LD_{50}) (mg/kg)	≤50	>50–300	>300–2,000	>2,000	–
Dermal LD_{50} (mg/kg)	≤200	>200–1,000	>1,000–2,000	>2,000	–
Inhalation median lethal concentration (LC_{50}) - vapor/gas (mg/L)	≤2	>2–10	>10–20	>20	–
Inhalation LC_{50} - dust/mist/ fume (mg/L)	≤0.5	>0.5–1.0	>1–5	>5	–
Carcinogenicity					
Carcinogenicity	*Known or presumed human carcinogen* (equivalent to Globally Harmonized System of Classification and Labeling of Chemicals (GHS) Categories 1A and 1B)	*Suspected human carcinogen* (equivalent to GHS Category 2)	*Limited or marginal evidence of carcinogenicity in animals* (and inadequate evidence in humans)	*Negative studies or robust mechanism-based Structure Activity Relationship (SAR)* (as described above)	–

Mutagenicity/Genotoxicity					
Germ cell mutagenicity	GHS Category 1A or 1B: Substances known to induce heritable mutations or to be regarded as if they induce heritable mutations in the germ cells of humans	GHS Category 2: Substances which cause concern for humans owing to the possibility that they may induce heritable mutations in the germ cells of humans OR	Evidence of mutagenicity supported by positive results in *in vitro* OR *in vivo* somatic cells of humans or animals	Negative for chromosomal aberrations and gene mutations, or no structural alerts.	--
Mutagenicity and genotoxicity in somatic cells		Evidence of mutagenicity supported by positive results in *in vitro* AND *in vivo* somatic cells and/or germ cells of humans or animals			
Reproductive toxicity					
Oral (mg/kg/day)	–	<50	50–250	>250-1,000	>1,000
Dermal (mg/kg/day)	–	<100	100–500	>500-2,000	>2,000
Inhalation - vapor, gas (mg/L/day)	–	<1	1–2.5	>2.5-20	>20
Inhalation - dust/mist/fume (mg/L/day)	–	<0.1	0.1–0.5	>0.5-5	>5
Developmental toxicity					
Oral (mg/kg/day)	–	<50	50–250	>250-1,000	>1,000
Dermal (mg/kg/day)	–	<100	100–500	>500-2,000	>2,000
Inhalation - vapor, gas (mg/L/day)	–	<1	1–2.5	>2.5-20	>20
Inhalation - dust/mist/fume (mg/L/day)	–	<0.1	0.1–0.5	>0.5-5	>5
Neurotoxicity					
Oral (mg/kg/day)	–	<10	10–100	>100	–
Dermal (mg/kg/day)	–	<20	20–200	>200	–
Inhalation - vapor, gas (mg/L/day)	–	<0.2	0.2–1.0	>1.0	–
Inhalation - dust/mist/fume (mg/L/day)	–	<0.02	0.02–0.2	>0.2	–
Repeated-dose toxicity					
Oral (mg/kg/day)	–	<10	10–100	>100	–
Dermal (mg/kg/day)	–	<20	20–200	>200	–

Inhalation - vapor, gas (mg/L/day)	–	<0.2	0.2–1.0	>1.0	–
Inhalation - dust/mist/fume (mg/L/day)	–	<0.02	0.02–0.2	>0.2	–
Sensitization					
Skin sensitization	–	High frequency of sensitization in humans and/or high potency in animals (GHS Category 1A)	Low to moderate frequency of sensitization in human and/or low to moderate potency in animals (GHS Category 1B)	Adequate data available and not GHS Category 1A or 1B	–
Respiratory sensitization	–	Occurrence in humans or evidence of sensitization in humans based on animal or other tests (equivalent to GHS Category 1A and 1B)	Limited evidence including the presence of structural alerts	Adequate data available indicating lack of respiratory sensitization	–
Irritation/corrosivity					
Eye irritation/corrosivity	Irritation persists for >21 days or corrosive	Clearing in 8–21 days, severely irritating	Clearing in ≤7 days, moderately irritating	Clearing in <24 hours, mildly irritating	Not irritating
Skin irritation/corrosivity	Corrosive	Severe irritation at 72 hours	Moderate irritation at 72 hours	Mild or slight irritation at 72 hours	Not irritating
Endocrine activity					
Endocrine Activity	*For this endpoint, High/Moderate/Low etc. characterizations will not apply. A qualitative assessment of available data will be prepared.*				
Environmental Toxicity and Fate					
Aquatic toxicity					
Acute aquatic toxicity – LC_{50} or half maximal effective concentration (EC_{50}) (mg/L)	<1.0	1–10	>10–100	>100 or No Effects at Saturation (NES)	–
Chronic aquatic toxicity – lowest observed effect concentration (LOEC) or chronic value (ChV) (mg/L)	<0.1	0.1–1	>1–10	>10 or NES	–

Environmental persistence					
Persistence in water, soil, or sediment	Half-life >180 days or recalcitrant	Half-life of 60–180 days	Half-life <60 but ≥16 days	Half-life <16 days OR passes Ready Biodegradability test not including the 10-day window. No degradation products of concern.	Passes Ready Biodegradability test with 10-day window. No degradation products of concern.
Persistence in air (half-life days)	*For this endpoint, High/Moderate/Low etc. characterizations will not apply. A qualitative assessment of available data will be prepared.*				
Bioaccumulation					
Bioconcentration Factor (BCF)/Bioaccumulation Factor (BAF)	>5,000	5,000–1,000	<1,000–100	<100	–
Log BCF/BAF	>3.7	3.7–3	<3-2	<2	–

Very High or Very Low designations (if an option for a given endpoint in Table 5-2) were assigned only when there were experimental data located for the chemical under evaluation. In addition, the experimental data must have been collected from a well conducted study specifically designed to evaluate the endpoint under review. If the endpoint was estimated using experimental data from a close structural analog, by professional judgment, or from a computerized model, then the next-level designation was assigned (e.g., use of data from a structural analog that would yield a designation of very high would result in a designation of high for the chemical in review). One exception is for the estimated persistence of polymers with an average MW >1,000 daltons, which may result in a Very High designation.

5.1.3 Endpoints Characterized but Not Evaluated

Several additional endpoints were characterized, but not evaluated against hazard criteria. This is because the endpoints lacked a clear consensus concerning the evaluation criteria (endocrine activity), data and expert judgment were limited for industrial chemicals (persistence in air, terrestrial ecotoxicology), or the information was valuable for the interpretation of other toxicity and fate endpoints (including toxicokinetics and transport in the environment).

Table 5-3: Definitions of Endpoints and Information Characterized but Not Evaluated Against Hazard Criteria

Toxicological Endpoint	Definition
Toxicokinetics	The determination and quantification of the time course of absorption, distribution, biotransformation, and excretion of chemicals (sometimes referred to as *pharmacokinetics*).
Biomonitoring Information	The measured concentration of a chemical in biological tissues where the analysis samples were obtained from a natural or non-experimental setting.
Environmental Transport	The potential movement of a chemical, after it is released to the environment, within and between each of the environmental compartments, air, water, soil, and sediment. Presented as a qualitative summary in the alternatives assessment based on physical-chemical properties, environmental fate parameters, and simple volatilization models. Also includes distribution in the environment as estimated from a fugacity model[5].

Toxicological Endpoint	Definition
Persistence in Air	The half-life for destructive removal of a chemical substance in the atmosphere. The primary chemical reactions considered for atmospheric persistence include hydrolysis, direct photolysis, and the gas phase reaction with hydroxyl radicals, ozone, or nitrate radicals. Results are used as input into the environmental transport models.
Immunotoxicology	Adverse effects on the normal structure or function of the immune system caused by chemical substances (e.g., gross and microscopic changes to immune system organs, suppression of immunological response, autoimmunity, hypersensitivity, inflammation, and disruption of immunological mechanistic pathways).
Terrestrial Ecotoxicology	Reported experimental values from guideline and nonguideline studies on adverse effects on the terrestrial environment. Studies on soil, plants, birds, mammals, invertebrates were also included.
Endocrine Activity	A change in endocrine homeostasis caused by a chemical or other stressor from human activities (e.g., application of pesticides, the discharge of industrial chemicals to air, land, or water, or the use of synthetic chemicals in consumer products.)

[1]A fugacity model predicts partitioning of chemicals among air, soil, sediment, and water under steady state conditions for a default model "environment" (U.S. EPA 2011e).

5.2 Data Sources and Assessment Methodology

This section explains how data were collected (Section 5.2.1), prioritized and reviewed (Section 5.2.2) for use in the development of hazard profiles. High-quality experimental studies lead to a thorough understanding of behavior and effects of the chemical in the environment and in living organisms. Analog approaches and SAR-based estimation methods are also useful tools and are discussed throughout this section. Information on how polymers differ from discrete chemicals in terms of how they are evaluated is presented in Section 5.2.3.

5.2.1 Identifying and Reviewing Measured Data

For each chemical assessed, data were collected in a manner consistent with the *High Production Volume (HPV) Chemical Challenge Program Guidance* (U.S. EPA 1999) on searching for existing chemical information. This process resulted in a comprehensive search of the literature for available experimental data. For chemicals well characterized by experimental studies, this usually resulted in the collection of recent high-quality reviews or peer-reviewed risk assessments. These were supplemented by primary searches of scientific literature published after these secondary sources were released; this is explained in greater detail below. For chemicals that are not as well characterized, that is, where these secondary sources were not available or lacked relevant or adequate data, a comprehensive search of the primary scientific literature was done. Subsequently, these searches led to the collection and review of articles from the scientific literature, industrial submissions, encyclopedic sources, and government reports. In addition, data presented in EPA public databases (e.g., Integrated Risk Information System (IRIS); the High Production Volume Information System (HPVIS)) and confidential databases were obtained for this project. Generally, foreign language (non-English) reports were not used unless they provided information that was not available from other sources.

Chemical assessments were performed by first searching for experimental data for all endpoints in Table 5-2. For most alternatives assessed, high quality secondary sources were not available;

therefore a comprehensive search of the literature was performed to identify experimental data. In some cases, confidential studies submitted to EPA by chemical manufacturers were also available to support hazard designations. For those chemicals that were expected to form stable metabolites, searches were performed to identify relevant fate and toxicity information for the metabolite or degradation product.

Well Studied Chemicals – Literature Search Strategy

As mentioned above, for chemicals that have been well characterized, the literature review focused primarily on the use of secondary sources, such as Agency for Toxic Substances and Disease Registry (ATSDR) Toxicological Profiles or IRIS assessments. Using high-quality secondary sources maximized available resources and eliminated potential duplication of effort. However, more than one secondary source was typically used to verify reported values, which also reduced the potential for presenting a value that was transcribed incorrectly from the scientific literature. Although other sources might also contain the same experimental value for an endpoint, effort was not focused on building a comprehensive list of these references, as it would not have enhanced the ability to reach a conclusion in the assessment. When data for a selected endpoint could not be located in a secondary source for an otherwise well studied chemical, the primary literature was searched by endpoint and experimental studies were assessed for relevant information.

Making Predictions in the Absence of Measured Data

In the absence of primary or secondary data, hazard designations were based on (1) Quantitative Structure Activity Relationships (QSAR)-based estimations from the EPA New Chemical Program's predictive methods; (2) analog data; (3) class-based assignments from the EPA Chemical Categories document, and (4) expert judgment by EPA subject matter experts.

For chemicals that lacked experimental information, QSAR assessments were made using either EPA's Estimation Programs Interface (EPISuite™) for physical-chemical property and environmental fate endpoints or EPA's Ecological Structure Activity Relationships (ECOSAR™) QSARs for ecotoxicity. For the cancer endpoint, estimates were also obtained from EPA's OncoLogic expert system. These estimation methods have been automated, and are available for free (U.S. EPA 2012c). Often analog data were used to support predictions from models. These approaches were described in the EPA Pollution Prevention (P2) Framework and Sustainable Futures (SF) program (U.S. EPA 2005b; U.S. EPA 2011e).

For some physical-chemical properties that could not be estimated using EPISuite™, such as acid/base dissociation constants, other available methods (e.g., the ACE acidity and basicity calculator website for dissociation constants) were used (ACE Organic 2013). All estimation methods employed were limited to those freely available in the public domain.

The methodology and procedures used to assess polymers are described in Section 5.2.3. In addition, the endpoints for impurities or oligomers with a MW >1,000 daltons were estimated using professional judgment and the results assessed for inclusion in the overall hazard

designation. This process is described, as appropriate, under the corresponding endpoints appearing in Section 5.3.

When QSAR models were not available, professional judgment was used to identify hazards for similar chemicals using the guidance from EPA's New Chemicals Categories (U.S. EPA 2010b). The categories identify substances that share chemical and toxicological properties and possess potential health or environmental concerns (U.S. EPA 2010a). In the absence of an identified category, analogs for which experimental data are available were identified using EPA's Analog Identification Methodology (AIM) or by substructure searches of confidential EPA databases (U.S. EPA 2012a). If a hazard designation was still not available, the expert judgment of scientists from EPA's New Chemical Program would provide an assessment of the physical-chemical properties, environmental fate, aquatic toxicity and human health endpoints to fill remaining data gaps.

Expandable graphite was a unique substance compared to the other alternatives in this report. Although expandable graphite has some structural features in common with carbon-based nanoparticles, its cross-section diameter is far greater, and it would be less likely to pass through biological membranes. As a result, it was not considered a nano-sized substance and available nanoparticle data were not used as analog data in the evaluation. At the time of this report, DfE is not using the hazard criteria to assess nanoparticles.

5.2.2 Hierarchy of Data Adequacy

Once the studies were obtained, they were evaluated to establish whether the hazard data were of sufficient quality to meet the requirements of the assessment process. The adequacy and quality of the studies identified in the literature review are described in the Data Quality field of the chemical assessments presented in Section 7. The tiered approach described below represents a general preferred data hierarchy, but the evaluation of toxicological data also requires flexibility based on expert judgment.

1. One or more studies conducted in a manner consistent with established testing guidelines
2. Experimentally valid but nonguideline studies (i.e., do not follow established testing guidelines)
3. Reported data without supporting experimental details
4. Estimated data using SAR methods or professional judgment based on an analog approach
5. Expert judgment based on mechanistic and structural considerations

In general, data were considered adequate to characterize an endpoint if they were obtained using the techniques identified in the HPV data adequacy guidelines (U.S. EPA 1999). Studies performed according to Harmonized EPA or Organisation for Economic Cooperation and Development guidelines were reviewed to confirm that the studies followed all required steps.

Experimental studies published in the open literature were reviewed for their scientific rigor and were also compared and contrasted to guideline studies to identify potential problems arising from differences in the experimental design. Data from adequate, well-performed, experimental

studies were used to assign hazard designations in preference to those lacking in sufficient experimental detail. When multiple adequate studies were available for a given endpoint, any discrepancies that were identified within the set of data were examined further and addressed using a weight-of-evidence approach that was described in the data entry to characterize the endpoint whenever possible.

When available, experimental data from guideline or well-performed experimental studies were preferred (Items 1 and 2 in the hierarchy list). Information from secondary sources such as Material Safety Data Sheets (MSDSs), or online databases (such as the National Library of Medicine's Hazardous Substances Data Bank (HSDB), Item 3 in the hierarchy list) was considered appropriate for some endpoints when it included numerical values for effect levels that could be compared to the evaluation criteria.

5.2.3 Assessment of Polymers and Oligomers

The methodology and procedures used to assess polymers were slightly different than those used for oligomers, discrete compounds and simple mixtures. Although experimental data for polymers were identified using the literature search techniques discussed above in Section 5.2.1, in the absence of experimental data, estimates were performed using professional judgment as presented in the literature (Boethling and Nabholz 1997). The polymers are a mixture of molecules with a distribution of components (e.g., different chain lengths) that depend on the monomers used, their molar ratios, the total number of monomeric units in the polymer chain, and the manufacturing conditions. To account for this variation, the average MW profile (also referred to as the number average molecular weight (MW_n)) was used in their assessment, as the individual chains rarely have the same degree of polymerization and weight, yet their physical, chemical, and environmental properties are essentially identical for the purposes of this assessment. The polymers evaluated as alternatives typically have average MWs ranging from >1,000 to <100,000 daltons.

For polymers with relatively low average MWs (i.e., those with average MWs generally less than 2,000), the alternatives assessment also determined the amount of oligomers and unchanged monomers (starting materials) in the MW profile with MWs <1,000 daltons. Special attention was paid to materials that have a MW <1,000 daltons, as these materials often have the highest hazard (potentially bioavailable substances) in the mixture. This type of assessment was similar to the evaluation of the hazards of impurities present in discrete chemical products. Methodological differences between the evaluation of discrete products and polymers are discussed in Section 5.3. Although the MW of expandable graphite is >1,000, it was not explicitly evaluated as a polymer. However, the chemical property and hazard designation cutoffs associated with polymers and other high MW materials were used in its evaluation.

For this alternatives assessment, there were chemicals that are mixtures of low MW oligomers comprised of 2 or 3 repeating units. The hazard assessment evaluated all oligomers present. From all the oligomers, the higher concern material was used to assign the hazard designation. This process is essentially identical to the evaluation of the hazards associated with impurities or byproducts present in discrete chemical products. As a result, the alternatives assessment process determined the amount of oligomers and unchanged monomers (starting materials) present, and considered their potential hazards in the alternatives designation.

5.3 Importance of Physical and Chemical Properties, Environmental Transport, and Biodegradation

Physical-chemical properties provide basic information on the characteristics of a chemical substance, and were used throughout the alternatives assessment process. These endpoints provide information required to assess potential environmental release, exposure, and partitioning, as well as insight into the potential for adverse toxicological effects. The physical-chemical properties are provided in the individual chemical hazard profiles presented in Section 7. Descriptions of relevant physical-chemical properties and how they contribute to the hazard assessments are presented below.

Molecular Weight (MW)

MW informs how a chemical behaves in a physical or biological system, including bioavailability and environmental fate. In general, but not strictly, larger compounds tend to be less mobile in biological and environmental systems. Their large size restricts their transport through biological membranes and lowers their vapor pressure. Polymers and oligomers evaluated in this alternatives assessment were mixtures that contain a distribution of components, and they may not have a unique MW (see also Section 5.2.3). To account for variation in these mixtures, the average MW or MW_n, determined experimentally (typically using high pressure liquid chromatography, viscosity, or light-scattering), was used in the assessment of polymers. The assessment of polymers also includes oligomers and unchanged monomers (starting materials) that have MW of <1,000 daltons, as these were often the highest concern materials (bioavailable substances) in the mixture.

Melting Point and Boiling Point

These two properties provide an indication of the physical state of the material at ambient temperature. Chemicals with a melting point more than 25°C were assessed as a solid. Those with a melting point less than 25°C and a boiling point more than 25°C were assessed as a liquid, and those with a boiling point less than 25°C were assessed as a gas. The physical state was used throughout the assessment, such as in the determination of potential routes of human and environmental exposure. The melting and boiling points were also useful in determining the potential environmental fate, ecotoxicity, and human health hazards of a chemical. For example, organic compounds with high melting points generally have low water solubility and low rates of dissolution. These properties influence a material's bioavailability, and were therefore taken into account in both the assessment process and the evaluation of experimental studies. Similarly, chemicals with a low melting point also have a higher potential to be absorbed through the skin, gastrointestinal tract, and lungs.

In the absence of experimental data, the melting point value was not reported, and no estimations were performed. If a chemical decomposes before it melts, this information was included in the assessment. For boiling point, the maximum value reported in the assessment was 300°C for high boiling materials, including polymers (U.S. EPA 1999). Melting points for polymers and/or oligomers were not reported, as these materials typically reach a softening point and do not undergo the phase change associated with melting (i.e., solid to liquid).

Vapor Pressure

Vapor pressure is useful in determining the potential for a chemical substance to volatilize to the atmosphere from dry surfaces, from storage containers, or during mixing, transfer, or loading/unloading operations. In the assessment process, chemicals with a vapor pressure less than 1×10^{-6} mm Hg have a low potential for inhalation exposure resulting from gases or vapors. Vapor pressure is also useful for determining the potential environmental fate of a substance. Substances with a vapor pressure more than 1×10^{-4} mm Hg generally exist in the gas phase in the atmosphere. Substances with a vapor pressure between 1×10^{-4} and 1×10^{-8} mm Hg exist as a gas/particulate mixture. Substances with a vapor pressure less than 1×10^{-8} mm Hg exist as a particulate. The potential atmospheric degradation processes described below in the reactivity section generally occur when a chemical exists in the gas phase. Gases in the atmosphere also have the potential to travel long distances from their original point of release. Materials in the liquid or solid (particulate) phases in the atmosphere generally undergo deposition onto the Earth's surface.

A maximum vapor pressure of 1×10^{-8} mm Hg was assigned for chemicals without experimental data, or for those substances that were anticipated by professional judgment to be nonvolatile (U.S. EPA 1999). The maximum vapor pressure of 1×10^{-8} mm Hg was also the default value reported for the vapor pressure of polymers and other high MW materials with a MW >1,000 daltons (U.S. EPA 1999).

Water Solubility

The water solubility of a chemical provides an indication of its distribution between environmental media, potential for environmental exposure through release to aquatic compartments, and potential for human exposure through ingestion of drinking water. Water solubility was also used extensively to determine potential human health and ecotoxicity hazards. In general, chemicals with water solubility less than 1×10^{-5} g/L indicate a lower concern for both the expression of adverse effects and potential aquatic and general population exposure, due to their low bioavailability. However, chemicals with a low bioavailability also tend to be more environmentally persistent. Low bioavailability is different than no bioavailability, and the two should not be used interchangeably.

Within the context of this alternatives assessment, the following descriptors were used according to ranges of water solubility values: more than 10,000 mg/L was considered very soluble; 1,000–10,000 mg/L represents soluble; 100–1,000 mg/L represents moderately soluble, 1–100 mg/L represents slightly soluble, and less than 1 mg/L was considered to be insoluble, noting that these guidelines might not match what is used elsewhere within the scientific literature for other disciplines. Chemicals with higher water solubility are more likely to be transported into groundwater with runoff during storm events, be absorbed through the gastrointestinal tract or lungs, partition to aquatic compartments, undergo atmospheric removal by rain washout, and possess a greater potential for human exposure through the ingestion of contaminated drinking water. Chemicals with lower water solubility are generally more persistent, and have a greater potential to bioconcentrate.

The water solubility of a substance was also used to evaluate the quality of experimental aquatic toxicity and oral exposure human health studies, as well as the reliability of aquatic toxicity estimates. If the water solubility of a substance was lower than the reported exposure level in these experiments, then the study was likely to be regarded as inadequate, due to potentially confounding factors arising from the presence of un-dissolved material. For aquatic toxicity estimates obtained using SARs, when the estimated toxicity was higher than a chemical's water solubility (i.e., the estimated concentration in water at which adverse effects appear cannot be reached because it was above the material's water solubility), the chemical was described as having NES. An NES designation is equivalent to a low aquatic toxicity hazard designation for that endpoint.

While assessing the water solubility of a chemical substance, its potential to disperse in an aqueous solution was also considered. Ideally, a chemical's potential to disperse would be obtained from the scientific literature. In the absence of experimental data, the potential for dispersion can be determined from chemical structure and/or comparison to closely related analogs. There are two general structural characteristics that lead to the formation of dispersions in water: (1) chemicals that have both a hydrophilic (polar) head and a hydrophobic (nonpolar) tail (e.g., surfactants), and (2) molecules that have a large number of repeating polar functional groups (e.g., polyethylene oxide).

The potential for a chemical to disperse influences potential exposure, environmental fate, and toxicity. Dispersible chemicals have greater potential for human and environmental exposure, leachability, and aquatic toxicity than what might be anticipated based on the material's water solubility alone.

Chemicals without experimental data, or chemicals that were anticipated by professional judgment to be sufficiently insoluble and thus were not bioavailable, were assigned a water solubility maximum value of 1×10^{-3} mg/L (U.S. EPA 1999). A water solubility of 1×10^{-3} mg/L is the default value used for discrete organics, as well as non-ionic polymers with a MW > 1,000 daltons, according to information contained in the literature concerning polymer assessment (Boethling and Nabholz 1997). This assignment is consistent with an analysis of the chemicals used in the development of the water solubility estimation program in EPA's EPISuite™ software. The training set for this model included 1,450 chemicals with a MW range 27-628 daltons and experimental water solubility values ranging from miscible to 4×10^{-7} mg/L (Meylan, Howard et al. 1996; U.S. EPA 2011i). Given that water solubility decreases with MW, a default value of 1×10^{-3} mg/L is consistent with the limited bioavailability expected for materials with a MW >1,000 daltons.

Octanol/Water Partition Coefficient (K_{ow})

The octanol/water partition coefficient, commonly expressed as its log value (i.e., log K_{ow}) is one of the most useful properties for performing a hazard assessment. The log K_{ow} indicates the partitioning of a chemical between octanol and water, where octanol is used to mimic fat and other hydrophobic components of biological systems. Chemicals with a log K_{ow} less than 1 are highly soluble in water (hydrophilic), while those with a log K_{ow} more than 4 are not very soluble in water (hydrophobic). A log K_{ow} more than 8 indicates that the chemical is not readily

bioavailable and is essentially insoluble in water. In addition, a log K_{ow} greater than approximately 8 may be difficult to obtain experimentally.

The log K_{ow} can be used as a surrogate for the water solubility in a hazard assessment, and is frequently used to estimate the water solubility if an experimental value is not available. It can also be used to estimate other properties important to the assessment, including bioconcentration and soil adsorption, and is a required input for SAR models used to estimate ecotoxicity values.

For chemicals without data, that are not within the domain of EPISuite™ or that were expected to be insoluble in water (WS <1 x 10^{-3} mg/L), a minimum value of 10 was assigned for the log K_{ow} (U.S. EPA 1999). Insoluble chemicals that could be run through EPISuite™ software may use a log K_{ow} >10 if the result appeared to be valid based on expert review. This assignment is consistent with an analysis of the chemicals ("training set") used in the development of the octanol/water partition coefficient estimation program in the EPISuite™ software. The training set for this model included 10,946 chemicals with a MW range 18-720 daltons and experimental log K_{ow} values ranging from -3.89 to 8.70 (Meylan and Howard 1995; U.S. EPA 2011h). Given that log K_{ow} increases with MW, a default value of 10 is consistent with the limited bioavailability expected for materials with a MW >1,000 daltons. A maximum log K_{ow} of -2 was used for water soluble materials. For most polymers and other materials that are anticipated to be insoluble in both water and octanol, the log K_{ow} cannot be measured and was therefore not listed.

Flammability (Flash Point)

The flash point of a substance is defined as the minimum temperature at which the substance emits sufficient vapor to form an ignitable mixture with air. Flash point can be used to identify hazards associated with the handling of volatile chemicals. Substances with a flash point above 37.8°C (100°F) were commonly referred to as non-flammable, as this is the flammability definition used in the shipping industry. There are exceptions to this definition, such as chemicals that may form explosive mixtures in the presence of air.

Explosivity

Explosivity refers to the potential for a chemical to form explosive mixtures in air, and can be defined using the limits of flammability. The lower limit of flammability (LFL) is defined as the minimum concentration of a combustible substance that is capable of propagating a flame through a homogenous mixture in the presence of an ignition source. The upper limit of flammability (UFL) is similarly defined as the highest concentration that can propagate a flame. LFLs and UFLs are commonly reported as the volume percent or volume fraction of the flammable component in air at 25°C. If the ambient air concentration of the gas (or vapor) is between the upper and lower explosion limit, then the material has the potential to explode if it comes in contact with an ignition source. Knowledge regarding the explosivity of a given material in air is also useful in identifying potential hazards associated with the manufacture and use of that material.

pH

The pH scale measures how acidic or basic a substance is on a range from 0 to 14. A pH of 7 is neutral. A pH less than 7 is acidic, and a pH greater than 7 is basic. This scale is used primarily to identify potential hazards associated with skin or eye contact with a chemical or its aqueous solutions. The corrosive nature of chemicals that form either strongly basic (high pH) or strongly acidic (low pH) solutions are generally likely to result in harm to skin and other biological membranes. For corrosive chemicals, some experimental studies, such as biodegradation tests, require additional analysis to determine if the tests were performed at concentrations that cause harm to microbes in the test (and, therefore, may result in incorrectly identifying a chemical as persistent in the environment). For chemicals that form moderately basic or acidic solutions in water, the pH of the resulting solution can be used in lieu of a measured dissociation constant.

Dissociation Constant in Water (pKa)

The dissociation constant determines if a chemical will ionize under environmental conditions. The dissociation constant in water provides the amount of the dissociated and undissociated forms of an acid, base, or organic salt in water. Knowledge of the dissociation constant is required to assess the importance of the other physical-chemical properties used in the hazard assessment. As the percentage of ionization increases, the water solubility increases while the vapor pressure, Henry's Law constant, and octanol/water partition coefficient decrease. For acids and bases, the dissociation constant is expressed as the pK_A and pK_B, respectively.

Henry's Law Constant

Henry's Law constant is the ratio of a chemical's concentration in the gas phase to that in the liquid phase (at equilibrium). In environmental assessments, the Henry's Law constant is typically measured in water at 25°C. The Henry's Law constant provides an indication of a chemical's volatility from water, which can be used to derive partitioning within environmental compartments and the amount of material removed by stripping in a sewage treatment plant. Henry's Law constant values less than 1×10^{-7} atm-m^3/mole indicate slow volatilization from water to air (the Henry's Law constant for the volatilization of water from water is 1×10^{-7} atm-m^3/mole) and values more than 1×10^{-3} atm-m^3/mole indicate rapid volatilization from water to air. To aid in determining the importance of volatilization, the assessment uses two models based on the Henry's Law constant. These models determine the half-life for volatilization from a model river and a model lake. A maximum value of 1×10^{-8} atm-m^3/mole for the Henry's Law constant was assigned for chemicals without experimental data or for those that were anticipated by professional judgment to be nonvolatile.

Sediment/Soil Adsorption/Desorption Coefficient (K_{oc})

The soil adsorption coefficient provides a measure of a chemical's ability to adsorb to the organic portion of soil and sediment. This provides an indication of the potential for the chemical to leach through soil and be introduced into groundwater, which may lead to environmental exposures to wildlife or humans through the ingestion of drinking water drawn from underground sources. Chemicals with high soil adsorption coefficients are expected to be

strongly adsorbed to soil and are unlikely to leach into ground water. The soil adsorption coefficient also describes the potential for a chemical to partition from environmental waters to suspended solids and sediment. The higher the $K_{oc,}$ the more strongly a chemical is adsorbed to soil. Strong adsorption may impact other fate processes, such as the rate of biodegradation, by making the chemical less bioavailable.

The soil adsorption coefficient, K_{oc}, is normalized with respect to the organic carbon content of the soil to account for geographic differences. The assignments for the degree that a chemical is adsorbed to soil within the context of the assessment were described qualitatively as very strong (above 30,000), strong (above 3,000), moderate (above 300), low (above 30), and negligible (above 3). When determining the potential for a chemical to adsorb to soil and suspended organic matter, the potential for a chemical to form chemical bonds with humic acids and attach to soil also needs to be considered, although this process is generally limited to a small number of chemical classes.

A maximum value of 30,000 for the K_{oc} was assigned for chemicals without experimental data or for those that were anticipated by professional judgment to be strongly absorbed to soil (U.S. EPA 2005b). A default K_{oc} of 30,000 was used for polymers and other high MW materials with a MW >1,000 daltons.

Reactivity

The potential for a substance to undergo irreversible chemical reactions in the environment can be used in the assessment of persistence. The primary chemical reactions considered in an environmental fate assessment are: hydrolysis, photolysis, and the gas phase reaction with hydroxyl radicals, ozone, or nitrate radicals. The most important reaction considered in the hazard assessment of organic compounds is hydrolysis, or the reaction of a chemical substance with water. Because the rate of hydrolysis reactions can change substantially as a function of pH, studies performed in the pH range typically found in the environment (pH 5–9) were considered. The second reaction considered in the assessment is photolysis, the reaction of a chemical with sunlight. Both hydrolysis and photolysis occur in air, water, and soil, while only hydrolysis was considered in sediment. The half-lives for reactive processes, if faster than removal via biodegradation, were used to assign the hazard designation by direct comparison to the DfE persistence criteria.

For the atmospheric compartment, persistence also includes the evaluation of oxidative gas-phase processes. These processes include the reaction with ozone, hydroxyl radicals, and nitrate radicals. Since the average concentration of these oxidative species in the atmosphere has been measured, the experimental or estimated rate constants were converted to, and reported as, a half-life in the assessment using standard pseudo first-order kinetics (U.S. EPA 2011f; U.S. EPA 2011d).

For inorganic compounds, an additional chemical process was considered, the potential to be reduced or oxidized (undergo a redox reaction) under environmental conditions. Redox reactions change the oxidation state of the species through the transfer of electrons to form another compound (such as the reduction of Cr(VI) to Cr(III)). A change in the oxidation state of a metal

or inorganic species can result in significant changes in the material's hazard designation. In this example, going from Cr(VI) to Cr(III) makes the compound less toxic.

Environmental Transport

The persistence of a chemical substance is based on determining the importance of removal processes that may occur once a chemical enters the environment. Chemicals with a half-life of less than 60 days are expected to be at most a Moderate hazard designation for persistence. Persistence does not directly address the pathways in which a chemical substance might enter the environment (e.g., volatilization or disposal in a landfill) and focuses instead on the removal processes that are expected to occur once it is released into air, water, soil, or sediment. Similarly, the persistence assessment does not address what might happen to a chemical substance throughout its life cycle, such as disposal during incineration of consumer or commercial products. Understanding the environmental transport of a chemical substance can help identify processes relevant to environmental assessment. For example, if a chemical is toxic to benthic organisms and partitions primarily to sediment, its potential release to water should be carefully considered in the selection of alternatives.

Biodegradation

In the absence of rapid hydrolysis or other chemical reactions, biodegradation is typically the primary environmental degradation process for organic compounds. Determining the importance of biodegradation is, therefore, an important component of the assessment. Biodegradation processes are divided into two types. The first is primary biodegradation, in which a chemical substance is converted to another substance. The second is ultimate biodegradation, in which a chemical is completely mineralized to small building-block components (e.g., CO_2 and water). DfE persistence criteria use data that are reported as percent of theoretical ultimate degradation in the guideline Ready Biodegradability test or as a half-life in other experimental studies; both of these measurements can be compared directly to the DfE criteria in 5.1.2. When considering primary degradation, the assessment process includes an evaluation of the potential for the formation of metabolites that were more persistent than the parent materials. Chemical substances that undergo rapid primary degradation but only slow ultimate biodegradation were considered to have stable metabolites. In the absence of measured data on the substance of interest, DfE evaluated the potential for biodegradation for chemicals with a MW <1,000 daltons using the EPA EPISuite™ models. EPISuite™ estimates the probability for ready biodegradation as well as the potential for primary and ultimate removal, as described in Section 5.3. A default Very High persistence hazard designation was assigned for polymers and other high MW materials with a MW >1,000 daltons, according to information contained in the literature concerning polymer assessment (Boethling and Nabholz 1997).

5.4 Evaluating Human Health Endpoints

After data collection and analysis of the physical-chemical properties for the chemicals being assessed, the comparison of the data against the hazard criteria can begin. Section 5.4.1 discusses how measured data are used to make hazard designations for human health endpoints and Section 5.4.2 presents the approach for filling in data gaps to make these hazard designations.

5.4.1 Endpoints Characterized and Evaluated Against Criteria Based on Measured Data

This section provides a short description of how measured data were used to designate the level of hazard for each endpoint. As a reminder, the criteria for the hazard designations are in Table 5-2.

For acute mammalian toxicity the median lethal doses or concentrations were used to assign the hazard designation. Four levels of hazard designation have been defined ranging from Low to Very High.

For cancer, the hazard designation was contingent on the level of evidence for increased incidence of cancer, and not potency. The definitions applied in DfE criteria are based on International Agency for Research on Cancer (IARC) levels of evidence (International Agency for Research on Cancer 2006). For example, a designation of Very High concern requires that the substance be characterized as a "known or presumed human carcinogen," whereas a designation of Low concern requires either negative studies or robust SAR conclusions. A designation of Moderate was applied as a default value when there was an absence of data suggesting High carcinogenicity, and an absence of data supporting Low carcinogenicity (i.e., a lack of negative studies or weak SAR conclusions).

Similarly, the hazard designation for mutagenicity/genotoxicity was also based on the level of evidence rather than potency. Complete data requirements for this endpoint were both gene mutation and chromosomal aberration assays. For instances of incomplete or inadequate mutagenicity/genotoxicity data, a Low hazard designation cannot be given.

For chronic endpoints, such as reproductive, developmental, neurological, and repeated dose toxicity, the hazard designation was based on potency. The evaluation considers both lowest observed adverse effect levels (LOAELs) and identification of no observed adverse effect levels (NOAELs), when available. The LOAEL and the NOAEL are experimental dose levels, and their reliability is dictated by the study design. In studies for which the lowest dose tested resulted in an adverse effect (and therefore a NOAEL was not established), and in studies for which the highest dose tested was a NOAEL, a conservative approach using professional judgment was used to address uncertainty regarding the lowest dose or exposure level that might be expected to cause a particular adverse effect. For example, in the absence of an established a NOAEL, an identified LOAEL might fall within the range of a Moderate hazard; however, it is uncertain if a lower dose, such as one that falls within the range of High hazard exists because no lower doses were tested. In such cases, professional judgment was applied to assign a hazard designation, when possible. Some degree of uncertainty was evident in results from studies in which a NOAEL may fall within one hazard range (e.g., Moderate hazard) and the identified LOAEL falls within a different hazard range (e.g., Low hazard) because the true LOAEL may fall in either category, but there were not enough experimental data points to determine the true LOAEL. Professional judgment was also applied to these cases to assign a hazard descriptor, when possible, and the rationale used was described in the assessment. Developmental neurotoxicity was considered, and was evaluated using the developmental toxicity criteria, which are more stringent than the criteria for neurotoxicity and thus designed to be more protective (U.S. EPA 2011b).

The criteria for skin and respiratory sensitization, which are immune-based responses, consider the frequency and potency of the reactions. For skin sensitization, categories were based on the weight of evidence[6] from traditional animal bioassays, but *in vitro* alternative studies were also considered. At this time, there are no standard test methods for respiratory sensitization; as a result, there was often no designation for this endpoint.

The evaluation of skin and eye irritation and corrosivity were based on the time to recovery.

5.4.2 SAR – Application of SAR and Expert Judgment to Endpoint Criteria

If measured data pertaining to human health criteria were not available, potential adverse effects were estimated with SAR analysis. To make these estimates, DfE relied on the expertise of scientists in EPA's New Chemicals Program (NCP) who have reviewed thousands of chemicals and associated data using these methods. SAR uses the molecular structure of a chemical to infer a physicochemical property that can be related to specific effects on human health. These correlations may be qualitative ("simple SAR") or quantitative (QSAR). Information on EPA's use of SAR analysis has been published by U.S. EPA (1994). Public access to free validated quantitative SAR models for human health endpoints is far more limited than physical-chemical properties, environmental fate parameters, or ecotoxicology. Carcinogenicity was assessed using the OncoLogic expert system that provides a qualitative result directly applicable to the DfE criteria. For other endpoints that required SAR approaches, an analog approach using expert judgment was used as discussed in Section 5.2. All estimates obtained in this project were reviewed by EPA scientists having subject matter expertise. Estimates for the other human health endpoints were based on expert judgment using an analog approach, and not through the use of computerized SAR methodologies.

Carcinogenicity

The potential for a chemical to cause cancer in humans was estimated using the OncoLogic expert system. This program uses a decision tree based on the known carcinogenicity of chemicals with similar chemical structures, information on mechanisms of action, short-term predictive tests, epidemiological studies, and expert judgment.

Polymer Assessment

Estimates for polymers were obtained using information contained in the literature concerning polymer assessment based on the MW profile (Boethling and Nabholz 1997). Those polymers with MW >1,000 were assessed using an appropriate representative structure that has a MW less than or equal to the average MW. For polymers with an average MW >1,000 daltons and a significant amount of low MW material <1,000 daltons, the low MW components were also assessed for their environmental fate and potential toxicity in order to identify any possible hazards for the most bioavailable fraction. Similarly, the presence of unreacted monomers requires that the assessment consider these components for polymers of any MW range. The

[6] Generally, weight of evidence is defined as the process for characterizing the extent to which the available data support a hypothesis that an agent causes a particular effect (U.S. EPA 1999; U.S. EPA 2002; U.S. EPA 2005b).

properties for polymers with an average MW >1,000 with no low MW components were generally evaluated as a single high MW material for each of the properties described below. In general, polymers with an average MW >1,000 were not amenable to the available SAR estimation methods, and based on the SF guidance are assumed to have low to no bioavailability. Polymers with MW >1,000 that were not degradable or reactive are also typically not bioavailable. Polymers with an average MW >10,000 have potential for adverse effects due to lung overloading when respirable particles are present (less than ten microns). There may be exceptions to the rules of thumb outlined above, and as such this guidance should not be held as absolute thresholds.

Polymers and oligomers with MWs <1,000 were assessed using a representative structure for all the MW species anticipated to be present in the mixture. The procedures were essentially identical to those employed for the evaluation of impurities or byproducts in discrete chemicals, although in this case the oligomer with the highest concern was used to drive the hazard designation. Unreacted monomers, if present, were also assessed and considered in the hazard evaluation.

5.5 Evaluating Environmental Toxicity and Fate Endpoints

As with endpoints previously mentioned, the preferred method for the evaluation of environmental endpoints is the use of experimental data. In their absence, the alternatives assessment uses computerized QSAR models developed by EPA for the evaluation of environmental endpoints that can be directly compared to the DfE criteria. When measured data were unavailable, the hazard designation for aquatic toxicity was estimated using EPA's ECOSAR™ software, and the persistence designation was estimated using models in EPA's EPISuite™ software. As a direct result of the design of these models and their direct application to DfE criteria, the evaluation of environmental endpoints using experimental or estimated data was discussed together in the following subsections.

5.5.1 Aquatic Toxicity

For environmental toxicity, the alternatives assessment focused on the hazard designations for acute and chronic studies on freshwater species of algae, invertebrates, and fish, (often referred to as the "three surrogate species"). Aquatic toxicity values were reported in the assessment as follows:

- Acute (estimated or experimental) - LC_{50} in mg/L
- Chronic (experimental) - No observed effect concentration (NOEC) in mg/L
- Chronic (estimated) - ChV, or the geometric mean between the NOEC and the LOEC, in mg/L

Experimental data reported in the alternatives assessment also included information on the species tested. Test data on other organisms (e.g., worms) were included in the assessment if data were readily available. These data would be evaluated using professional judgment to support hazard designations assigned using the three surrogate species; however, they were not used by themselves to assign a hazard designation, as DfE criteria are not available. Poorly soluble

substances for which the water column exposures may not be adequate to describe sediment and particulate exposures will be identified by a footnote.

If an experimental or estimated effect level exceeded the known water solubility of a chemical substance, or if the log K_{ow} exceeded the estimated ECOSAR™ cut-off values for acute and chronic endpoints (which are class specific), NES were predicted for the aquatic toxicity endpoints. NES indicates that at the highest concentration achievable, the limit of a chemical's water solubility, no adverse effects were observed (or would be expected). In these cases, a Low hazard designation was assigned. In the cases where both an estimated water solubility and ECOSAR™ estimate were used, then an additional factor of ten was applied to the water solubility before a NES designation was assigned, to account for the combined uncertainty in the model estimates.

In the case where an experimental aquatic toxicity value was significantly higher than the chemical's water solubility, it was likely the result of a poorly conducted study. In this circumstance, which is generally more frequent for formulated products or mixtures, additional details were provided in the Data Quality section to describe why the reported values could not be used to assign a hazard designation.

EPA's ECOSAR™ estimation program uses chemical structure to estimate toxicity of a chemical substance using class-specific QSARs. ECOSAR™ automatically determines all of the classes that a chemical substance may belong to and, therefore, may provide a number of different ecotoxicity estimates for some or all of the species and durations estimated. Modeled results are dependent on the functional groups present on the molecule, as well as the diversity of chemicals with experimental data that were used to build the models. However, if the chemical substance is not anticipated to lie within the domain of the class-specific estimates provided by ECOSAR, or to undergo the same mode of action of the chemicals that appear in their training sets, then the narcosis (baseline toxicity) associated with the neutral organic class will be used. Experimental log K_{ow} values were used preferentially as input into ECOSAR™. In their absence, estimated log K_{ow} values from EPISuite™ were used. ECOSAR™ is maintained and developed as a stand-alone program, but is also accessible through the EPA EPISuite™ program after it is installed; therefore, the Estimations Program Interface (EPI) program was cited for the ECOSAR™ values in this report.

The QSARs for ECOSAR™ were built using experimental data for several chemical classes. For a chemical class to be defined within ECOSAR™, sufficient acute experimental data were required to build a QSAR for all three species included in the model. The equations in ECOSAR are derived from surrogate species of fish, zooplankton, and phytoplankton. While these surrogate species can comprise several genera as well as families, the equations are not intended to be species-specific, but rather estimates of toxicity to the general trophic levels they represent (fish, aquatic invertebrates, and aquatic plants). There were instances, however, where sufficient experimental data were not available to build a chronic QSAR for some of the three surrogate species. When ECOSAR™ did not provide chronic estimates, the acute value (experimental or estimated) was divided by an acute to chronic ratio (ACR) to arrive at the ChV. ACRs of 10 were used for fish and daphnid, and an ACR of 4 was used for algae (Mayo-Bean, Nabholz et al. 2011).

For phosphate esters and phosphonate esters in this report, alternative predictive methodologies such as data derived acute-to-chronic ratios (ACRs) and read across to analogous substances were reported to address data gaps, using a weight of evidence approach instead of ECOSAR predictions. Many of the chemicals and chemical mixture components in this assessment are phosphate or phosphonate esters, including Diethyl bis(2-hydroxyethyl)aminomethyl-phosphonate, Emerald Innovation™ NH-1, Fyrol™ HF-5, Isopropylated triphenyl phosphate, Oligomeric ethyl ethylene phosphate, Oligomeric phosphonate polyol, Phosphoric acid, P,P'-[2,2-bis(chloromethyl)-1,3-propanediyl] P,P,P',P'-tetrakis(2-chloroethyl) ester, Tricresyl phosphate, Triphenyl phosphate, Tris (1,3-dichloro-2-propyl) phosphate, Tris (2-chloro-1-methylethyl) phosphate, Tris (2-chloroethyl) phosphate, and Tris (p-t-butylphenyl) phosphate. ECOSAR v1.11 provides estimates for these compounds based on the esters, esters (phosphate), and neutral organic classes. These compounds are not well represented by ECOSAR v1.11 esters (phosphate) QSAR, which is based on underlying Log K_{ow} methodology that does not adequately distinguish weak-to-strong esterase inhibition, resulting in low correlation of the class members. Additionally, certain modes of action have been previously associated with phosphate ester chemicals (i.e., potential for esterase inhibition and alkylation); therefore, the ECOSAR v1.11 esters and neutral organics QSARs are also not well representative of these chemicals. The ECOSAR v1.11 esters estimated values are reported in the assessment for comparative purposes.

An estimate of NES is the default value used for organics, oligomers, or non-ionic polymers with a MW >1,000 daltons in the assignment of aquatic toxicity hazard. In EPA's New Chemical program, aquatic toxicity is not predicted for chemicals with a MW >1,000 daltons, as uptake has been found to decrease exponentially with MWs >600 daltons (Nabholz, Clements et al. 1993), due to a decrease in passive absorption through respiratory membranes (Mayo-Bean, Nabholz et al. 2011). This methodology was also used in the evaluation of expandable graphite, a large, insoluble material with a MW >1,000 daltons.

5.5.2 Bioaccumulation

Bioaccumulation is a process in which a chemical substance is absorbed in an organism by all routes of exposure as occurs in the natural environment (e.g., from dietary and ambient environment sources). Bioaccumulation is the net result of the competing processes; this includes uptake, metabolism, and elimination of a chemical in an organism. Bioaccumulation can be evaluated using the BAF, the steady state ratio of a chemical in an organism relative to its concentration in the ambient environment, where the organism is exposed through ingestion and direct contact. Experimental BAFs have not been widely available in the scientific literature and, as a result, experimental BCFs are more commonly used to evaluate the bioaccumulation hazard. BCFs are defined as the ratio of the concentration of a chemical in an organism to the concentration of the chemical in the organism's surroundings; BCFs are typically measured for fish (in water) using guideline studies.

Experimental BAF or BCF values can be compared directly to the DfE criteria for this endpoint to assign a hazard designation. The BCF/BAF designations range from <100 for a Low designation to >5,000 for a Very High designation (see Section 5.1.2). If experimental values were available for both of these endpoints, and the BCF and BAF were >100 (i.e., above the Low designation), the largest factor was used to assign hazard designation. If experimental BCFs

<100 were available, the estimated upper trophic BAF from EPISuite™ was used preferentially if its use resulted in a more conservative hazard designation, and if the potential for metabolism was accurately accounted for within the model estimates.

In the absence of experimental data, evaluation of bioaccumulation potential can be done using the log K_{ow} and the log octanol/air partition coefficient $K_{oa,}$ as estimated by EPISuite™. However, analysis using K_{oa} requires the use of metabolism data for higher trophic, air breathing organisms, which can be difficult to obtain from the scientific literature and cannot be readily estimated. BAFs and BCFs from EPISuite™ were, therefore, typically used for the bioaccumulation hazard designation when experimental data were lacking. These values can be compared directly to DfE criteria, and the most conservative result was used for the hazard designation. For chemicals that had estimated bioaccumulation data, available experimental monitoring data were used to provide insight into the reliability of the model results. For example, an estimated Low bioaccumulation potential may be increased to a Moderate designation if a chemical was routinely identified in samples from higher trophic levels, or a High designation if the chemical was routinely measured in animals at the top of the food chain.

An estimate of Low is the default value used for discrete organics with a MW >1,000 daltons in the assignment of bioaccumulation hazard. This assignment is consistent with an analysis of the chemicals used in the development of the bioconcentration and bioaccumulation estimation programs in the EPISuite™ software (U.S. EPA 2011g). The training sets for these models included 527 and 421 chemicals, respectively, with a MW range 68-992 daltons (959 daltons for BAF). Given that BCF and BAF reach a maximum and then decrease with increasing log K_{ow}, a default value of Low is, in general, consistent with the limited bioavailability expected for materials with a MW >1,000 daltons. DfE uses all available well-conducted studies when evaluating bioaccumulation potential for materials with a MW >1,000, including environmental biomonitoring data on higher trophic levels.

In general, for polymers and other materials with a MW >1,000 daltons, the default bioaccumulation designation of Low was assigned, arising from their predicted limited bioavailability (Boethling and Nabholz 1997). A more detailed analysis was performed for compounds at or near this bright line cutoff, as well as for polymers with components where residuals <1,000 had the potential to be present.

5.5.3 Environmental Persistence

A chemical's persistence in the environment is evaluated by determining the type and rate of potential removal processes. These removal processes were generally divided into two categories: chemical and biological. Of the chemical degradation processes, an evaluation of environmental persistence includes the reaction of a chemical with water, also known as hydrolysis, because water is ubiquitous in the environment. Hydrolysis rate constants can be obtained from the literature or estimated, and the resulting half-lives can be compared directly to DfE criteria. For commercial chemicals, hydrolysis tends to be a slower environmental removal process than biodegradation. Direct and indirect photolysis also represents other potential chemical degradation processes that are considered in the alternative assessment, and they are discussed later in this section.

Biodegradation, the most prevalent biological removal process, was divided into two types. The first is primary biodegradation, in which a chemical substance is converted to another substance through a single transformation. The second is ultimate biodegradation, in which a chemical is completely degraded to CO_2, water, and mineral oxides (such as phosphates for chemicals containing phosphorus). DfE criteria utilize ultimate biodegradation preferentially for the persistence hazard designation, although primary removal rates were informative in assigning hazard designations, particularly for materials that were transformed slowly, and to a lesser extent for those that are transformed rapidly.

If ultimate biodegradation data were not available, primary removal data were used in some cases. For primary removal processes, the potential for the formation of degradation products that are more persistent than the parent compounds must be considered in the hazard designation. When present, the persistent degradation products should be evaluated for fate and toxicity. Half-life data on the persistent degradation products, if available, were used to determine the assignment for the persistence designation. In the absence of persistent degradation products, primary biodegradation half-life data were compared directly to the DfE criteria to assign a hazard designation.

Biodegradation processes can be classified as either aerobic or anaerobic. Aerobic biodegradation is an oxidative process that occurs in the presence of oxygen. Anaerobic biodegradation is a reductive process that occurs only in the absence of oxygen. Aerobic biodegradation is typically assessed for soil and water, while anaerobic biodegradation is generally assessed in sediment. For determining the persistence hazard, the importance of both aerobic and anaerobic biodegradation, as well as partitioning and transport in the environment, were considered to determine what removal processes were most likely to occur. Anaerobic degradation may use any of several electron acceptors, depending on their availability in a given environment and the prevailing redox potential (E_h). The biodegradative populations that are dominant in a given environment vary with the conditions, and so do their biodegradative capabilities.

One aspect of the assessment is to determine the potential for removal of a chemical substance, and especially removal attributable to biodegradation within a sewage treatment plant and other environments. In this assessment, the term “ready biodegradability” refers to a chemical’s potential to undergo ultimate degradation in guideline laboratory studies. A positive result in a test for ready biodegradability can be considered as indicative of rapid and ultimate degradation in most environments, including biological sewage treatment plants. Ready tests typically include a 10-day window, beginning when the biodegradation parameter (e.g., disappearance of dissolved organic carbon from test substance, or theoretical oxygen demand) reaches 10%. The 10-day window must occur within the 28-day length of the test. If the pass level of the test (60% for oxygen demand and CO2 production; 70% for dissolved organic carbon disappearance) is met in the 10-day window, the chemical received a Very Low hazard designation. Those that did not pass the 10-day window criterion but met the pass level in 28 days received a Low hazard designation. If ready biodegradability test data were available but the chemical did not meet the pass level, the chemical was evaluated based on measured data using the DfE half-life criteria (Table 5-2). These half-life criteria were also used to assign a hazard designation for non-guideline ultimate biodegradation studies reported in the scientific literature.

In the absence of a reported half-life, experimental data were also used to approximate half-life, as appropriate. For example, a chemical that undergoes <5% removal in 30 days would be expected to have a half-life >60 days, and would be assigned a High persistence concern.

When experimental data on the biodegradation of a chemical substance were not available, the potential of that substance to undergo this removal process was assessed from the results of the EPISuite™ models. These models fall into one of four classes: rapid biodegradation models based on linear and non-linear regressions that estimate the probability that a chemical substance will degrade fast; expert survey models that estimated the rate of ultimate and primary biodegradation using semi-quantitative methods; probability of ready biodegradability in the OECD 301C test; and probability of rapid biodegradation under methanogenic anaerobic conditions. Each of these is discussed in the following paragraphs.

The first models (Biowin 5 and 6) used in the screening assessment estimated ready biodegradability in the OECD 301C test, and are also known as Japanese Ministry of International Trade and Industry (MITI) models. These models provided the probability that a material passes this standardized test. Those chemicals that were estimated to pass the ready biodegradability test received a Low persistence designation. If a chemical was not estimated to pass the MITI test, the results of the other EPISuite™ biodegradation models were used.

The rapid biodegradation potential models within EPISuite™ (Biowin 1 and 2) were useful for determining if a chemical substance was expected to biodegrade quickly in the environment. If a chemical was likely to biodegrade quickly, it was generally assigned a Low hazard designation for persistence. The results of the estimates from these models may be used in concert with the semi-quantitative output from a second set of models, which include ultimate and primary biodegradation survey models (Biowin 3 and 4) for evaluating persistence. These models provide a numeric result, ranging from 1 to 5, which relates to the amount of time required for complete ultimate degradation (Biowin 3) and removal of the parent substance by primary degradation (Biowin 4) of the test compound. The numeric result from Biowin 3 is converted to an estimated half-life for removal that can be compared directly to DfE criteria. If results from different models (other than the MITI models) led to a different hazard designation, then the ultimate biodegradation model results were used preferentially. If the transport properties indicate the potential for the material to partition to sediment, an anoxic compartment, then the results of the anaerobic probability model (Biowin 7) are also evaluated.

Half-lives for hydrolysis from experimental studies or EPISuite™ estimates were used in preference to biodegradation data when they suggested that hydrolysis is a more rapid removal process. Hydrolysis half-lives were compared directly to DfE criteria to assign the persistence designation. Similar to primary biodegradation, breakdown products resulting from hydrolysis were evaluated for fate and toxicity when they were expected to be more persistent than the parent compound.

Photolysis may also be an important environmental removal process. In general, environmental removal rates from photolysis do not compete with biodegradation or hydrolysis, although there are exceptions, such as iodides. Photolysis may be an important removal process for chemicals

that were not bioavailable because of their limited water solubility. Estimation methods for photolysis rates were not available using computerized SAR tools. If experimental or suitable analog data were available, the rate of photolysis was evaluated relative to other removal processes.

When evaluating the environmental persistence designation, it should be noted that chemicals with a High or Very High designation can degrade over time, although this process may occur at a very slow rate. As a result, a Very High designation may have been assigned if persistent degradates were expected to be produced, even at a very slow rate, in the absence of experimental biodegradation data for the parent substance.

Chemicals that contain a metal are assigned a High persistence designation in DfE alternatives assessments, as these inorganic moieties are recalcitrant. In this instance, an 'R' footnote is added to the hazard summary table to indicate that the persistence potential was based on the presence of a recalcitrant inorganic moiety. The assessment process also includes the evaluation of the potential chemical reactions of metal-containing and inorganic moieties to determine if they were potentially transformed to more or less hazardous forms. However, no alternatives that contain metals were evaluated in this updated assessment.

Polymers with a MW >1,000 generally received a Very High persistence designation due to their lack of bioavailability.

5.6 Endocrine Activity

Chemicals included in DfE alternatives assessments are screened for potential endocrine activity, consistent with the DfE Alternatives Assessment Criteria. **Endocrine activity** refers to a change in endocrine homeostasis caused by a chemical or other stressor. An **endocrine disruptor** is an external agent that interferes in some way with the role of natural hormones in the body, in a manner causing adverse effects. Relevant data are summarized in the hazard assessments for each chemical, located in Section 7. Data on endocrine activity were available for twelve of the chemicals included in this report. For chemicals without available data on endocrine activity, this was acknowledged with a "no data located" statement. When endocrine activity data were available, the data are summarized as a narrative. A unique hazard designation of Low, Moderate or High is not provided for this endpoint in Table 5-2, for reasons discussed below.

The document *Special Report on Environmental Endocrine Disruption: An Effects Assessment and Analysis* describes EPA's activities regarding the evaluation of endocrine disruption (U.S. EPA 1997). This report was requested by the Science Policy Council and prepared by EPA's Risk Assessment Forum. This report states that "Based on the current state of the science, the Agency does not consider endocrine disruption to be an adverse endpoint per se, but rather to be a mode or mechanism of action potentially leading to other outcomes, for example, carcinogenic, reproductive or developmental effects, routinely considered in reaching regulatory decisions" (U.S. EPA 1997). The report also states that "Evidence of endocrine disruption alone can influence priority setting for further testing and the assessment of results of this testing could lead to regulatory action if adverse effects are shown to occur" (U.S. EPA 1997).

The 1996 Food Quality Protection Act (FQPA) directed EPA to develop a scientifically validated screening program to determine whether certain substances may cause hormonal effects in humans. In response, EPA established the Endocrine Disruptor Screening Program (EDSP) (U.S. EPA 2012b). The EDSP is developing requirements for the screening and testing of thousands of chemicals for their potential to affect the endocrine system. When complete, EPA will use these screening and testing approaches to set priorities and conduct further testing, when warranted. The science related to measuring and demonstrating endocrine disruption is relatively new, and validated testing methods at EPA are still being developed.

The EDSP proposes a two-tiered approach that includes initial screening followed by more in-depth testing, when warranted (U.S. EPA 2011a). The Tier 1 screening battery is intended to identify chemicals with the potential to interact with the estrogen, androgen, or thyroid hormone systems through any of several recognized modes of action. Positive findings for Tier 1 tests identify the potential for an interaction with endocrine systems, but do not fully characterize the nature of possible effects in whole animals. Tier 2 testing is intended to confirm, characterize, and quantify the effects for chemicals that interact with estrogen, androgen, and thyroid hormone systems. These test methods must undergo a four-stage validation process (protocol development, optimization/prevalidation, validation, and peer-review) prior to regulatory acceptance and implementation. Validation is ongoing for Tier 1 and Tier 2 methods[7]. Once validated test methods have been established for screening and testing of potential endocrine disruptors, guidance must be developed for interpretation of these test results using an overall weight-of-evidence characterization.

To assess the data on endocrine activity, DfE applies the weight of evidence approach developed by the EDSP (U.S. EPA 2011c). This process integrates and evaluates data, and always relies on professional judgment (U.S. EPA 2011c). To evaluate endocrine activity with this weight of evidence approach, DfE examined multiple lines of evidence (when available) and considered the nature of the effects within and across studies, including number, type, and severity/magnitude of effects, conditions under which effects occurred (e.g., dose, route, duration), consistency, pattern, range, and interrelationships of effects observed within and among studies, species, strains, and sexes, strengths and limitations of the *in vitro* and *in vivo* information, and biological plausibility of the potential for an interaction with the endocrine, androgen, or thyroid hormonal pathways.

Most test data for chemicals in this report consist of *in vitro* assays, but results of *in vitro* assays alone were not generally expected to provide a sufficient basis to support a hazard designation for endocrine disruption. EPA expects that *in vivo* evidence would typically be given greater overall influence in the weight of evidence evaluation than *in vitro* findings, because of the inherent limitations of such assays. Although *in vitro* assays can provide insight into the mode of action, they have limited ability to account for normal metabolic activation and clearance of the compound, as well as normal intact physiological conditions (e.g., the ability of an animal to compensate for endocrine alterations).

[7] Information on the status of assay development and validation efforts for each assay in EPA's EDSP can be found at: http://www.epa.gov/oscpmont/oscpendo/pubs/assayvalidation/status.htm

As described in the DfE Alternatives Assessment Criteria, endocrine activity was summarized in a narrative, rather than by High, Moderate or Low hazard designation. The endocrine activity summaries can be found in the hazard profiles. This is an appropriate approach because there is no consensus on what constitutes high, moderate or low concern for this endpoint. The summary of endocrine activity largely relies on representative studies and expert review summaries.

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7 Hazard Evaluations

Ammonium polyphosphate (APP)

Screening Level Toxicology Hazard Summary

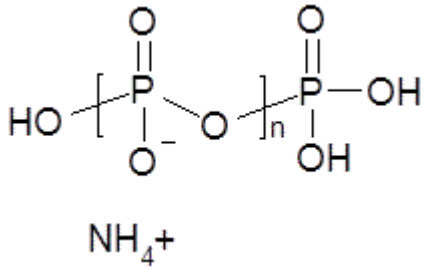
This table contains hazard information for each chemical; evaluation of risk considers both hazard and exposure. Variations in end-of-life processes or degradation and combustion by-products are discussed in the report but not addressed directly in the hazard profiles. The caveats listed below must be taken into account when interpreting the information in the table.

VL = Very Low hazard L = Low hazard M = Moderate hazard H = High hazard VH = Very High hazard – Endpoints in colored text (VL, L, M, H, and VH) were assigned based on empirical data. Endpoints in black italics *(VL, L, M, H,* and *VH*) were assigned using values from estimation software and professional judgment [(Quantitative) Structure Activity Relationships "(Q)SAR"].

[d] This hazard designation would be assigned MODERATE for a potential for lung overloading if >5% of the particles are in the respirable range as a result of dust forming operations.

Chemical	CASRN	Human Health Effects										Aquatic Toxicity**		Environmental Fate	
		Acute Toxicity	Carcinogenicity	Genotoxicity	Reproductive	Developmental	Neurological	Repeated Dose	Skin Sensitization	Respiratory Sensitization	Eye Irritation	Dermal Irritation	Acute	Chronic	Persistence	Bioaccumulation
Ammonium polyphosphate (APP)	68333-79-9	L	*L*	*L*	*L*	*L*	*L*	*L*[d]	L		VL	L	*L*	*L*	*VH*	*L*

**Aquatic toxicity: EPA/DfE criteria are based in large part upon water column exposures which may not be adequate for poorly soluble substances such as many flame retardants that may partition to sediment and particulates.



CASRN: 68333-79-9

MW: ~100,000

MF: $(NH_4)_k \cdot H_{(n+2-k)}P_nO_{(3n+1)}$ (NAS, 2000)

Physical Forms:
Neat: Solid

Use: Flame retardant

SMILES: This polymer inorganic salt with MW >1,000 and no low MW components is not amenable to SMILES notation.

Synonyms: Polyphosphoric acids, ammonium salts; Ammonium polyphosphate; Ammonium polyphosphates; Polymetaphosphoric acid, ammonium salt, Polyphosphoric acid, ammonium salt APP; APP I; APP II
Trade names: AP 422, AP 462, APP (fireproofing agent), APP 422, Albaplas AP 95, Amgard CL, Amgard MC, Amgard TR, Antiblaze MC, Antiblaze MCM, Budit 3076, Budit 3076DC, Budit 3077, Budit 365, DFP-I, EINECS 269- 789-9, Exolit 462, Exolit 263, Exolit 422, Exolit 442, Exolit 454, Exolit 455, Exolit 462, Exolit 470, Exolit AP 422, Exolit AP 423, Exolit AP 462, FR-Cros 480, FR-Cros 484,Fire-Trol LCG-R, Flameguard PT 8, Hostaflam 423, Hostaflam AP 420, Hostaflam AP 422, Hostaflam AP 462, Hostaflam AP 464, Hostaflam TP-AP 751, Hostaflam TP-AP 752, Novawhite, Phos-Chek P 30, Phos-Chek P 40, Phos-Chek P 60, Poly-N 10-34-0, Poly-N 11-37-0, Sumisafe, Taien A, Taien H

Chemical Considerations: High-MW ammonium polyphosphate (n>50) with a minimum of water-soluble fractions are being used to an increasing extent in flame retardants (Gard, 2005, Schrödter et al., 2005). These insoluble ammonium polyphosphates are long chain, ionic phosphate polymers with the following MF: $(NH_4)_k \cdot H_{(n+2-k)}P_nO_{(3n+1)}$, where n typically can range from 70 (Wanjie International Co., 2007) to >1,000 (PINFA, 2010) and k represents the degree of replacement of hydrogen ions with ammonium ions. MWs can be as high as 100,000 g/mole and oligomers with a MW <1,000 are not expected. The high MW inorganic polymer was assessed as a non-bioavailable material. Prior assessments for similar polyphosphates evaluated the lower, water soluble moieties, which also have application as a flame retardant (Professional judgment; SinoHarvest, 2013).

Polymeric: Yes
Oligomeric: Not applicable

Metabolites, Degradates and Transformation Products: Ammonia; phosphate (Leisewitz et al., 2000)

Analog: None
Endpoint(s) using analog values: Not applicable

Analog Structure: Not applicable

Structural Alerts: Not applicable

Risk Phrases: This substance is not classified in the Annex 1 of Directive 67/548/EEC (ESIS, 2012).

Hazard and Risk Assessments: The Maine Department of Environmental Protection (MDEP) Safer Alternative Assessment for Decabromodiphenyl Ether Flame Retardant in Plastic Pallets includes a GreenScreen Assessment of Ammonium Polyphosphate although these were performed on lower MW materials (MDEP, 2007).

Ammonium polyphosphate CASRN 68333-79-9			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
PHYSICAL/CHEMICAL PROPERTIES			
Melting Point (°C)	Decomposes at > 275°C (Measured)	IUCLID, 2000	Consistent with values reported in other secondary sources.
	Decomposes at 300°C for long chain ammonium polyphosphate (Measured)	OECD-SIDS, 2007	Consistent with values reported in other secondary sources.
	Decomposes at approx. 150°C for short chain ammonium polyphosphate (Measured)	OECD-SIDS, 2007	Reported for the low MW ammonium polyphosphate.
Boiling Point (°C)	>275 decomposition with evolution of ammonia and phosphoric acid (Measured)	Clariant, 2011	Reported in chemical datasheet, consistent with the high melting point expected for this chemical.
Vapor Pressure (mm Hg)	$<10^{-8}$ at 25°C (Estimated)	Professional judgment; Boethling and Nabholz, 1997	Cutoff value for large high MW polymers.
	<0.75 at 20°C reported as < 1 hPa (Measured)	IUCLID, 2000; OECD-SIDS, 2007	Ammonium polyphosphate will have negligible vapor pressure as an inorganic salt. Any measurable vapor pressure is due to decomposition and the release of ammonia gas.
Water Solubility (mg/L)	0.5 % (w/w) at 25°C in 10% suspension (Measured)	Clariant, 2011	Reported in chemical datasheet.
	0.05-0.5% max at 25°C in 10% suspension (Measured)	Wanjie International Co, 2007	Inadequate. This value likely represents a dispersion and is not an indication of the material's true water solubility.
	10,000 (Measured) Reported as approximately 10 g/L at 25°C and at pH 5.5	IUCLID, 2000	This value is not consistent with the other secondary sources; the value is most likely for the low MW ammonium polyphosphate.

Ammonium polyphosphate CASRN 68333-79-9				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		Reported as 100% at 25°C; considered to be miscible. (Measured)	OECD-SIDS, 2007	This value is not consistent with the other secondary sources; it is likely for the low MW ammonium polyphosphate.
Log K_{ow}				No data located; polymers with a MW >1,000 are outside the domain of the available estimation methods.
Flammability (Flash Point)		Not flammable (Measured)	OECD-SIDS, 2007	Reported in chemical datasheet.
Explosivity		Not explosive (Measured)	OECD-SIDS, 2007	Reported in chemical datasheet.
Pyrolysis				No data located.
pH		5.5-7.5 At 25°C in 10% suspension (Measured)	Clariant, 2011	Measured by chemical supplier. Data are likely for the formulated material in water, and would be dependent on the ammonium/polyphosphate ratios.
pK_a				No data located.
HUMAN HEALTH EFFECTS				
Toxicokinetics		**Absorption is not expected for any route of exposure. This inorganic polymer moiety is large with a MW >1,000. Based on professional judgment, it is expected to have limited bioavailability and therefore is not expected to be readily absorbed, distributed or metabolized in the body.**		
Dermal Absorption *in vitro*				No data located.
Absorption, Distribution, Metabolism & Excretion	**Oral, Dermal or Inhaled**	Gastrointestinal absorption of higher polyphosphates following ingestion is probably low; they are most likely hydrolyzed by stomach acids to phosphate and ammonium ions.	NAS, 2000	Limited study details reported in a secondary source.
	Other	No absorption is expected for all routes of exposure if insoluble in water. (Estimated)	Professional judgment	Estimated based on physical/chemical properties and limited bioavailability.

Ammonium polyphosphate CASRN 68333-79-9				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Acute Mammalian Toxicity		**LOW: This polymer is large, with a MW >1,000. It is expected to have limited bioavailability and therefore is of low potential for acute mammalian toxicity. This low hazard designation is also supported by a rat oral LD_{50} of >2,000 mg/kg, a rat dermal LD_{50} of >2,000 mg/kg, and a 4-hour rat LC_{50} of >5.09 mg/L.**		
Acute Lethality	**Oral**	Rat oral LD_{50} >2,000 mg/kg	OECD-SIDS, 2007	Limited study details reported in a secondary source.
		Rat oral LD_{50} = 4,740 mg/kg	IUCLID, 2000; Clariant, 2009	Although limited study details were reported in a secondary source, results indicated that LD_{50} values were greater than the high dosages tested; data for commercial mixture Exolit 422 (purity not specified).
		Rabbit oral LD_{50} >2,000 mg/kg	OECD-SIDS, 2007	Although limited study details were reported in a secondary source, results indicated that LD_{50} values were greater than the high dosages tested.
	Dermal	Rat dermal LD_{50} >5,000 mg/kg	IUCLID, 2000; NAS, 2000; OECD-SIDS, 2007	Although limited study details were reported in a secondary source, results indicated that LD_{50} values were greater than the high dosages tested; data for commercial mixture Exolit 456 (90% ammonium polyphosphate and 10% monoammonium phosphate).
		Rat dermal LD_{50} >2,000 mg/kg	OECD-SIDS, 2007	Although limited study details were reported in a secondary source, results indicated that LD_{50} values were greater than the high dosages tested.
	Inhalation	Rat Inhalation 4-hour LC_{50} >5.09 mg/L (nose-only exposure, aerosol)	NAS, 2000; OECD-SIDS, 2007	Although limited study details were reported in a secondary source, results indicate that LC_{50} values are

Ammonium polyphosphate CASRN 68333-79-9				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
				greater than the highest concentration tested; it is unspecified if the inhaled substance is a vapor/gas or dust/mist/fume.
Carcinogenicity		**LOW: This polymer is large, with a MW >1,000. It is expected to have few to no residual monomers. Additionally, crosslinking, swellability, dispersability, reactive functional groups, inhalation potential, and hindered amine groups are not expected. Therefore, there is low potential for carcinogenicity based on professional judgment. No data located.**		
	OncoLogic Results			No data located.
	Carcinogenicity (Rat and Mouse)			No data located.
	Combined Chronic Toxicity/Carcinogenicity			No data located.
	Other	Limited bioavailability expected; crosslinking swellability, dispersability, reactive functional groups, inhalation potential, and hindered amine groups are not expected. (Estimated)	Professional judgment; Boethling and Nabholz, 1997	Based on cutoff value for large high MW polymers.
Genotoxicity		**LOW: This polymer is large, with a MW >1,000. It is expected to have limited bioavailability and therefore has low potential for genotoxicity.**		
	Gene Mutation *in vitro*	Limited bioavailability expected (Estimated)	Professional judgment; Boethling and Nabholz, 1997	Based on cutoff value for large high MW polymers.
		Negative, Ames assay, *Salmonella Typhimurium* TA98. TA100, TA1535, TA1537, TA1538, and *E. coli* WP2uvrA; with and without metabolic activation	IUCLID, 2000; NAS, 2000	Reported in a secondary source, study details and test conditions were not provided.
	Gene Mutation *in vivo*			No data located.
	Chromosomal Aberrations *in vitro*			No data located.

Ammonium polyphosphate CASRN 68333-79-9				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Chromosomal Aberrations *in vivo*			No data located.
	DNA Damage and Repair			No data located.
	Other			No data located.
Reproductive Effects		**LOW: This polymer is large, with a MW >1,000. It is expected to have limited bioavailability and therefore has low potential for reproductive effects based on professional judgment and the polymer assessment literature. No data located.**		
	Reproduction/Developmental Toxicity Screen			No data located.
	Combined Repeated Dose with Reproduction/ Developmental Toxicity Screen			No data located.
	Reproduction and Fertility Effects			No data located.
	Other	Limited bioavailability expected	Professional judgment; Boethling and Nabholz, 1997	Based on cutoff value for large high MW polymers.
Developmental Effects		**LOW: This polymer is large, with a MW >1,000. It is expected to have limited bioavailability and therefore has low potential for developmental effects based on professional judgment and polymer assessment literature. No data located.**		
	Reproduction/ Developmental Toxicity Screen			No data located.
	Combined Repeated Dose with Reproduction/ Developmental Toxicity Screen			No data located.
	Prenatal Development			No data located.
	Postnatal Development			No data located.
	Prenatal and Postnatal Development			No data located.

Ammonium polyphosphate CASRN 68333-79-9				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Developmental Neurotoxicity			No data located.
	Other	Limited bioavailability expected	Professional judgment; Boethling and Nabholz, 1997	Based on cutoff value for large high MW polymers.
Neurotoxicity		**LOW: This polymer is large, with a MW >1,000. It is expected to have limited bioavailability and therefore has low potential for neurotoxicity based on professional judgment and the polymer assessment literature. No data located.**		
	Neurotoxicity Screening Battery (Adult)			No data located.
	Other	Limited bioavailability expected (Estimated)	Professional judgment; Boethling and Nabholz, 1997	Based on cutoff value for large high MW polymers.
Repeated Dose Effects		**LOW: This polymer is large, with a MW >1,000. It is expected to have limited bioavailability; however, because the MWn is >10,000, there is the possibility of lung overloading if >5% of the particles are in the respirable range as a result of dust forming operations. No experimental data located.**		
		Limited bioavailability expected (Estimated)	Professional judgment; Boethling and Nabholz, 1997	Based on cutoff value for large high MW polymers.
		This polymer MWn is >10,000; There is uncertain potential for lung effects from lung overload if respirable particles are inhaled; Polymers with a MW >10,000 have the potential for irreversible lung damage as a result of lung overloading. (Estimated)	Professional judgment; Boethling and Nabholz, 1997	Based on cutoff value for large high MW polymers.
Skin Sensitization		**LOW: Not a skin sensitizer in guinea pigs.**		
	Skin Sensitization	Not a skin sensitizer, guinea pigs	SafePharm Labs, 1993; NAS, 2000	Reported in chemical data sheet; adequate study details provided.
Respiratory Sensitization		**No data located.**		
	Respiratory Sensitization			No data located.

Ammonium polyphosphate CASRN 68333-79-9				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Eye Irritation		**VERY LOW: Mixtures containing primarily ammonium polyphosphate were not irritating to rabbit eyes.**		
	Eye Irritation	Not irritating, rabbits	OECD-SIDS, 2007	Reported in secondary source; study details and test conditions were not provided; data for commercial mixture (70% ammonium polyphosphate and 30% monoammonium phosphate).
		Not irritating, rabbits	IUCLID, 2000	Reported in a secondary source; study details and test conditions were not provided; data for commercial mixture Exolit 456 (90% ammonium polyphosphate and 10% monoammonium phosphate). Study in accordance with OECD 405 guideline.
Dermal Irritation		**LOW: Mixtures containing primarily ammonium polyphosphate were not irritating to slightly irritating to skin.**		
	Dermal Irritation	Not irritating, rabbits 4-hour occlusion	OECD-SIDS, 2007	Reported in a secondary source; study details and test conditions were not provided; data for commercial mixture (70% ammonium polyphosphate and 30% monoammonium phosphate).
		Slightly irritating, rabbits; 24-hour occlusive patch test	IUCLID, 2000	Reported in a secondary source; study details and test conditions were not provided; data for commercial mixture Exolit 422 (purity not specified).
		Not irritating	IUCLID, 2000	Reported in a secondary source; study details and test conditions were not provided; data for commercial mixture Exolit 456

Ammonium polyphosphate CASRN 68333-79-9				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
				(90% ammonium polyphosphate and 10% monoammonium phosphate). Study in accordance with OECD 404 guideline.
		Not irritating, rabbits. Very slight erythema in 2/3 animals 1-hour after exposure to AMGARD LR4; however, no skin reaction was observed after 24 and 72 hours.	NAS, 2000	Limited study details reported in a secondary source. Study was conducted using AMGARD LR2 (liquid containing test substance, urea and water) and AMGARD L4 (powder).
		Not irritating, rabbits exposed 5 times (23 hours for each exposure) to fabric treated with LR2	NAS, 2000	Limited study details reported in a secondary source. Study was conducted using AMGARD LR2 (liquid containing test substance, urea and water).
		Not irritating, human volunteers.	NAS, 2000	Limited study details reported in a secondary source. Study was conducted using AMGARD LR2 (liquid containing test substance, urea and water).
Endocrine Activity		**This polymer is large, with a MW >1,000. It is not expected to have endocrine activity due to its poor bioavailability and inability to be readily metabolized in the body based on professional judgment.**		
		Limited bioavailability expected	Professional judgment; Boethling and Nabholz, 1997	Based on cutoff value for large high MW polymers.
Immunotoxicity		**This polymer is large, with a MW >1,000. It is expected to have limited bioavailability and therefore has low potential for immunotoxicity based on professional judgment and the polymer assessment literature. No data located.**		
	Immune System Effects	Limited bioavailability expected	Professional judgment; Boethling and Nabholz, 1997	Based on cutoff value for large high MW polymers.

Ammonium polyphosphate CASRN 68333-79-9			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
ECOTOXICITY			
ECOSAR Class	Not applicable		
Acute Aquatic Toxicity	**LOW: Water insoluble polymers with a MW >1,000 that do not contain reactive functional groups and are comprised of minimal low MW oligomers are estimated to have no effects at saturation (NES). These polymers have NES because the amount dissolved in water is not anticipated to reach a concentration at which adverse effects may be expressed. Based on professional judgment, guidance for the assessment of aquatic toxicity hazard leads to a low concern for those materials that display NES. Experimental data are also consistent with this hazard designation.**		
Fish LC_{50}	NES (Estimated)	Professional judgment	The large MW, limited bioavailability and low water solubility suggest there will be NES.
	Oncorhynchus mykiss 96-hour LC_{50} >101 mg/L (Experimental)	IUCLID, 2000; OECD-SIDS, 2007	Inadequate; limited study details reported in a secondary source and value is much greater than the anticipated water solubility.
	Danio rerio 96-hour LC_{50} = 100 - 1,000 mg/L (Experimental)	Clariant, 2009	Inadequate; limited study details reported in a secondary source and value is much greater than the anticipated water solubility.
	Brachydanio rerio 96-hour LC_{50} >500 mg/L (Experimental)	IUCLID, 2000	Guideline study red in a secondary source with limited study details; OECD 203. Test substance: Exolit 456 (90% ammonium polyphosphate and 10% of ammonium phosphate).
	Freshwater fish (*Oncorhynchus mykiss*) 96-hour LC_{50} = 123 - 1326 mg/L (Experimental)	EPA, 2013	Limited study details reported in a secondary source.
	Freshwater fish (*Oncorhynchus tshawytscha*) 96-hour LC_{50} = 685-1195 mg/L (Experimental)	Buhl and Hamilton, 1998	Limited study details reported in a secondary source. Study conducted with Fire-Trol LCG-R (composed primarily of liquid ammonium polyphosphate with attapulgite clay,

Ammonium polyphosphate CASRN 68333-79-9			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
			a corrosion inhibitor and iron oxide).
	Freshwater fish (*Oncorhynchus mykiss*) LC_{50} = 872 - > 10,000 mg/L (Experimental)	Gaikowski et al., 1996	Limited study details reported in a secondary source. Study conducted with Fire-Trol LCG-R (composed primarily of liquid ammonium polyphosphate with attapulgite clay, a corrosion inhibitor and iron oxide).
	Freshwater fish (*Oncorhynchus mykiss*) 96-hour LC_{50} = 1,006 – 10,000 mg/L (Experimental)	EPA, 2013	Limited study details reported in a secondary source.
	Freshwater fish (*Pimephales promelas*) 96-hour LC_{50} = 519-1080 mg/L (Experimental)	EPA, 2013	Limited study details reported in a secondary source.
Daphnid LC_{50}	*Hyalella azteca* 96-hour LC_{50} = 73 mg/L (Experimental)	McDonald et al., 1997	Limited study details reported in a secondary source. Study conducted with Fire-Trol LCG-R (composed primarily of liquid ammonium polyphosphate with attapulgite clay, a corrosion inhibitor and iron oxide).
	Daphnia magna 48-hour EC_{50} = 90.89 mg/L (Experimental)	EPA, 2013	Limited study details provided in a secondary source.
	Daphnia magna 48-hour EC_{50} = 848 – 1,036 mg/L (Experimental)	EPA, 2013	Limited study details reported in a secondary source.
	Daphnia magna 24-hour EC_{50} = 1,007 mg/L Range = 780 - 1,300 mg/L (Experimental)	EPA, 2013	Limited study details reported in a secondary source.
	NES (Estimated)	Professional judgment	The large MW, limited bioavailability and low water solubility suggest there will be NES.

Ammonium polyphosphate CASRN 68333-79-9				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Green Algae EC_{50}		NES (Estimated)	Professional judgment	The large MW, limited bioavailability and low water solubility suggest there will be NES.
Chronic Aquatic Toxicity		**LOW: Water insoluble polymers with a MW >1,000 that do not contain reactive functional groups and are comprised of minimal low MW oligomers are estimated to have NES. These polymers have NES because the amount dissolved in water is not anticipated to reach a concentration at which adverse effects may be expressed. Based on professional judgment, guidance for the assessment of aquatic toxicity hazard leads to a low potential for those materials that display NES.**		
Fish ChV		NES (Estimated)	Professional judgment	The large MW, limited bioavailability and low water solubility suggest there will be NES.
Daphnid ChV		NES (Estimated)	Professional judgment	The large MW, limited bioavailability and low water solubility suggest there will be NES.
Green Algae ChV		NES (Estimated)	Professional judgment	The large MW, limited bioavailability and low water solubility suggest there will be NES.
ENVIRONMENTAL FATE				
Transport		**The estimated negligible water solubility and estimated negligible vapor pressure indicate that this ionic polymer is anticipated to partition predominantly to soil and sediment. The estimated Henry's Law Constant of $<10^{-8}$ atm-m^3/mole indicates that it is not expected to volatilize from water to the atmosphere. The estimated Koc of >30,000 indicates that it is not anticipated to migrate from soil into groundwater and also has the potential to adsorb to sediment.**		
	Henry's Law Constant (atm-m^3/mole)	$<10^{-8}$ (Estimated)	Professional judgment; Boethling and Nabholz, 1997	Cutoff value for large high MW polymers.
	Sediment/Soil Adsorption/Desorption - K_{oc}	>30,000 (Estimated)	Professional judgment; Boethling and Nabholz, 1997	High MW polymers are expected to adsorb strongly to soil and sediment.
	Level III Fugacity Model			This substance is not amenable to the model.

Ammonium polyphosphate CASRN 68333-79-9				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Persistence		**VERY HIGH: This polymer is large, with a MW >1,000. It is expected to have negligible water solubility and poor bioavailability to microorganisms indicating that biodegradation is not expected to be an important removal process in the environment. Hydrolysis is expected for ammonium polyphosphates, mainly via end-clipping of a monophosphate unit to form monoammonium phosphate. Hydrolysis rates increase with increasing chain lengths, but reach a limit when n>50. Qualitative statements from manufacturers indicate hydrolysis is slow, but increases with prolonged exposure to water and elevated temperatures. Therefore, hydrolysis is not expected to occur at a rate that would greatly reduce the polymeric chain. Furthermore, long-chain ammonium polyphosphates produced for flame retardant applications may be formulated with melamine or other stabilizers that impede hydrolysis. Evaluation of these values suggest that APP polymer size will be reduced by primary degradation but ultimate degradation of the HMW polymer is >180 days.**		
Water	**Aerobic Biodegradation**	Recalcitrant (Estimated)	Professional judgment; Boethling and Nabholz, 1997	Cutoff value for large high MW polymers.
	Volatilization Half-life for Model River	>1 year (Estimated)	Professional judgment	Based on the magnitude of the estimated Henry's Law Constant.
	Volatilization Half-life for Model Lake	>1 year (Estimated)	Professional judgment	Based on the magnitude of the estimated Henry's Law Constant.
Soil	**Aerobic Biodegradation**	The half-life values ranged from 5.2-8.7 days in soil under aerobic conditions for liquid ammonium polyphosphate. Liquid ammonium polyphosphate hydrolyzed faster than solid ammonium polyphosphate and anaerobic conditions, caused by subsequent flooding, accelerated hydrolysis. (Measured)	OECD-SIDS, 2007	Not applicable; this non-guideline study is for the low MW, liquid form of ammonium polyphosphate.
		Ammonium polyphosphate breaks down to ammonia and phosphate rapidly in soil and sewage sludge. (Measured)	Leisewitz et al., 2000	Not applicable; biodegradation data is expected for the more soluble low MW ammonium polyphosphate. Reported in a secondary source.

Ammonium polyphosphate CASRN 68333-79-9				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Anaerobic Biodegradation	Recalcitrant	Professional judgment	The substance has a MW >1,000 and is not anticipated to be assimilated by microbial populations; therefore, biodegradation is not expected.
		Study results: 50%/1.6 days Test method: Field Test The half-life values ranged from 1.6-2.0 days in soil under anaerobic soil conditions for liquid ammonium polyphosphate. Liquid ammonium polyphosphate hydrolyzed faster than solid ammonium polyphosphate and anaerobic conditions, caused by flooding, accelerated hydrolysis. (Measured)	OECD-SIDS, 2007	Not applicable; this nonguideline study is for the liquid form of ammonium polyphosphate.
	Soil Biodegradation with Product Identification			No data located.
	Sediment/Water Biodegradation			No data located.
Air	**Atmospheric Half-life**	Not a significant fate process (Estimated)	Professional judgment	This substance is expected to exist entirely in particulate form in air and is not anticipated to undergo gas-phase chemical reactions.
Reactivity	**Photolysis**	Not a significant fate process (Estimated)	Professional judgment; Mill, 2010	The substance does not contain functional groups that would be expected to absorb light at environmentally significant wavelengths.
	Hydrolysis	Not a significant fate process (Estimated)	Professional judgment; Gard, 2005; Wanjie International Co, 2007; PINFA, 2010; EFRA, 2011	Hydrolysis is expected, mainly via end-clipping of a monophosphate unit to form monoammonium phosphate. Qualitative statements from manufacturers indicate

Ammonium polyphosphate CASRN 68333-79-9				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
				hydrolysis is slow, but increases with prolonged exposure to water and elevated temperatures. Hydrolysis is not expected to occur at a rate that would greatly reduce the polymeric chain to a MW <1,000 g/mole.
		Chemical hydrolysis of polyphosphates proceeds slowly in sterile, neutral solutions at room temperature. Solubility is pH dependent: at pH > 7 the substance will completely hydrolyze to HPO_4^{2-} and at pH 4-7 the substance will completely hydrolyze to $H_2PO_4^-$. (Measured)	OECD-SIDS, 2007	Consistent with values reported in other secondary sources.
Environmental Half-life		>180 days (Estimated)	Professional judgment	The substance has a MW >1,000 and is not anticipated to be assimilated by microorganisms. Therefore, biodegradation is not expected to be an important removal process. It is also not expected to be removed by other degradative processes under environmental conditions because of limited water solubility and limited partitioning to air.
Bioaccumulation		**LOW: This ionic polymer is large, with a MW >1,000. It is expected to have negligible water solubility and poor bioavailability indicating that it will have low potential for bioaccumulation based on professional judgment.**		
	Fish BCF	<100 (Estimated)	Professional judgment	The substance has a MW >1,000 and is not anticipated to be assimilated by aquatic organisms; therefore, bioconcentration is not expected.
	Other BCF			No data located.

Ammonium polyphosphate CASRN 68333-79-9				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	BAF			No data located.
	Metabolism in Fish			No data located.
ENVIRONMENTAL MONITORING AND BIOMONITORING				
Environmental Monitoring		No data located.		
Ecological Biomonitoring		No data located.		
Human Biomonitoring		This chemical was not included in the NHANES biomonitoring report (CDC, 2013).		

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Benzoic acid, 2,3,4,5-tetrabromo-, 2-ethylhexyl ester (TBB)

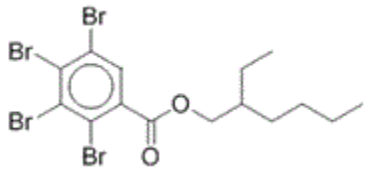
Screening Level Toxicology Hazard Summary

This table contains hazard information for each chemical; evaluation of risk considers both hazard and exposure. Variations in end-of-life processes or degradation and combustion by-products are discussed in the report but not addressed directly in the hazard profiles. The caveats listed below must be taken into account when interpreting the information in the table.

VL = Very Low hazard L = Low hazard M = Moderate hazard H = High hazard VH = Very High hazard – Endpoints in colored text (VL, L, M, H, and VH) were assigned based on empirical data. Endpoints in black italics *(VL, L, M, H,* and *VH*) were assigned using values from estimation software and professional judgment [(Quantitative) Structure Activity Relationships "(Q)SAR"].

Chemical	CASRN	Human Health Effects											Aquatic Toxicity**		Environmental Fate	
		Acute Toxicity	Carcinogenicity	Genotoxicity	Reproductive	Developmental	Neurological	Repeated Dose	Skin Sensitization	Respiratory Sensitization	Eye Irritation	Dermal Irritation	Acute	Chronic	Persistence	Bioaccumulation
Benzoic acid, 2,3,4,5-tetrabromo-, 2-ethylhexyl ester (TBB)	183658-27-7	*L*	*M*	*L*	*M*	*M*	*M*	*M*	*M*		*M*	*L*	*L*	*L*	*H*	*H*

**Aquatic toxicity: EPA/DfE criteria are based in large part upon water column exposures which may not be adequate for poorly soluble substances such as many flame retardants that may partition to sediment and particulates.



	CASRN: 183658-27-7
	MW: 549.9
	MF: $C_{15}H_{18}Br_4O_2$
	Physical Forms: Liquid **Neat:** Liquid
	Use: Flame retardant

SMILES: O=C(c1c(Br)c(Br)c(Br)c(Br)c1)OCC(CCCC)CC

Synonyms: Benzoic acid, 2,3,4,5-tetrabromo-, 2-ethylhexyl ester; TBB; EH-TBB. Related trade names: this chemical is one of the components of the commercial products BZ-54, CN-2065 and Firemaster 550 (FM550).

Chemical Considerations: This is a discrete organic chemical with a MW below 1,000. EPI v4.11 was used to estimate physical/chemical and environmental fate values where adequate experimental data were lacking.

Polymeric: No
Oligomeric: Not applicable

Metabolites, Degradates and Transformation Products: 2,3,4,5-tetrabromobenzoic acid (TBBA CASRN 27581-13-1) (and the corresponding 2-ethylhexanol 104-76-7) by metabolism and hydrolysis (Estimated); 2,3,4,5-tetrabromomethylbenzoate by metabolism di- and tri-brominated analogs by anaerobic biodegradation (Estimated) and photodegradation (Davis and Stapleton, 2009; Bearr et al., 2012; Roberts et al., 2012; Patisaul et al., 2013).

Analog: Confidential analogs **Endpoint(s) using analog values:** Reproductive, developmental, repeated dose effects, carcinogenicity, eye irritation and dermal irritation	**Analog Structure:** Not applicable

Structural Alerts: Polyhalogenated aromatic hydrocarbons, immunotoxicity (EPA, 2012).

Risk Phrases: Not classified by Annex VI Regulation (EC) No 1272/2008 (ESIS, 2012).

Hazard and Risk Assessments: None identified.

Benzoic acid, 2,3,4,5-tetrabromo-, 2-ethylhexyl ester CASRN 183658-27-7			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
PHYSICAL/CHEMICAL PROPERTIES			
Melting Point (°C)			No data located.
Boiling Point (°C)	>300 (Estimated)	EPI v4.11; EPA, 1999	Cutoff value for high boiling point compounds according to HPV assessment guidance.
Vapor Pressure (mm Hg)	$<10^{-8}$ at 25°C (Estimated)	EPI v4.11; EPA, 1999	Cutoff value for nonvolatile compounds according to HPV assessment guidance.
Water Solubility (mg/L)	0.000011 (Estimated)	EPI v4.11; EPA, 1999	Estimated value is less than the cutoff value, <0.001 mg/L, for non-soluble compounds according to HPV assessment guidance.
Log K_{ow}	8.8 (Estimated)	EPI v4.11	
Flammability (Flash Point)	Flash Point: 215°C Performed according to EEC Methods, Directive 92/69/EEC (OJ No. L383A, 29.12.92), Part A, Method A9, flash point (Measured)	Chemtura, 2013	Adequate guideline study.
Explosivity	Not expected to form explosive mixtures with air (Estimated)	Professional judgment	No experimental data located; based on its use as a flame retardant.
Pyrolysis			No data located.
pH	Not applicable (Estimated)	Professional judgment	Does not contain functional groups that are expected to ionize under environmental conditions.
pK_a	Not applicable (Estimated)	Professional judgment	Does not contain functional groups that are expected to ionize under environmental conditions.

Benzoic acid, 2,3,4,5-tetrabromo-, 2-ethylhexyl ester CASRN 183658-27-7				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
HUMAN HEALTH EFFECTS				
Toxicokinetics		**TBB is estimated to have poor absorption by all routes of exposure based on analogy to a structurally similar confidential analog; however, experimental data for Firemaster 550 (a mixture made up of a sum total of TBB and TBPH of 50%) indicate that absorption of TBB can occur in rats following oral exposure from gestation through lactation. TBB was detected in tissues of exposed dams and the pups following exposure to FM550. The primary metabolite of TBB (TBBA) was also detected in dam livers. TBB from a BZ-54 (TBB and TBPH mixture) was shown to be metabolized by hepatic subcellular fractions in fathead minnow, carp, and mouse. The final metabolite is tetrabromobenzoic acid TBBA (27581-13-1). This was confirmed *in vitro* using liver and intestinal subcellular fraction. In all experiments, TBB was consistently metabolized to TBBA via cleavage of the 2-ethylhexyl chain without requiring added cofactors. No phase II metabolites of TBBA were detected. The metabolism of TBB in humans has not been evaluated.**		
Dermal Absorption *in vitro*				No data located.
Absorption, Distribution, Metabolism & Excretion	**Oral, Dermal or Inhaled**	Pregnant rats were administered 0, 0.1 or 1 mg/kg-day of FM550 in the diet across gestation and through lactation (Gestation day (GD) 8 - PND 21) FM550 components including TBPH was detected in adipose, liver, and muscle tissues in Dams at PND 21 with the highest concentration in the adipose tissue (768 ng/g w.w. in high dose, 29.6 ng/g w.w. in low dose, < 7.0 ng/g w.w. in controls). The primary metabolite of TBB (TBBA) was also detected in liver tissue of dams on PND 21. TBB was detected in pooled PND21 pup adipose tissue. TBB was not detected in pooled pup adipose tissue by PND220.	Patisaul et al., 2013	Non guideline study indicates that absorption of this compound can occur in rats through oral exposure; the test substance identified as FM550 is a mixture made up of TBB, TBPH (sum total of TBB and TBPH is approximately 50%), TPP and IPTPP; it is unclear if absorption in pups occurred due to gestational exposure or through lactation.

Benzoic acid, 2,3,4,5-tetrabromo-, 2-ethylhexyl ester CASRN 183658-27-7				
PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
	Other	*In vitro* metabolism experiments with liver and intestinal subcellular fractions following exposure to TBB. TBB was rapidly metabolized to 2,3,4,5-tetrabromobenzoic acid (TBBA) via cleavage of the 2-ethylhexyl chain without requiring added cofactors. The Km and Vmax values for TBB metabolism was estimated to be 11.1 ± 3.9 µM and 0.644 ± 0.144 nmol min-1 mg protein-1, respectively in human microsomes. No phase II metabolites of TBBA were detected. The metabolism of TBB in humans has not been evaluated.	Roberts et al., 2012	Adequate study details reported.
		Metabolism was measured in the fat head minnow, common carp, mouse, and snapping turtle by measuring the loss of the parent compound (TBB and TBPH) in hepatic subcellular fractions Metabolic loss of TBB was observed for all species with the exception of snapping turtles; metabolism rates of TBB were similar between the subcellular fractions in the fathead minnow and carp. There were differences in the rated of metabolism between the subcellular fraction in mice with greater metabolism in microsomal fractions than in cytosolic or S9 fractions. Observed metabolites, including 2,3,4,5-tetrabromomethylbenzoate (TBMB),	Bearr et al., 2012	Test substance identified as Firemaster BZ-54 (TBB and TBPH in approximate 3:1 ratio).

Benzoic acid, 2,3,4,5-tetrabromo-, 2-ethylhexyl ester CASRN 183658-27-7				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		appeared to be derived from TBB. It was concluded by the authors that some species can metabolize TBB and TBPH to form varying metabolites.		
		Estimated to have poor absorption by all routes of exposure.	Professional judgment	Based on a closely related confidential analog and professional judgment.
Acute Mammalian Toxicity		**LOW: Based on a rat oral LD_{50} >2,000 mg/kg. Acute toxicity values are estimated to be a Low hazard for components of a commercial mixture containing TBB and TBPH (Firemaster 550).**		
Acute Lethality	**Oral**	Rat oral LD_{50} >2,000 mg/kg	Submitted confidential study	Confidential study submitted to EPA; test substance purity: 99.7%; conducted according to 92/69/EEC guideline consistent with OECD guideline 401.
		Rat oral LD_{50} > 5,000 mg/kg (Estimated based on analogy)	Chemtura, 2006	No study details reported in an MSDS; estimated based on analogy to a similar compound to a component of Firemaster 550 (commercial mixture containing TBB and TBPH); it is not certain if this component contains TBB.
		Rat oral LD_{50} > 5,000 mg/kg (Estimated)	Chemtura, 2006	No study details reported in an MSDS; estimated based on one component of Firemaster 550 (commercial mixture containing TBB and TBPH); it is not certain if this component contains TBB.
	Dermal	Rabbit dermal LD_{50} > 2,000 mg/kg (Estimated based on analogy)	Chemtura, 2006	No study details reported in an MSDS; estimated based on analogy to a similar compound to a component of Firemaster 550 (commercial mixture containing TBB

Benzoic acid, 2,3,4,5-tetrabromo-, 2-ethylhexyl ester CASRN 183658-27-7				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
				and TBPH); it is not certain if this component contains TBB.
		Rabbit dermal LD_{50} > 2,000 mg/kg (Estimated)	Chemtura, 2006	No study details reported in an MSDS; estimated based on one component of Firemaster 550 (commercial mixture containing TBB and TBPH); it is not certain if this component contains TBB.
	Inhalation	Rat 1-hr inhalation LC_{50} > 200 mg/L (Estimated based on analogy)	Chemtura, 2006	No study details reported in an MSDS; estimated based on analogy to a similar compound to a component of Firemaster 550 (commercial mixture containing TBB and TBPH); it is not certain if this component contains TBB.
Carcinogenicity		**MODERATE: There is uncertainty due to lack of data for this substance. TBB is estimated to have uncertain potential for carcinogenicity based on analogy to a closely related confidential analog and professional judgment; carcinogenic effects cannot be ruled out.**		
	OncoLogic Results			No data located.
	Carcinogenicity (Rat and Mouse)			No data located.
	Combined Chronic Toxicity/Carcinogenicity			No data located.
	Other	Estimated to have uncertain potential for carcinogenicity.	Professional judgment	Based on analogy to closely related chemical classes and professional judgment. (Estimated by analogy)

Benzoic acid, 2,3,4,5-tetrabromo-, 2-ethylhexyl ester CASRN 183658-27-7				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Genotoxicity		**LOW: Estimated based on negative results for mutagenicity in bacteria and chromosomal aberrations in clastogenicity assays for a component of Firemaster 550 (a commercial mixture containing TBB and TBPH).**		
	Gene Mutation *in vitro*	Negative; an unspecified component of a commercial mixture was not mutagenic in *Salmonella typhimurium* or *Escherichia coli* when tested in dimethyl sulphoxide. (Estimated)	Chemtura, 2006	No study details reported in an MSDS; estimated based on one component of Firemaster 550 (commercial mixture containing TBB and TBPH); it is not certain if this component contains TBB.
	Gene Mutation *in vivo*			No data located.
	Chromosomal Aberrations *in vitro*	Negative; an unspecified component of a commercial mixture showed no evidence of clastogenicity in an *in vitro* cytogenic test. (Estimated)	Chemtura, 2006	No study details reported in an MSDS; estimated based on one component of Firemaster 550 (commercial mixture containing TBB and TBPH); it is not certain if this component contains TBB.
		Negative; a similar compound to an unspecified component of a commercial mixture did not induce chromosome aberrations in human peripheral blood lymphocytes with and without metabolic activation. (Estimated based on analogy)	Chemtura, 2006	Limited study details reported in an MSDS; estimated based on analogy to a similar compound to a component of Firemaster 550 (commercial mixture containing TBB and TBPH); it is not certain if this component contains TBB; study conducted according to OECD 422.
	Chromosomal Aberrations *in vivo*			No data located.
	DNA Damage and Repair			No data located.
	Other			No data located.

Benzoic acid, 2,3,4,5-tetrabromo-, 2-ethylhexyl ester CASRN 183658-27-7				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Reproductive Effects		**MODERATE: No reproductive effects were reported in a 2-generation oral (gavage) reproductive toxicity study in rats at doses up to 165 mg/kg-day (highest dose tested) of Firemaster BZ 54 (commercial mixture of TBB and TBPH) with a larger constituent of TBB. The NOAEL of 165 mg/kg-day falls within the Moderate hazard criteria range; it is possible that effects driven by either component may occur within the Moderate hazard range if tested at a higher dose. It is not clear which component or components of the commercial mixture caused the reported developmental effects. Data from a reproductive/developmental toxicity screen in rats exposed to a similar compound to a component of Firemaster 550 (commercial mixture containing TBB and TBPH) indicated histopathological effects in female reproductive organs at doses ≥ 25 mg/kg-day (lowest dose tested; a NOAEL was not identified). It is uncertain if the commercial mixture contained TBB.**		
	Reproduction/Developmental Toxicity Screen	Estimated to have moderate potential for reproductive effects. (Estimated by analogy)	Professional judgment	Estimated based on a closely related confidential analog and professional judgment.
		2-generation oral (gavage) reproductive toxicity study in rats administered 15, 50, or 165 mg/kg-day; F0 generation was treated 10 weeks prior to pairing through the mating period. Males were treated until termination; females were treated through gestation and lactation, and until termination on PND 21; pup selected (30/sex/dose) to continue as F1 parental generation began treatment on PND 22 and continued treatment similar to the F0 generation. No adverse effects on reproductive performance or fertility in rats. NOAEL: 165 mg/kg-day (highest dose tested) LOAEL: Not established (Estimated)	MPI Research, 2008a	Test substance: Firemaster BZ 54 (commercial mixture of TBB and TBPH) with a larger constituent of TBB; it is not clear which component or components of the mixture are driving the reported developmental effects.

Benzoic acid, 2,3,4,5-tetrabromo-, 2-ethylhexyl ester CASRN 183658-27-7				
PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
	Combined Repeated Dose with Reproduction/ Developmental Toxicity Screen	Reproductive/developmental toxicity screen in rats orally administered 0, 25, 100, 400 mg/kg-day of a similar compound to an unspecified component of a commercial mixture. Reduced number of successful pregnancies and viable offspring at doses of 100 and 400 mg/kg-day; histopathological effects reported in thymus and male reproductive organs (testes and epididymides) at 400 mg/kg-day; histopathological effects in female reproductive organs and adrenals at doses of ≥ 25 mg/kg-day. NOAEL: Not established LOAEL: 25 mg/kg-day (lowest dose tested) (Estimated based on analogy)	Chemtura, 2006	Limited study details reported in an MSDS; estimated based on analogy to a similar compound to a component of Firemaster 550 (commercial mixture containing TBB and TBPH); it is not certain if this component contains TBB; study conducted according to OECD 422.
	Reproduction and Fertility Effects			No data located.
	Other	Potential for reproductive effects following long-term exposure to BZ-54 HP (Estimated)	Chemtura, 2008	No study details reported in an MSDS; Estimated based on BZ-54 HP (commercial mixture containing TBB and TBPH); it is not clear which component is driving repeated dose effects.

Benzoic acid, 2,3,4,5-tetrabromo-, 2-ethylhexyl ester CASRN 183658-27-7				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Developmental Effects		**MODERATE: Developmental effects were reported in a 2-generation reproductive toxicity study in rats and a prenatal study in rats exposed to CN-2065 (a commercial mixture of TBB and TBPH with the predominant constituent being TBB). Developmental effects were reported at doses of 165 mg/kg-day and 100 mg/kg-day in the 2-generation and prenatal studies, respectively. Both studies had a NOAEL of 50 mg/kg-day which falls within the Moderate hazard criteria range. It is not clear which component or components of the commercial mixture caused the reported developmental effects. Development/neurodevelopmental effects were reported in a study in pregnant Wistar rats administered a FM550 mixture (sum total of TBB and TBPH approximately 50%) during gestation though lactation (GD8 - PND21); developmental effects included early female puberty, weight gain, altered exploratory behavior, and increased male left ventricle thickness (LOAEL = 1 mg/kg-day, NOAEL = 0.1 mg/kg-day). It is uncertain which component or components of the FM 550 mixture is driving the reported developmental effects. While the FM 550 mixture data indicates a High hazard potential, it may be the other components driving the reported toxicity. Experimental data indicated no effects on embryonic survival or development in exposed zebrafish embryos.**		
	Reproduction/ Developmental Toxicity Screen	2-generation oral (gavage) reproductive toxicity study in rats administered 15, 50, or 165 mg/kg-day; F0 generation was treated 10 weeks prior to pairing through the mating period. Males were treated until termination; females were treated through gestation and lactation, and until termination on PND 21; pup selected (30/sex/dose) to continue as F1 parental generation began treatment on PND 22 and continued treatment similar to the F0 generation. Parental toxicity: lower body weights and body weight gains during premating period in parental and F1 females at highest dose; Lower body weights in the premating period in F1 males; body weight gains were not affected in males Developmental toxicity: at highest dose,	MPI Research, 2008a	Study details reported in an unpublished report; test substance: Firemaster BZ 54 (CN-2065) (commercial mixture of TBB and TBPH) with the predominant constituent being TBB; it is not clear which component or components of the mixture are driving the reported developmental effects.

Benzoic acid, 2,3,4,5-tetrabromo-, 2-ethylhexyl ester CASRN 183658-27-7				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		lower body weights at birth and throughout lactation was reported in both generations of offspring (F1 and F2); this resulted in lower premating body weights of the first female generation. Decreased spleen weights at lactation day (LD) 21 in F1 male pups and F2 male and female pups. Parental toxicity: NOAEL: 50 mg/kg-day LOAEL: 165 mg/kg-day Developmental toxicity: NOAEL: 50 mg/kg-day LOAEL: 165 mg/kg-day (Estimated)		
		Estimated to have moderate potential for developmental/ neurodevelopmental effects. (Estimated by analogy)	Professional judgment	Estimated based on a closely related confidential analog and professional judgment.
	Combined Repeated Dose with Reproduction/ Developmental Toxicity Screen			No data located.

Benzoic acid, 2,3,4,5-tetrabromo-, 2-ethylhexyl ester CASRN 183658-27-7				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Prenatal Development	Prenatal study in rats exposed to 0, 50, 100, 300 mg/kg-d Firemaster BZ54 (CN-2065) on GD 6-19. Maternal toxicity: increased incidence of animals with sparse hair in abdominal region, lower gestation body weights and body weight gain, and lower gestation food consumption at doses ≥ 100 mg/kg-day. Developmental toxicity: decreased fetal weight at 100 mg/kg-day; increased incidence of fused cervical vertebral neural arches (litter incidence of 8%) in fetuses at 300 mg/kg-day; increased litter incidence of fetal ossification variations involving additional ossification centers to the cervical vertebral neural arches, incomplete ossified skull bones (jugal, parietal, and squamosal), and unossified sternebrae. Maternal toxicity: NOAEL: 50 mg/kg-day LOAEL: 100 mg/kg-day Developmental toxicity: NOAEL: 50 mg/kg-day LOAEL (developmental): 100 mg/kg-day based on decreased fetal weight (Estimated)	MPI Research, 2008b	Study details reported in an unpublished report; test substance: Firemaster BZ54 (CN-2065); commercial mixture of TBB and TBPH with the predominant constituent being TBB; it is not clear which component or components of the mixture are driving the reported developmental effects.
	Postnatal Development			No data located.
	Prenatal and Postnatal Development	Pregnant Wistar rats were administered 0, 0.1 or 1 mg/kg-day of FM550 in the	Patisaul et al., 2013	Estimated based on data for FM550 mixture; non guideline study; the test

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		diet during gestation and through lactation (GD8 - PND 21); Maternal toxicity: Increased serum thyroxine (T4) levels in the high dose dams compared to controls was reported. There was no significant change in triiodothyronine (T3) levels in dam serum. Decreased hepatic carboxylesterease activity was also reported in dams in the high dose group. Developmental toxicity: female offspring in the high dose group displayed a significantly earlier vaginal opening when compared to controls. A statistically significant increase in weight was reported in both males and females in the high dose group at PND 120. This effect persisted through PND 180 to PND 220 with high dose males and females having significantly higher weights than same sex controls. A dose-dependent decrease in the number of rats to enter with open arms, (indicating anxiety), was reported in both male and female offspring. Increased blood glucose levels were reported in male offspring in the high-dose group compared to controls. There was no statistically significant difference in heart weight of male or female offspring. Left ventricular (LV) free wall thickness was significantly increased in male offspring in the high dose group; there were no changes in LV thickness in		substance identified as FM550 is a mixture made up of TBB, TBPH (sum total of TBB and TBPH is approximately 50%), TPP and IPTPP; it is not clear which component or components of the mixture are driving the reported developmental effects.

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		females at any dose. Maternal Toxicity: NOAEL: 0.1 mg/kg-day LOAEL: 1 mg/kg-day Developmental toxicity: NOAEL: 0.1 mg/kg-day LOAEL: 1 mg/kg-day (based on early vaginal opening in females, increased weight in males and females, decreased open arm behavior, increased blood glucose levels in males and increased LV thickness in males) (Estimated)		
	Developmental Neurotoxicity			No data located.
	Other	Potential for developmental effects following long-term exposure to BZ-54 HP (Estimated)	Chemtura, 2008	No study details reported in an MSDS; Estimated based on BZ-54 HP (commercial mixture containing TBB and TBPH); it is not clear which component is driving repeated dose effects.
		Zebrafish embryos were exposed under static conditions to purified TBB at concentrations up to 10 µM from 5.25 - 96 hours post fertilization (hpf); There were no effects on embryonic survival or development. NOAEL: Not established LOAEL: Not established	McGee et al., 2013	Zebrafish is a nonstandard species; current DfE criteria for this endpoint are based on gestational and/or postnatal exposure to mammalian species. Thus, this study cannot be used to assign a hazard designation for the developmental endpoint.

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Neurotoxicity		**MODERATE: Estimated based on analogy to a similar compound to a component of Firemaster 550 (commercial mixture containing TBB and TBPH). There is potential for neurological effects after breathing or swallowing large amounts or after long-term exposure to this analog. There were no neurotoxic effects reported in a 28-day oral toxicity study in rats treated with the analog.**		
	Neurotoxicity Screening Battery (Adult)			No data located.
	Other	Potential for neurological effects following long-term exposure to BZ-54 HP (Estimated)	Chemtura, 2008	No study details reported in an MSDS; Estimated based on BZ-54 HP (commercial mixture containing TBB and TBPH); it is not clear which component is driving repeated dose effects.
		Potential for neurological effects after breathing or swallowing large quantities or repeated exposure over a prolonged period of time is possible for a similar compound to an unspecified component of the commercial mixture. (Estimated based on analogy)	Chemtura, 2006	No study details reported in an MSDS; estimated based on analogy to a similar compound to a component of Firemaster 550 (commercial mixture containing TBB and TBPH); it is not certain if this component contains TBB.
		28-day sub-chronic oral toxicity study in rats treated with 0, 160, 400, 1,000 mg/kg-day; No neurotoxicity effects were reported. NOAEL: 1,000 mg/kg-day (highest dose tested) LOAEL: Not established (Estimated)	Chemtura, 2006	Limited study details reported in an MSDS; neurotoxicity was evaluated in this study; estimated based on one component of Firemaster 550 (commercial mixture containing TBB and TBPH); it is not certain if this component contains TBB.

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Repeated Dose Effects		**MODERATE: Estimated based on an increased incidence of sparse hair in abdominal region, reduced body weight, and reduced food consumption in dams during gestation in a prenatal study in rats exposed to CN-2065 (commercial mixture of TBB and TBPH with the predominant constituent being TBB) on GD 6-19 at doses ≥ 100 mg/kg-day (NOAEL = 50 mg/kg-day). Reduced body weight and body weight gain during the premating period in parental F0 and F1 female rats treated with 165 mg/kg-day CN-2065 (NOAEL = 50 mg/kg-day) was also reported in a 2-generation oral reproductive toxicity in rats. In addition, TBB is Estimated to have a moderate potential for liver effects and cerebral hemorrhages based on a closely related confidential analog and professional judgment and is estimated to have kidney, liver, adrenal, thymus, developmental, reproductive, and neurological effects following long-term exposure to commercial mixtures that included TBB.**		
		In a prenatal study in rats exposed to 0, 50, 100, 300 mg/kg-d on GD 6-19; dams experienced increased incidence of animals with sparse hair in abdominal region, lower gestation body weights and body weight gain, and lower gestation food consumption at doses ≥ 100 mg/kg-day. NOAEL: 50 mg/kg-day LOAEL (maternal): 100 mg/kg-day (Estimated)	MPI Research, 2008b	Study details reported in an unpublished report Test substance: Firemaster BZ54 (CN-2065); commercial mixture of TBB and TBPH with the predominant constituent being TBB; it is not clear which component or components of the mixture are driving the reported effects.
		2-generation oral (gavage) reproductive toxicity study in rats administered 15, 50, or 165 mg/kg-day; F0 generation was treated 10 weeks prior to pairing through the mating period. Males were treated until termination; females were treated through gestation and lactation, and until termination on PND 21; pup selected (30/sex/dose) to continue as F1 parental generation began treatment on PND 22 and continued treatment similar	MPI Research, 2008a	Study details reported in an unpublished report; test substance: Firemaster BZ 54 (CN-2065) commercial mixture of TBB and TBPH with the predominant constituent being TBB; it is not clear which component or components of the mixture are driving the reported developmental effects.

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PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
		to the F0 generation Parental toxicity: lower body weights and body weight gains during premating period in parental and F1 females at highest dose; Lower body weights in the premating period in F1 males; body weight gains were not affected in males Parental toxicity: NOAEL: 50 mg/kg-day LOAEL: 165 mg/kg-day (reduced body weight and body weight gain) (Estimated)		
		Estimated to have moderate potential for liver effects and concern for cerebral hemorrhages. (Estimated by analogy)	Professional judgment	Estimated based on a closely related confidential analog and professional judgment.
		28-day sub-chronic oral toxicity study in rats treated with 0, 160, 400, 1,000 mg/kg-day; Kidney effects were only reported at 1,000 mg/kg-day. No systemic effects were reported at 160 mg/kg-day (NOEL). NOEL: 160 mg/kg-day NOAEL: 400 mg/kg-day LOAEL: 1,000 mg/kg-day based on kidney effects (Estimated)	Chemtura, 2006	Limited study details reported in an MSDS; neurotoxicity was evaluated in this study; estimated based on one component of Firemaster 550 (commercial mixture containing TBB and TBPH); it is not certain if this component contains TBB. The NOAEL of 400 mg/kg is assumed based on the information in the report.
		Potential for neurological effects after breathing or swallowing large quantities or repeated exposure over a prolonged	Chemtura, 2006	No study details reported in an MSDS; estimated based on analogy to a similar compound to a

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		period of time is possible for a similar compound to an unspecified component of the commercial mixture (Estimated based on analogy)		component of Firemaster 550 (commercial mixture containing TBB and TBPH); it is not certain if this component contains TBB.
		Potential for kidney and liver effects following long-term exposure to BZ-54 HP (Estimated)	Chemtura, 2008	No study details reported in an MSDS; Estimated based on BZ-54 HP (commercial mixture containing TBB and TBPH); it is not clear which component is driving repeated dose effects.
Skin Sensitization		**MODERATE: Estimated based on positive results for skin sensitization following exposure to components of commercial mixtures containing TBB. It is not certain which component or components caused the reported effects.**		
	Skin Sensitization	The commercial mixture Firemaster BZ 54 is a skin sensitizer. (Estimated)	Chemtura, 2013	Limited study details reported in an MSDS; Test substance: Firemaster BZ 54 (commercial mixture of TBB and TBPH) with a larger constituent of TBB; it is not clear which component or components of the mixture are driving the reported effects.
		An unspecified component of the commercial mixture was not sensitizing in a Buehler test. (Estimated)	Chemtura, 2006	No study details reported in an MSDS; estimated based on one component of Firemaster 550 (commercial mixture containing TBB and TBPH); it is not certain if this component contains TBB.
		An unspecified component of the commercial mixture was reported to be a sensitizer in a M&K sensitization assay. (Estimated)	Chemtura, 2006	No study details reported in an MSDS; estimated based on one component of Firemaster 550 (commercial mixture containing TBB and TBPH); it is not certain if this component contains TBB.

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Respiratory Sensitization		**No data located.**		
	Respiratory Sensitization			No data located.
Eye Irritation		**MODERATE: Estimated to be irritating to mildly irritating based on experimental data reporting irritation from a commercial mixture containing TBB, mild eye irritation in rabbits from a closely related confidential analog and professional judgment.**		
		Irritating; effects reversible by day 4 (Estimated)	Submitted confidential study	Confidential study submitted to EPA. Limited study details reported for a commercial mixture containing TBB.
		Mild eye irritation in rabbits (Estimated by analogy)	Professional judgment	Estimated based on a closely related confidential analog and professional judgment.
		The commercial mixture Firemaster BZ 54 is a slight eye irritant. (Estimated)	Chemtura, 2013	Limited study details reported in an MSDS; Test substance: Firemaster BZ 54 (commercial mixture of TBB and TBPH) with a larger constituent of TBB; it is not clear which component or components of the mixture are driving the reported effects.
		An unspecified component of the commercial mixture was reported to be a slight eye irritant in rabbits. (Estimated)	Chemtura, 2006	No study details reported in an MSDS; estimated based on one component of Firemaster 550 (commercial mixture containing TBB and TBPH); it is not certain if this component contains TBB.
		No eye irritation was reported in rabbits for a similar compound to an unspecified component of the commercial mixture. (Estimated based on analogy)	Chemtura, 2006	No study details reported in an MSDS; estimated based on analogy to a similar compound to a component of Firemaster 550 (commercial mixture containing TBB and TBPH); it is not certain if this component contains TBB.

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Dermal Irritation		**LOW: Estimated to have mild skin irritation based on a closely related confidential analog, experimental data reporting mild irritation to components of a commercial mixture, and professional judgment.**		
	Dermal Irritation	Mild skin irritation in rabbits (Estimated based on analogy)	Professional judgment	Estimated based on a closely related confidential analog and professional judgment.
		The commercial mixture Firemaster BZ 54 is a mild skin irritant. (Estimated)	Chemtura, 2013	Limited study details reported in an MSDS; Test substance: Firemaster BZ 54 (commercial mixture of TBB and TBPH) with a larger constituent of TBB; it is not clear which component or components of the mixture are driving the reported effects.
		No skin irritation was reported in rabbits for a similar compound to an unspecified component of the commercial mixture. (Estimated based on analogy)	Chemtura, 2006	No study details reported in an MSDS; estimated based on analogy to a similar compound to a component of Firemaster 550 (commercial mixture containing TBB and TBPH); it is not certain if this component contains TBB.
		An unspecified component of the commercial mixture was reported to be a slight skin irritant in rabbits. (Estimated)	Chemtura, 2006	No study details reported in an MSDS; estimated based on one component of Firemaster 550 (commercial mixture containing TBB and TBPH); it is not certain if this component contains TBB.

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PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
Endocrine Activity	**Increased serum thyroxine (T4) levels were reported in the serum of dams following oral administration to FM550 (mixture of 50% sum total of TBB and TBPH); other components of the mixture were not identified. It is unclear which component or components of the mixture are driving the endocrine activity effects. There was no experimental data located specifically for the TBB compound.**		
	Potential for adrenal effects following long-term exposure to BZ-54 HP (Estimated)	Chemtura, 2008	No study details reported in an MSDS; Estimated based on BZ-54 HP (commercial mixture containing TBB and TBPH); it is not clear which component is driving repeated dose effects.
	Pregnant Wistar rats were administered 0, 0.1 or 1 mg/kg-day of FM550 in the diet during gestation and through lactation (GD8 - PND 21); Increased serum thyroxine (T4) levels (increase of 65%) in the high dose dams compared to controls was reported. There was no significant change in triiodothyronine (T3) levels in dam serum. There was no reported statistically significant change in T4 or T3 levels in pup serum on PND 21 when compared to controls. (Estimated)	Patisaul et al., 2013	Estimated based on data for FM550 mixture; non guideline study; test substance identified as FM550 is a mixture made up of TBB, TBPH (sum total of TBB and TBPH is approximately 50%), TPP and IPTPP; it is not clear which component or components of the mixture are driving the reported endocrine activity effects.
	Reproductive/developmental toxicity screen in rats orally administered 0, 25, 100, 400 mg/kg-day of a similar compound to an unspecified component of a commercial mixture. Reduced number of successful pregnancies and viable offspring at doses of 100 and 400 mg/kg-day; histopathological effects reported in	Chemtura, 2006	Limited study details reported in an MSDS; estimated based on analogy to a similar compound to a component of Firemaster 550 (commercial mixture containing TBB and TBPH); it is not certain if this component contains TBB; study conducted according to OECD 422.

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		thymus and male reproductive organs (testes and epididymides) at 400 mg/kg-day; histopathological effects in female reproductive organs and adrenals at doses of 25 mg/kg-day. NOAEL: Not established LOAEL: 25 mg/kg-day (lowest dose tested) (Estimated based on analogy)		
Immunotoxicity		**Estimated to have potential for immunotoxicity based on a structural alert for polyhalogenated aromatic hydrocarbons.**		
	Immune System Effects	Potential for thymus effects following long-term exposure to BZ-54 HP (Estimated)	Chemtura, 2008	No study details reported in an MSDS; Estimated based on BZ-54 HP (commercial mixture containing TBB and TBPH); it is not clear which component is driving repeated dose effects.
		Potential for immunotoxicity based on structural alert for polyhalogenated aromatic hydrocarbons (Estimated)	Professional judgment; EPA, 2012	Estimated based on structural alert for polyhalogenated aromatic hydrocarbons and professional judgment.
ECOTOXICITY				
ECOSAR Class		Esters		
Acute Aquatic Toxicity		**LOW: Based on an estimated log Kow of 8.8 and the fact that the experimental effect levels in fish, daphnia, and algae were well above the estimated water solubility (0.00001 mg/L), NES are predicted for this endpoint.**		
Fish LC_{50}		Fish 96-hour LC_{50} = No effects at saturation (NES) (Experimental)	Submitted confidential study	No study details reported in a submitted confidential study report. Species, test conditions, and toxicity values not specified.
		Oncorhynchus mykiss rainbow trout 96-	Chemtura, 2006	No study details reported in an

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	hour LC_{50} = 1.6 mg/L (Estimated by analogy)		MSDS; estimated based on analogy to a similar compound to a component of Firemaster 550 (commercial mixture containing TBB and TBPH); it is not certain if this component contains TBB. Based on log K_{ow} of 8.8 and the reported effect level was above the estimated water solubility (0.000011 mg/L), NES are predicted for this endpoint.
	Fathead minnow 96-hour LC_{50} = 10.8 mg/L (Estimated by analogy)	Chemtura, 2006	No study details reported in an MSDS; estimated based on analogy to a similar compound to a component of Firemaster 550 (commercial mixture containing TBB and TBPH); it is not certain if this component contains TBB. Based on log K_{ow} of 8.8 and the reported effect level was above the estimated water solubility (0.000011 mg/L), NES are predicted for this endpoint.
	Oncorhynchus mykiss rainbow trout 96-hour LC_{50}> 12 mg/L (Estimated)	Chemtura, 2006, 2013	No study details reported in an MSDS; estimated based on one component of Firemaster 550 and for Firemaster BZ-54 (commercial mixtures containing TBB and TBPH); Based on log K_{ow} of 8.8 and the reported effect level was above the estimated water solubility (0.000011 mg/L), NES are predicted for this endpoint.
	Fish 96-hour LC_{50} = 0.008 mg/L (Estimated)	ECOSAR v1.11	NES: The estimated log K_{ow} of 8.8 for this chemical exceeds the SAR

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PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	ECOSAR: Esters		limitation for log K_{ow} of 5.0; NES are predicted for these endpoints.
	Fish 96-hour LC_{50} < 0.001 mg/L (Estimated) ECOSAR: Neutral organics	ECOSAR v1.11	NES: The estimated log K_{ow} of 8.8 for this chemical exceeds the SAR limitation for log K_{ow} of 5.0; NES are predicted for these endpoints. Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.
Daphnid LC_{50}	*Daphnia magna* 48-hour EC_{50} = 0.42 mg/L. (Experimental)	Chemtura, 2006, 2013	No study details reported in an MSDS; estimated based on one component of Firemaster 550 and for Firemaster BZ-54 (commercial mixture containing TBB and TBPH); Based on log K_{ow} of 8.8 and the reported effect level was above the estimated water solubility (0.000011 mg/L), NES are predicted for this endpoint.
	Daphnia magna 24-hour EC_{50} = 1.2 mg/L. (Experimental)	Chemtura, 2006, 2013	No study details reported in an MSDS; estimated based on one component of Firemaster 550 and for Firemaster BZ-54 (commercial mixtures containing TBB and TBPH); Based on log K_{ow} of 8.8 and the reported effect level was above the estimated water solubility (0.000011 mg/L), NES are predicted

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PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
			for this endpoint.
	Daphnia magna 48-hour LC_{50} = 2.44 mg/L (Estimated by analogy)	Chemtura, 2006	No study details reported in an MSDS; estimated based on analogy to a similar compound to a component of Firemaster 550 (commercial mixture containing TBB and TBPH); it is not certain if this component contains TBB. Based on log K_{ow} of 8.8 and the reported effect level was above the estimated water solubility (0.000011 mg/L), NES are predicted for this endpoint.
	Daphnia 48-hour LC_{50} = 0.008 mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	NES: The estimated log K_{ow} of 8.8 for this chemical exceeds the SAR limitation for log K_{ow} of 5.0; NES are predicted for these endpoints.
	Daphnia 48-hour LC_{50} < 0.001 mg/L (Estimated) ECOSAR: Neutral organics	ECOSAR v1.11	NES: The estimated log K_{ow} of 8.8 for this chemical exceeds the SAR limitation for log K_{ow} of 5.0; NES are predicted for these endpoints. Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.
Green Algae EC_{50}	Green algae 96 hour LC_{50} = No effects at saturation (NES). (Experimental)	Submitted confidential study	Limited study details reported in submitted confidential study report.
	Green algae 96-hour EC_{50} = 0.001 mg/L (Estimated)	ECOSAR v1.11	NES: The estimated log K_{ow} of 8.8 for this chemical exceeds the SAR

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PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	ECOSAR: Esters		limitation for log K_{ow} of 6.4; NES are predicted for these endpoints.
	Selenastrum capricornutum 96-hour EC_{50} >5.1 mg/L (Estimated)	Chemtura, 2006, 2013	No study details reported in an MSDS; estimated based on one component of Firemaster 550 and for Firemaster BZ-54 (commercial mixture containing TBB and TBPH); based on log K_{ow} of 8.8 and the reported effect level was above the estimated water solubility (0.000011 mg/L), NES are predicted for this endpoint.
	Green algae 96-hour EC50 < 0.001 mg/L (Estimated) ECOSAR: Neutral organics	ECOSAR v1.11	NES: The estimated log K_{ow} of 8.8 for this chemical exceeds the SAR limitation for log K_{ow} of 5.0; NES are predicted for these endpoints. Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.
Chronic Aquatic Toxicity	**LOW: Based on estimated chronic toxicity values for fish, daphnid, and algae that indicate no effects at saturation (NES).**		
Fish ChV	Fish ChV < 0.001 mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	NES: The estimated log K_{ow} of 8.8 for this chemical exceeds the SAR limitation for log K_{ow} of 8.0; NES are predicted for these endpoints.

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	Green algae 96-hour EC_{50} < 0.001 mg/L (Estimated) ECOSAR: Neutral organics	ECOSAR v1.11	NES: The estimated log K_{ow} of 8.8 for this chemical exceeds the SAR limitation for log K_{ow} of 5.0; NES are predicted for these endpoints. Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.
Daphnid ChV	*Daphnia carinata* 15-day NOEC: 15.6 µg/l (repro) NOEC: 62.5 µg/l (mortality) LC50: 79.3 µg/l	Submitted confidential study	Limited study details reported in a submitted confidential Chronic Toxicity/Reproductive toxicity test. NES are predicted for this endpoint based on a log K_{ow} of 8.8 and the reported effect level was above the estimated water solubility (0.000011 mg/L).
	Daphnia ChV < 0.001 mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	NES: The estimated log K_{ow} of 8.8 for this chemical exceeds the SAR limitation for log K_{ow} of 8.0; NES are predicted for these endpoints.

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PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	Daphnia ChV < 0.001 mg/L (Estimated) ECOSAR: Neutral organics	ECOSAR v1.11	NES: The estimated log K_{ow} of 8.8 for this chemical exceeds the SAR limitation for log K_{ow} of 8.0; NES are predicted for these endpoints. Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.
Green Algae ChV	Green algae ChV = 0.003 (Estimated) ECOSAR: Esters	ECOSAR v1.11	NES: The estimated log K_{ow} of 8.8 for this chemical exceeds the SAR limitation for log K_{ow} of 8.0; NES are predicted for these endpoints.
	Green algae ChV = 0.004 (Estimated) ECOSAR: Neutral organics	ECOSAR v1.11	NES: The estimated log K_{ow} of 8.8 for this chemical exceeds the SAR limitation for log K_{ow} of 8.0; NES are predicted for these endpoints. Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
ENVIRONMENTAL FATE				
Transport		**Level III fugacity models incorporating available physical and chemical property data indicate that at steady state, TBB is expected to be found primarily in soil and to a lesser extent, water. Hydrolysis of TBB is not expected to occur at a significant rate at environmentally-relevant pH conditions. TBB is expected to have low mobility in soil based on its measured K_{OC}. Therefore, leaching of TBB through soil to groundwater is not expected to be an important transport mechanism. Estimated volatilization half-lives indicate that it will be slightly volatile from surface water. In the atmosphere, TBB is expected to exist in the particulate phase, based on its estimated vapor pressure. Particulates will be removed from air by wet or dry deposition.**		
	Henry's Law Constant (atm-m^3/mole)	$7.1x10^{-6}$ (Estimated)	EPI v4.11	Estimated by the HENRYWIN Group SAR Method with no measured chemical property inputs.
	Sediment/Soil Adsorption/Desorption - K_{oc}	>28840 (Measured)	Submitted confidential study	Limited study details available; the degree of precision reported is atypical for this type of study.
	Level III Fugacity Model	Air = 0.3% Water = 12% Soil = 87% Sediment = 1% (Estimated)	EPI v4.11	This estimation was obtained using the Level III Fugacity model based on the equal emissions distribution assumption with no measured chemical property inputs.

Benzoic acid, 2,3,4,5-tetrabromo-, 2-ethylhexyl ester CASRN 183658-27-7				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Persistence		**HIGH: The persistence hazard designation for TBB is based on estimated rates of removal in soil and the persistence of degradation products. Confidential experimental biodegradation studies reported half-lives of 3.5 days in water and 8.5 days in sediment with a shake flask die-away test and 6% degradation after 28 days in a closed bottle test. There was 93% removal of a commercial mixture containing TBB in an activated sludge simulation test due to sorption to sludge. TBB has an estimated half-life of 120 days in soil where fugacity models indicate that it is expected to partition. Although TBB may undergo hydrolysis under basic conditions, the resulting hydrolysis products are expected to have high persistence. TBB has the potential to undergo photodegradation, under laboratory conditions when dissolved in organic solvents, however the importance of this process under environmental conditions cannot be determined. The vapor phase reaction half-life of TBB with atmospheric hydroxyl radicals is estimated at < 1 day, although it is expected to exist primarily in the particulate phase in air.**		
Water	**Aerobic Biodegradation**	Passes Ready Test: No Test method: OECD TG 301D: Closed Bottle Test 6% biodegradation after 28 days (Measured)	Submitted confidential study	Adequate guideline study.
		Study results: 50% in 3.5 days Test method: Shake Flask Shake flask die-away test (Measured)	Submitted confidential study	Adequate guideline study. Although limited experimental data were available, the anticipated degradation product, 2,3,4,5-tetrabromobenzoic acid, is anticipated to be resistant to degradation under the test conditions.
		Weeks-months (Primary Survey Model) Months (Ultimate Survey Model) (Estimated for degradation product)	EPI v4.11	Estimated for the degradation product 2,3,4,5-tetrabromobenzoic acid (CASRN 27581-13-1).
		Study results: 50% in 8.5 days Test method: Shake Flask Performed in water with suspended sediment (Measured)	Submitted confidential study	Adequate guideline study. Although limited experimental data were available, the anticipated degradation product, 2,3,4,5-tetrabromobenzoic acid, is anticipated to be resistant to degradation under the test conditions.
		>93% removal	Submitted confidential study	Guideline study, submitted for a

Benzoic acid, 2,3,4,5-tetrabromo-, 2-ethylhexyl ester CASRN 183658-27-7				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		Test method: 303A: Activated Sludge Units - Simulation Test (Measured)		commercial mixture containing TBB. The substances did not biodegrade but showed removal (>93%) due to sorption to sludge.
	Volatilization Half-life for Model River	8 days (Estimated)	EPI v4.11	Based on the magnitude of the estimated Henry's Law constant.
	Volatilization Half-life for Model Lake	98 days (Estimated)	EPI v4.11	Based on the magnitude of the estimated Henry's Law constant.
Soil	**Aerobic Biodegradation**			No data located.
	Anaerobic Biodegradation	Not probable	Holliger et al., 2004; EPI v4.11	The estimated value addresses the potential for ultimate biodegradation. However, there is potential for primary anaerobic biodegradation of haloaromatic compounds by reductive dehalogenation.
	Soil Biodegradation with Product Identification			No data located.
	Sediment/Water Biodegradation			No data located.
Air	**Atmospheric Half-life**	1 day Based on a 12-hour day. (Estimated)	EPI v4.11	
Reactivity	**Photolysis**	Half-life = 95 min. in methanol Half-life = 86 min. in tetrahydrofuran Half-life = 162 min. in toluene Di- and tri-brominated analogues were identified by electron capture negative ion/mass spectrometry ECNI/MS as the most dominant photodegradation products (Measured)	Davis and Stapleton, 2009	The half-life and rate data are not relevant to removal rates in the environment as the test substance was dissolved in organic solvents. However, the results demonstrate the potential for some debromination.
	Hydrolysis	Half-life of 3.4 days at pH 8; 34 days at pH 7 (Estimated)	EPI v4.11	Hydrolysis rates are expected to be pH-dependent and may be limited the by low water solubility of this

Benzoic acid, 2,3,4,5-tetrabromo-, 2-ethylhexyl ester CASRN 183658-27-7				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
				compound.
		50%/>1 year at pH 4, 7, and 9 (Measured)	Submitted confidential study	Limited study details available. Data indicate the resistance of the material to hydrolysis under environmental conditions.
Environmental Half-life		Aquatic mesocosm study; a controlled source of TBB was applied and analyzed by GC-MS over the course of the study TBB was detected in both the particulate and sediment compartment samples. Degradation products were detected but not identified (Measured)	de Jourdan et al., 2013	This field study provides data about the partitioning and fate/persistence of this compound under environmental conditions.
		120 days Soil (Estimated)	PBT Profiler	Half-life estimated for the predominant compartment, oil, as determined by EPI methodology.
Bioaccumulation		**HIGH: The bioaccumulation hazard designation is estimated based on the estimated BAF and monitoring data reporting detections in many different species including those higher on the food chain. In addition, the stable metabolite and degradation product of TBB is expected to have a moderate Bioaccumulation designation based on an estimated BAF value.**		
	Fish BCF	BCFK edible tissue: 2.26 BCFK non-edible tissue: 2.70 BCFK whole fish: 2.47 According to OECD 305C in Trout (Measured)	Submitted confidential study	Guideline study, submitted for a commercial mixture containing TBB.
		6.2 Reported as a range: 1.7 - 6.2 (Measured)	Submitted confidential study	Adequate guideline study.
		10 for tetrabromobenzoic acid (TBBA), an expected metabolite and hydrolysis product of TBB (Estimated for metabolite)	EPI v4.11	Estimations run with using the SMILES: O=C(c1c(Br)c(Br)c(Br)c(Br)c1)O.

Benzoic acid, 2,3,4,5-tetrabromo-, 2-ethylhexyl ester CASRN 183658-27-7				
PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
	Other BCF			No data located.
	BAF	2100 (Estimated)	EPI v4.11	
		Fish were orally exposed to commercial flame retardant formulations including Firemaster BZ-54®, containing TBB for 56 days and depurated (e.g., fed clean food) for 22 days. Homogenized fish tissues were extracted and analyzed on day 0 and day 56 using gas chromatography electron-capture negative ion mass spectrometry (GC/ECNI-MS). TBB and TBPH, were detected in tissues at approximately 1% of daily dosage along with brominated metabolites. (Measured)	Bearr et al., 2010	BAFs were not calculated. Non guideline study indicates that absorption of this compound can occur in fish through dietary exposure.
		TBB was detected in adipose, liver, and muscle tissues in rat dams and rat pup adipose tissue. The primary metabolite of TBB (TBBA) was also detected in liver tissue of rat dams. The pregnant rats were administered 0, 0.1 or 1 mg/kg-day of FM550 by oral gavage across gestation and through lactation (GD8 - PND 21). (Measured)	Patisaul et al., 2013	BAFs were not calculated. Non guideline study indicates that absorption of this compound can occur in rats through oral exposure; the test substance identified as FM550 is a mixture made up of TBB, TBPH (CASRN 26040-51-7), IPTPP (CASRN 68937-41-7) and TPP (CASRN 115-86-6).
		835 for tetrabromobenzoic acid (TBBA), an expected metabolite and hydrolysis product of TBB (Estimated for metabolite)	EPI v4.11	Estimations run with using the SMILES: O=C(c1c(Br)c(Br)c(Br)c(Br)c1)O.
	Metabolism in Fish			No data located.

Benzoic acid, 2,3,4,5-tetrabromo-, 2-ethylhexyl ester CASRN 183658-27-7			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
ENVIRONMENTAL MONITORING AND BIOMONITORING			
Environmental Monitoring	TBB was detected in gas and particle-phase air samples collected from Denmark, near the shores of the Great Lakes, Norway and Sweden. TBB was detected in the marine atmosphere near Antarctica, the Arctic, East Asia and Southeast Asia. TBB was detected in sediment samples from Denmark, the Faroe Islands, Finland, Norway, Sweden and Yadkin River in North Carolina. TBB was detected in dust from Bavaria, Belgium, Canada, Kuwait, New Zealand, Pakistan, Sweden, United States, airplanes and a UK daycare (Stapleton et al., 2008, 2009; Ali et al., 2011, 2012, 2013; Covaci et al., 2012; Dodson et al., 2012; EFSA, 2012; Kopp et al., 2012; LaGuardia et al., 2012; Ma et al., 2012; Moller et al., 2012a, 2012b; Sahlstrom et al., 2012; Shoeib et al., 2012; Xiao et al., 2012; Allen et al., 2013).		
Ecological Biomonitoring	TBB was detected in bivalve (*Corbicula fluminea*); finless porpoise; gastropod (*Elimia proxima*); fish; ring-billed gulls; Black-legged kittiwake; Brünnich's guillemot; Capelin; Common eider; gastropod (*Elimia proxima*); polar bear; ringed seal; egg; pet cat and dog hair; artic fox (EPA, 2009; Lam et al., 2009; Sagerup et al., 2010; Zhou et al., 2010; Gentes et al., 2012; LaGuardia et al., 2012).		
Human Biomonitoring	This chemical was not included in the NHANES biomonitoring report (CDC, 2013).		

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Di(2-ethylhexyl) tetrabromophthalate (TBPH)

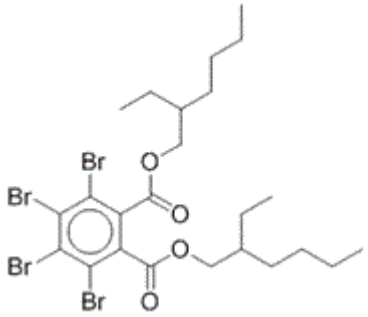
Screening Level Toxicology Hazard Summary

This table contains hazard information for each chemical; evaluation of risk considers both hazard and exposure. Variations in end-of-life processes or degradation and combustion by-products are discussed in the report but not addressed directly in the hazard profiles. The caveats listed below must be taken into account when interpreting the information in the table.

VL = Very Low hazard L = Low hazard M = Moderate hazard H = High hazard VH = Very High hazard – Endpoints in colored text (VL, L, M, H, and VH) were assigned based on empirical data. Endpoints in black italics *(VL, L, M, H,* and *VH*) were assigned using values from estimation software and professional judgment [(Quantitative) Structure Activity Relationships "(Q)SAR"].

Chemical	CASRN	Human Health Effects											Aquatic Toxicity**		Environmental Fate	
		Acute Toxicity	Carcinogenicity	Genotoxicity	Reproductive	Developmental	Neurological	Repeated Dose	Skin Sensitization	Respiratory Sensitization	Eye Irritation	Dermal Irritation	Acute	Chronic	Persistence	Bioaccumulation
Di(2-ethylhexyl) tetrabromophthalate	26040-51-7	*L*	*M*	M	*M*	*M*	*M*	M	L		L	L	*L*	*L*	*H*	*H*

**Aquatic toxicity: EPA/DfE criteria are based in large part upon water column exposures which may not be adequate for poorly soluble substances such as many flame retardants that may partition to sediment and particulates.



CASRN: 26040-51-7

MW: 706.14

MF: $C_{24}H_{34}Br_4O_4$

Physical Forms: Liquid
Neat: Liquid

Use: Flame retardant

SMILES: O=C(OCC(CCCC)CC)c1c(c(c(c(c1Br)Br)Br)Br)C(=O)OCC(CCCC)CC

Synonyms: 1,2-Benzenedicarboxylic acid, 3,4,5,6-tetrabromo-, 1,2-bis(2-ethylhexyl) ester; TBPH; BEH-TEBP. Related trade names: Uniplex FRP-45; this chemical is one of the components of the commercial products BZ-54, CN-2065 and Firemaster 550 (FM550).

Chemical Considerations: This is a discrete organic chemical with a MW below 1,000. EPI v4.11 was used to estimate physical/chemical and environmental fate values where experimental data were lacking.

Polymeric: No
Oligomeric: Not applicable

Metabolites, Degradates and Transformation Products: Mono(2-ethylhexyl) tetrabromophthalate (TBMEHP) by *in vitro* metabolism (and the corresponding 2-ethylhexanol 104-76-7) or hydrolysis (Estimated); di- and tri-brominated analogs of TBPH by anaerobic biodegradation (Estimated) and photodegradation (Davis and Stapleton, 2009; Bearr et al., 2012; Roberts et al., 2012; Patisaul et al., 2013).

Analog: Confidential analogs
Endpoint(s) using analog values: Carcinogenicity, reproductive, developmental effects and repeated dose effects

Analog Structure: Not applicable

Structural Alerts: Polyhalogenated aromatic hydrocarbons, immunotoxicity (EPA, 2012).

Risk Phrases: Not classified by Annex VI Regulation (EC) No 1272/2008 (ESIS, 2012).

Hazard and Risk Assessments: Di(2-ethylhexyl) tetrabromophthalate is part of the HPV Data Summary and Test Plan (ACC, 2004).

Di(2-ethylhexyl) tetrabromophthalate CASRN 26040-51-7			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
PHYSICAL/CHEMICAL PROPERTIES			
Melting Point (°C)	-20 Freezing point approximately -20°C (Measured)	Unitex Chemical Corporation, 2006	No study details obtained from a material safety data sheet (MSDS).
Boiling Point (°C)	>300 (Estimated)	EPI v4.11; EPA, 1999	Cutoff value for high boiling point compounds according to HPV assessment guidance.
Vapor Pressure (mm Hg)	$<10^{-8}$ at 25°C (Estimated)	EPI v4.11; EPA, 1999	Cutoff value for nonvolatile compounds according to HPV assessment guidance.
Water Solubility (mg/L)	$2x10^{-9}$ (Estimated)	EPI v4.11; EPA, 1999	Estimated value is less than the cutoff value, <0.001 mg/L, for nonsoluble compounds according to HPV assessment guidance.
Log K_{ow}	12 (Estimated)	EPI v4.11; EPA, 1999	Estimated value is greater than the cutoff value, >10, according to methodology based on HPV assessment guidance.
Flammability (Flash Point)	Flash Point: >265°C (Measured)	Unitex Chemical Corporation, 2006	Test substance identified as Uniplex FRP-45 (TBPH >99.5% purity).
Explosivity	Not expected to form explosive mixtures with air (Estimated)	Professional judgment	No experimental data located; based on its use as a flame retardant.
Pyrolysis			No data located.
pH	Not applicable (Estimated)	Professional judgment	Does not contain functional groups that are expected to ionize under environmental conditions.
pK_a	Not applicable (Estimated)	Professional judgment	Does not contain functional groups that are expected to ionize under environmental conditions.

Di(2-ethylhexyl) tetrabromophthalate CASRN 26040-51-7				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
HUMAN HEALTH EFFECTS				
Toxicokinetics		**TBPH is estimated to have poor absorption by all routes of exposure based on analogy to a structurally similar confidential analog; however, experimental data for the FM550 (a mixture made up of a sum total of TBB and TBPH of 50%) indicate that absorption of TBPH can occur in rats following oral exposure from gestation through lactation. TBPH was detected in liver tissues of dams following exposure to FM550, but not in any evaluated tissues in the offspring. The monoester, mono(2-ethylhexyl)tetrabromophthalate (TBMEHP 61776-60-1) was identified as the primary metabolite when tested *in vitro*. There were no metabolites of TBPH detected in human or rat subcellular fractions; however, in the presence of purified porcine carboxylesterase, the formation of TBMEHP was detected at a rate of 1.08 mol min^{-1} mg $protein^{-1}$. No phase II metabolites of TBMEHP were detected. TBPH in humans has not been evaluated. TBPH was also found to be metabolized in vitro in hepatic subcellular fractions of fathead minnow, common carp, wild-type mice, and snapping turtle. There were no data located regarding toxicokinetic properties of the pure TBPH compound following oral, dermal or inhaled routes of exposure.**		
Dermal Absorption *in vitro*				No data located.
Absorption, Distribution, Metabolism & Excretion	**Oral, Dermal or Inhaled**	Estimated to have poor absorption by all routes of exposure.	Professional judgment	Based on a closely related confidential analog and professional judgment.
		Pregnant rats (3/dose group) were administered 0, 0.1 or 1 mg/kg-day of FM550 in the diet across gestation and through lactation (GD8 - PND 21). FM500 components including TBPH were detected in the liver tissues in Dams at PND 21 (596 ng/g w.w. in high dose, 80.6 ng/g w.w. in low dose, < 18.0 ng/g w.w. in controls). TBPH was not detected in adipose or muscle tissue of dams. The primary metabolite of TBPH (TBMEHP) was not detected in any tissues in dams on PND 21. TBPH was not detected in any pup	Patisaul et al., 2013	Nonguideline study indicates that absorption of this compound can occur in rats through oral exposure; the test substance identified as FM550 is a mixture made up of TBB and TBPH (sum total of the TBB and TBPH components is approximately 50%) and other compounds including IPTPP (CASRN 68937-41-7) and TPP (CASRN 115-86-6); it is unclear if TBPH absorption in pups occurred due to gestational exposure or through lactation; this study was a non-guideline exploratory assessment and used a small number of animals per dose group.

Di(2-ethylhexyl) tetrabromophthalate CASRN 26040-51-7				
PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
		adipose tissue. (Estimated)		
	Other	*In vitro* metabolism experiments with liver and intestinal subcellular fractions following exposure to TBPH identified monoester, mono(2-ethylhexyl)tetrabromophthalate (TBMEHP 61776-60-1) as the primary metabolite when tested *in vitro*. There were no metabolites of TBPH detected in human or rat subcellular fractions; however, in the presence of purified porcine carboxylesterase, the formation of TBMEHP was detected at a rate of 1.08 mol min-1 mg protein-1. No phase II metabolites of TBMEHP were detected. TBPH in humans has not been evaluated.	Roberts et al., 2012	TBPH appears to be more recalcitrant to metabolism than TBB, and may have a longer half-life after absorption *in vivo* which may influence potential toxicity. The metabolism of TBPH to TBMEHP may also influence the toxicity of TBPH, but metabolism may not occur quickly enough to influence the bioaccumulation of TBPH.
		TBPH was metabolized to TBMEHP at a rate of 89 pmol/hr/mg esterase *in vitro* in the presence of hepatic porcine esterase.	Springer et al., 2012	Adequate.
		In vitro metabolism was measured in hepatic subcellular fractions in fat head minnow, common carp, wild-type mice, and snapping turtle exposed to by measuring the loss of the parent compound (TBB and TBPH) from the Firemaster BZ-54 mixture. Metabolic loss of TBPH was	Bearr et al., 2012	Test substance identified as Firemaster BZ-54 (TBB and TBPH in approximate 3:1 ratio).

Di(2-ethylhexyl) tetrabromophthalate CASRN 26040-51-7				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		observed for all species; metabolism of TBPH was generally at a lower rate than TBB in the fathead minnow, common carp and mouse; however, TBPH was metabolized in the snapping turtle while TBB was not. TBPH metabolism was significant for all species and cell fractions. It was concluded by the authors that some species can metabolize TBB and TBPH to form varying metabolites.		
Acute Mammalian Toxicity		**LOW: Based on oral and dermal LD_{50} values of ≥ 2,000 mg/kg in rats and rabbits, respectively. And an inhalation LC_{50} > 200 mg/L.**		
Acute Lethality	**Oral**	Rat oral LD_{50} = 2,000 mg/kg	Bradford et al., 1996	Procedure appears consistent with OECD methods for acute oral toxicity testing. Purity: 99.7%.
		Rat oral LD_{50} > 5,000 mg/kg	ACC, 2004; Chemtura, 2006	Study details reported in a secondary source; also reported in an MSDS; estimated based on one component of Firemaster 550 (commercial mixture containing TBB and TBPH); it is not certain if this component contains TBPH.
	Dermal	Rabbit dermal LD_{50} > 3,090 mg/kg	ACC, 2004	Study details reported in a secondary source. Test material was RC9927; FR-45B; CASRN 26040-51-7 (Purity > 95%).
		Rabbit dermal LD_{50} > 2,000 mg/kg (Estimated based on analogy)	Chemtura, 2006	No study details reported in an MSDS; estimated based on analogy to a similar compound to a component of Firemaster 550 (commercial mixture containing TBB and TBPH); it is not

Di(2-ethylhexyl) tetrabromophthalate CASRN 26040-51-7				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
				certain if this component contains TBPH.
		Rabbit dermal LD_{50} > 2,000 mg/kg (Estimated)	Chemtura, 2006	No study details reported in an MSDS; estimated based on one component of Firemaster 550 (commercial mixture containing TBB and TBPH); it is not certain if this component contains TBPH.
	Inhalation	Rat 1-hr inhalation LC_{50} > 200 mg/L (Estimated based on analogy)	Chemtura, 2006	No study details reported in an MSDS; estimated based on analogy to a similar compound to a component of Firemaster 550 (commercial mixture containing TBB and TBPH); it is not certain if this component contains TBPH.
Carcinogenicity		**MODERATE: There is uncertainty due to lack of data for this substance. EPA does not expect this substance to be carcinogenic; however, such effects cannot be ruled out. TBPH is estimated to have uncertain potential for carcinogenicity based on analogy to a closely related confidential analog and professional judgment.**		
	OncoLogic Results			No data located.
	Carcinogenicity (Rat and Mouse)			No data located.
	Combined Chronic Toxicity/Carcinogenicity			No data located.
	Other	Estimated to have uncertain potential for carcinogenicity. (Estimated by analogy)	Professional judgment	Based on analogy to closely related chemical classes and professional judgment.
Genotoxicity		**MODERATE: There was a weakly positive result for chromosome aberrations in human lymphocytes. There were negative results in 2 other *in vitro* chromosomal aberration assays using a component of Firemaster 550 (a commercial mixture containing TBB and TBPH). TBPH did not cause gene mutations in bacteria or chromosomal aberrations in an *in vivo* mouse micronucleus assay.**		
	Gene Mutation *in vitro*	Negative for gene mutation in	ACC, 2004	Study details reported in a secondary

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PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
		Salmonella typhimurium TA98, TA100, TA1535, TA1537, TA1538 with and without metabolic activation.		source. Test material was RC9927; FR-45B; CASRN 26040-51-7 (Purity > 95%).
		Negative; an unspecified component of a commercial mixture was not mutagenic in *Salmonella typhimurium* or *Escherichia coli* when tested in dimethyl sulphoxide. (Estimated)	Chemtura, 2006	No study details reported in an MSDS; estimated based on one component of Firemaster 550 (commercial mixture containing TBB and TBPH); it is not certain if this component contains TBPH.
	Gene Mutation *in vivo*			No data located.
	Chromosomal Aberrations *in vitro*	Weakly positive for chromosome aberrations in human lymphocytes with and without metabolic activation.	ACC, 2004	Study details reported in a secondary source. Test material was RC9927; FR-45B; CASRN 26040-51-7 (Purity > 95%).
		Negative; a similar compound to an unspecified component of a commercial mixture did not induce chromosome aberrations in human peripheral blood lymphocytes with and without metabolic activation. (Estimated based on analogy)	Chemtura, 2006	Limited study details reported in an MSDS; estimated based on analogy to a similar compound to a component of Firemaster 550 (commercial mixture containing TBB and TBPH); it is not certain if this component contains TBPH; study conducted according to OECD 422.
		Negative; an unspecified component of a commercial mixture showed no evidence of clastogenicity in an *in vitro* cytogenic test. (Estimated)	Chemtura, 2006	No study details reported in an MSDS; estimated based on one component of Firemaster 550 (commercial mixture containing TBB and TBPH); it is not certain if this component contains TBPH.
	Chromosomal Aberrations *in vivo*	Negative for clastogenic effects in an *in vivo* mouse micronucleus assay.	ACC, 2004	Study details reported in a secondary source. Test material was RC9927; FR-45B; CASRN 26040-51-7 (Purity >

Di(2-ethylhexyl) tetrabromophthalate CASRN 26040-51-7				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
				95%).
	DNA Damage and Repair			No data located.
	Other			No data located.
Reproductive Effects		**MODERATE: No reproductive effects were reported in a 2-generation oral (gavage) reproductive toxicity study in rats at doses up to 165 mg/kg-day (highest dose tested) of Firemaster BZ 54 (commercial mixture of TBB and TBPH) with a larger constituent of TBB. The NOAEL of 165 mg/kg-day falls within the Moderate hazard criteria range; it is possible that effects driven by either component may occur within the Moderate hazard range if tested at a higher dose. Exposure to TBPH did not cause adverse changes in testes or ovary weights in a 28-day repeat dose study in rats; however, while reproductive organs and tissues were examined, other reproductive parameters were not reported to have been examined. Data from a reproductive/developmental toxicity screen in rats exposed to a similar compound to a component of Firemaster 550 (commercial mixture containing TBB and TBPH) indicated histopathological effects in female reproductive organs at doses ≥ 25 mg/kg-day (lowest dose tested; a NOAEL was not identified). It is uncertain if the commercial mixture contained TBPH.**		
	Reproduction/Developmental Toxicity Screen	Reproductive/developmental toxicity screen in rats orally administered 0, 25, 100, 400 mg/kg-day of a similar compound to an unspecified component of a commercial mixture. Reduced number of successful pregnancies and viable offspring at doses of 100 and 400 mg/kg-day; histopathological effects reported in thymus and male reproductive organs (testes and epididymides) at 400 mg/kg-day; histopathological effects in female reproductive organs and adrenals at doses of ≥ 25 mg/kg-day. NOAEL: Not established	Chemtura, 2006	Limited study details reported in an MSDS; estimated based on analogy to a similar compound to a component of Firemaster 550 (commercial mixture containing TBB and TBPH); it is not certain if this component contains TBPH; study conducted according to OECD 422.

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PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
		LOAEL: 25 mg/kg-day (lowest dose tested) (Estimated based on analogy)		
		Estimated to have moderate potential for reproductive effects. (Estimated by analogy)	Professional judgment	Estimated based on a closely related confidential analog and professional judgment.
	Combined Repeated Dose with Reproduction/ Developmental Toxicity Screen	2-generation oral (gavage) reproductive toxicity study in rats administered 15, 50, or 165 mg/kg-day Firemaster BZ54; F0 generation was treated 10 weeks prior to pairing through the mating period. Males were treated until termination; females were treated through gestation and lactation, and until termination on PND 21; pup selected (30/sex/dose) to continue as F1 parental generation began treatment on PND 22 and continued treatment similar to the F0 generation. No adverse effects on reproductive performance or fertility in rats. NOAEL: 165 mg/kg-day (highest dose tested) LOAEL: Not established (Estimated)	MPI Research, 2008a	Test substance: Firemaster BZ 54 (commercial mixture of TBB and TBPH) with a larger constituent of TBB; it is not clear which component or components of the mixture are driving the reported developmental effects.
	Reproduction and Fertility Effects	Rat, 28-day repeat dose dietary toxicity study; 0, 200, 2,000, and 20,000 ppm in diet (~0, 21.1, 211, 2,110 mg/kg-day); There were no adverse effects on a full	ACC, 2004	Study details reported in a secondary source. Test material was RC9927; FR-45B; CASRN 26040-51-7 (Purity > 95%). It is reported that a full complement of male and female

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		complement of male and female reproductive organs and tissues examined by gross necropsy and histopathology; No changes in testes and ovary weights. NOAEL: 2,000 ppm (2,110 mg/kg-day - highest dose tested) LOAEL: Not established		reproductive tissues and organs were evaluated, however, the list of tissues and organs is unspecified. While reproductive organs and tissues were examined, other reproductive parameters were not reported to be examined.
	Other	Potential for reproductive effects following long-term exposure to BZ-54 HP (Estimated)	Chemtura, 2008	No study details reported in an MSDS; Estimated based on BZ-54 HP (commercial mixture containing TBB and TBPH); it is not clear which component is driving repeated dose effects.
Developmental Effects		**MODERATE: Developmental effects were reported in a 2-generation reproductive toxicity study in rats and a prenatal study in rats exposed to CN-2065 (a commercial mixture of TBB and TBPH with the predominant constituent being TBB). Developmental effects were reported at doses of 165 mg/kg-day and 100 mg/kg-day in the 2-generation and prenatal studies, respectively. Both studies had a NOAEL of 50 mg/kg-day which falls within the Moderate hazard criteria range. It is not clear which component or components of the commercial mixture caused the reported developmental effects. Development/neurodevelopmental effects were reported in a study in pregnant Wistar rats administered a FM550 mixture (sum total of TBB and TBPH approximately 50%) during gestation though lactation (GD8 - PND21); developmental effects included early female puberty, weight gain, altered exploratory behavior, and increased male left ventricle thickness (LOAEL = 1 mg/kg-day, NOAEL = 0.1 mg/kg-day). It is uncertain which component or components of the FM 550 mixture is driving the reported developmental effects. While the FM 550 mixture data indicates a High hazard potential, it may be the other components driving the reported toxicity. Gestational exposure to the TBPH monoester metabolite TBMEHP at a dose of 200 mg/kg-day resulted in an increased number of altered seminiferous cords (MNGs) per cord area in male fetuses from exposed rat dams. Experimental data indicated no effects on embryonic survival or development in exposed zebrafish embryos.**		
	Reproduction/ Developmental	Estimated to have moderate	Professional judgment	Estimated based on a closely related

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PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
	Toxicity Screen	potential for developmental effects. (Estimated by analogy)		confidential analog and professional judgment.
	Combined Repeated Dose with Reproduction/ Developmental Toxicity Screen	2-generation oral (gavage) reproductive toxicity study in rats administered 15, 50, or 165 mg/kg-day; F0 generation was treated 10 weeks prior to pairing through the mating period. Males were treated until termination; females were treated through gestation and lactation, and until termination on PND 21; pup selected (30/sex/dose) to continue as F1 parental generation began treatment on PND 22 and continued treatment similar to the F0 generation. Parental toxicity: lower body weights and body weight gains during premating period in parental and F1 females at highest dose; Lower body weights in the premating period in F1 males; body weight gains were not affected in males. Developmental toxicity: at highest dose, lower body weights at birth and throughout lactation were reported in both generations of offspring (F1 and F2); this resulted in lower premating body weights of the first female generation. Decreased spleen weights at lactation day 21 in F1 male pups	MPI Research, 2008a	Study details reported in an unpublished report; test substance: Firemaster BZ 54 (CN-2065) commercial mixture of TBB and TBPH with the predominant constituent being TBB; it is not clear which component or components of the mixture are driving the reported developmental effects.

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PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
		and F2 male and female pups. Parental toxicity: NOAEL: 50 mg/kg-day LOAEL: 165 mg/kg-day Developmental toxicity: NOAEL: 50 mg/kg-day LOAEL: 165 mg/kg-day		

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PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
	Prenatal Development	Prenatal study in rats exposed to 0, 50, 100, 300 mg/kg-d Firemaster BZ54 (CN-2065) on GD 6-19. Maternal toxicity: increased incidence of animals with sparse hair in abdominal region, lower gestation body weights and body weight gain, and lower gestation food consumption at doses ≥ 100 mg/kg-day. Developmental toxicity: decreased fetal weight at 100 mg/kg-day; increased incidence of fused cervical vertebral neural arches (litter incidence of 8%) in fetuses at 300 mg/kg-day; increased litter incidence of fetal ossification variations involving additional ossification centers to the cervical vertebral neural arches, incomplete ossified skull bones (jugal, parietal, and squamosal), and unossified sternebrae. Maternal toxicity: NOAEL: 50 mg/kg-day LOAEL: 100 mg/kg-day Developmental toxicity: NOAEL: 50 mg/kg-day LOAEL: 100 mg/kg-day based on decreased fetal weight (Estimated)	MPI Research, 2008b	Study details reported in an unpublished report Test substance: Firemaster BZ54 (CN-2065); commercial mixture of TBB and TBPH with the predominant constituent being TBB; it is not clear which component or components of the mixture are driving the reported developmental effects.

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PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
		Fischer Rats were administered the TBPH metabolite TBMEHP at 0, 200, and 500 mg/kg-day by oral gavage on GDs 18 and 19. Maternal toxicity: There were no treatment related effects on liver, kidney, adrenal gland, or ovary weights at any dose. At the highest dose, there was a significantly decreased level of the liver enzyme alkaline phosphatase and a decreased level of alanine transaminase. Decreased serum calcium levels and increased blood urea nitrogen levels were also reported at the highest dose. There was a dose-dependent decrease in cholesterol levels and serum T3 levels; there was no effect on serum T4 levels. There were no abnormalities in the kidneys or thyroids following treatment; however, there were effects (increased hepatocytes with mitotic spindles and increased hepatocytes with dense hypereosinophilic cytoplasm and condensed, fragmented nuclei) reported. These effects are indications of proliferation and apoptosis. Developmental toxicity: The	Springer et al., 2012	Estimated based on the assumption of total conversion of TBPH to TBMEHP; the test substance is identified as the TBPH metabolite TBMEHP; The doses reported are based on TBMEHP; though TBPH is expected to metabolize to TBMEHP, it is uncertain if these effects would occur or at what dose effects might occur following TBPH exposure.

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PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
		number of manifestation of altered seminiferous cords (MNGs) per cord area were significantly increased in fetuses from exposed dams. There were no reported significant changes in fetal testosterone production. Maternal toxicity: NOAEL: 200 mg/kg-day LOAEL: 500 mg/kg-day (liver effects) Developmental toxicity: NOAEL: Not established LOAEL: 200 mg/kg-day (increased number of fetal MNGs) (Estimated)		
	Postnatal Development			No data located.
	Prenatal and Postnatal Development			No data located.
	Developmental Neurotoxicity			No data located.
	Other	Potential for developmental effects following long-term exposure to BZ-54 HP (Estimated)	Chemtura, 2008	No study details reported in an MSDS; Estimated based on BZ-54 HP (commercial mixture containing TBB and TBPH); it is not clear which component is driving repeated dose effects.
		Pregnant Wistar rats were administered 0, 0.1 or 1 mg/kg-day of FM550 in the diet during gestation and through lactation	Patisaul et al., 2013	Estimated based on data for FM550 mixture; non guideline study; the test substance is a mixture made up of TBB and TBPH (sum total of TBB and

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PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
		(GD8 - PND 21); Maternal toxicity: Increased serum thyroxine (T4) levels in the high dose dams compared to controls was reported. There was no significant change in triiodothyronine (T3) levels in dam serum. Decreased hepatic carboxylesterease activity was also reported in dams in the high dose group. Developmental toxicity: female offspring in the high dose group displayed a significantly earlier vaginal opening when compared to controls. A statistically significant increase in weight was reported in both males and females in the high dose group at PND 120. This effect persisted through PND 180 to PND 220 with high dose males and females having significantly higher weights than same sex controls. A dose-dependent decrease in the number of rats to enter with open arms, (indicating anxiety), was reported in both male and female offspring. Increased blood glucose levels were reported in male offspring in the high-dose group compared to controls. There was no statistically significant difference in heart weight of male or female offspring. Left ventricular (LV) free wall thickness was significantly		TBPH approximately 50%) and other compounds including IPTPP (CASRN 68937-41-7) and TPP (CASRN 115-86-6); it is not clear which component or components of the mixture are driving the reported developmental effects.

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		increased in male offspring in the high dose group; there were no changes in LV thickness in females at any dose. Maternal Toxicity: NOAEL: 0.1 mg/kg-day LOAEL: 1 mg/kg-day Developmental toxicity: NOAEL: 0.1 mg/kg-day LOAEL: 1 mg/kg-day (based on early vaginal opening in females, increased weight in males and females, decreased open arm behavior, increased blood glucose levels in males and increased LV thickness in males) (Estimated)		
		Zebrafish embryos were exposed under static conditions to purified TBPH at concentrations up to 10 µM from 5.25 -96 hours post fertilization (hpf). There were no effects on embryonic survival or development.	McGee et al., 2013	Zebrafish is a nonstandard species; current DfE criteria for this endpoint are based on gestational and/or postnatal exposure to mammalian species. Thus, this study cannot be used to assign a hazard designation for the developmental endpoint.
Neurotoxicity		**MODERATE: Estimated based on analogy to a similar compound to a component of Firemaster 550 (commercial mixture containing TBB and TBPH). There is potential for neurological effects after breathing or swallowing large amounts or after long-term exposure to this analog. There were no neurotoxic effects reported in a 28-day oral toxicity study in rats treated with the analog.**		
	Neurotoxicity Screening Battery (Adult)	28-day sub-chronic oral toxicity study in rats treated with 0, 160, 400, 1,000 mg/kg-day;	Chemtura, 2006	Limited study details reported in an MSDS; neurotoxicity was evaluated in this study; estimated based on one

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PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
		No neurotoxicity effects were reported. NOAEL: 1,000 mg/kg-day (highest dose tested) LOAEL: Not established (Estimated)		component of Firemaster 550 (commercial mixture containing TBB and TBPH); it is not certain if this component contains TBPH.
	Other	Potential for neurological effects following long-term exposure to BZ-54 HP (Estimated)	Chemtura, 2008	No study details reported in an MSDS; Estimated based on BZ-54 HP (commercial mixture containing TBB and TBPH); it is not clear which component is driving repeated dose effects.
		Potential for neurological effects after breathing or swallowing large quantities or repeated exposure over a prolonged period of time is possible for a similar compound to an unspecified component of the commercial mixture. (Estimated based on analogy)	Chemtura, 2006	No study details reported in an MSDS; estimated based on analogy to a similar compound to a component of Firemaster 550 (commercial mixture containing TBB and TBPH); it is not certain if this component contains TBPH.

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Repeated Dose Effects		**MODERATE: There was a slight decrease in body weight along with decreased calcium and phosphorus levels in female rats with a LOAEL= 20,000 ppm (2,110 mg/kg-day). While this effect is known to occur at values that fall within the hazard criteria range for a LOW hazard designation, the NOAEL is identified as 2,000 ppm (211 mg/kg-day). The hazard criteria values are based on 90-day studies; therefore, the hazard criteria values are tripled for chemicals evaluated in 28-day studies. The LOAEL of 2,110 mg/kg-day remains in the Low hazard category, while the NOAEL of 211 mg/kg-day falls within the Moderate hazard designation (30 - 300 mg/kg-day). There is uncertainty as to where effects may occur. A Moderate hazard was designated as a conservative approach. TBPH is also estimated to have a Moderate potential for liver effects cerebral hemorrhages based on a closely related confidential analog and professional judgment and is estimated to have kidney, liver, adrenal, thymus, developmental, reproductive, and neurological effects following long-term exposure to commercial mixtures that included TBPH. There was an increased incidence of sparse hair in abdominal region, reduced body weight, and reduced food consumption in dams during gestation in a prenatal study in rats exposed to CN-2065 (commercial mixture of TBB and TBPH with the predominant constituent being TBB) on GD 6-19 at doses ≥ 100 mg/kg-day (NOAEL = 50 mg/kg-day). Reduced body weight and body weight gain during the premating period in parental F0 and F1 female rats treated with 165 mg/kg-day CN-2065 (NOAEL = 50 mg/kg-day) was also reported in a 2-generation oral reproductive toxicity in rats.**		
		Rat, 28-day dietary toxicity study; 0, 200, 2,000, and 20,000 ppm in diet (~0, 21.1, 211, 2,110 mg/kg-day); There was no mortality, clinical signs of toxicity, or adverse effects on examined organs or tissues; There was a slight decrease in body weight along with decreased calcium and phosphorus levels in females in the 20,000 ppm (2,110 mg/kg-day) group. NOAEL: 2,000 ppm (211 mg/kg-day) LOAEL: 20,000 ppm (2,110 mg/kg-	ACC, 2004	Study details reported in a secondary source. Test material was RC9927; FR-45B; CASRN 26040-51-7 (Purity > 95%). Doses were reported as ppm in the diet but were converted to mg/kg/day using EPA 1988 reference values for body weight and food consumption. The hazard criteria for repeat dose toxicity is based on 90 day studies; the hazard criteria values are tripled for chemicals evaluated in 28-day studies. The LOAEL of 2,110 mg/kg-day remains in the Low hazard category, while the NOAEL of 211 mg/kg-day falls within the Moderate

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PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
		day) based on slightly decreased body weight and decreased calcium and phosphorus levels (females)		hazard designation (30 - 300 mg/kg-day). There is uncertainty as to where effects may occur.
		Estimated to have moderate potential for liver effects and concern for cerebral hemorrhages. (Estimated by analogy)	Professional judgment	Estimated based on a closely related confidential analog and professional judgment.
		Potential for neurological effects after breathing or swallowing large quantities or repeated exposure over a prolonged period of time is possible for a similar compound to an unspecified component of the commercial mixture (Estimated based on analogy)	Chemtura, 2006	No study details reported in an MSDS; estimated based on analogy to a similar compound to a component of Firemaster 550 (commercial mixture containing TBB and TBPH); it is not certain if this component contains TBPH.
		Potential for kidney and liver effects following long-term exposure to BZ-54 HP (Estimated)	Chemtura, 2008	No study details reported in an MSDS; Estimated based on BZ-54 HP (commercial mixture containing TBB and TBPH); it is not clear which component is driving repeated dose effects.
		2-generation oral (gavage) reproductive toxicity study in rats administered 15, 50, or 165 mg/kg-day; F0 generation was treated 10 weeks prior to pairing through the mating period. Males were treated until termination; females were treated through gestation and lactation, and until termination on PND 21; pup selected (30/sex/dose) to continue as F1 parental generation began treatment on PND	MPI Research, 2008a	Study details reported in an unpublished report; test substance: Firemaster BZ 54 (CN-2065) commercial mixture of TBB and TBPH with the predominant constituent being TBB; it is not clear which component or components of the mixture are driving the reported developmental effects.

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PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
		22 and continued treatment similar to the F0 generation. Parental toxicity: lower body weights and body weight gains during premating period in parental and F1 females at highest dose; Lower body weights in the premating period in F1 males; body weight gains were not affected in males. Parental toxicity: NOAEL: 50 mg/kg-day LOAEL: 165 mg/kg-day (reduced body weight and body weight gain) (Estimated)		
		In a prenatal study in rats exposed to 0, 50, 100, 300 mg/kg-d on GD 6-19; dams experienced increased incidence of animals with sparse hair in abdominal region, lower gestation body weights and body weight gain, and lower gestation food consumption at doses ≥ 100 mg/kg-day. NOAEL: 50 mg/kg-day LOAEL (maternal): 100 mg/kg-day (Estimated)	MPI Research, 2008b	Study details reported in an unpublished report Test substance: Firemaster BZ54 (CN-2065); commercial mixture of TBB and TBPH with the predominant constituent being TBB; it is not clear which component or components of the mixture are driving the reported developmental effects.
		28-day sub-chronic oral toxicity study in rats treated with 0, 160, 400, 1,000 mg/kg-day; Kidney effects were reported.	Chemtura, 2006	Limited study details reported in an MSDS; neurotoxicity was evaluated in this study; estimated based on one component of Firemaster 550

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		NOAEL: 160 mg/kg-day LOAEL: 1,000 mg/kg-day based on kidney effects (Estimated)		(commercial mixture containing TBB and TBPH); it is not certain if this component contains TBPH.
Skin Sensitization		**LOW: TBPH is not a skin sensitizer in guinea pigs. There were positive results for skin sensitization following exposure to components of commercial mixtures containing TBPH. It is not certain which component or components caused the reported effects.**		
	Skin Sensitization	Negative for skin sensitization in guinea pigs	ACC, 2004	Study details reported in a secondary source. Test material was RC9927; FR-45B; CASRN 26040-51-7 (Purity > 95%).
		The commercial mixture Firemaster BZ 54 is a skin sensitizer. (Estimated)	Chemtura, 2013	Limited study details reported in an MSDS; Test substance: Firemaster BZ 54 (commercial mixture of TBB and TBPH) with a larger constituent of TBB; it is not clear which component or components of the mixture are driving the reported effects.
		An unspecified component of the commercial mixture was reported to be a sensitizer in a M&K sensitization assay. (Estimated)	Chemtura, 2006	No study details reported in an MSDS; estimated based on one component of Firemaster 550 (commercial mixture containing TBB and TBPH); it is not certain if this component contains TBPH.
		An unspecified component of the commercial mixture was not sensitizing in a Buehler test. (Estimated)	Chemtura, 2006	No study details reported in an MSDS; estimated based on one component of Firemaster 550 (commercial mixture containing TBB and TBPH); it is not certain if this component contains TBPH.

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Respiratory Sensitization		**No data located.**		
	Respiratory Sensitization			No data located.
Eye Irritation		**LOW: TBPH is a slight eye irritant in rabbits. Experimental studies reported mild irritation to components of a commercial mixture.**		
	Eye Irritation	Slight eye irritant in rabbits	ACC, 2004	Study details reported in a secondary source. Test material was RC9927; FR-45B; CASRN 26040-51-7 (Purity > 95%).
		The commercial mixture Firemaster BZ 54 is a slight eye irritant. (Estimated)	Chemtura, 2013	Limited study details reported in an MSDS; Test substance: Firemaster BZ 54 (commercial mixture of TBB and TBPH) with a larger constituent of TBB; it is not clear which component or components of the mixture are driving the reported effects.
		An unspecified component of the commercial mixture was reported to be a slight eye irritant in rabbits. (Estimated)	Chemtura, 2006	No study details reported in an MSDS; estimated based on one component of Firemaster 550 (commercial mixture containing TBB and TBPH); it is not certain if this component contains TBPH.
		No eye irritation was reported in rabbits for a similar compound to an unspecified component of the commercial mixture. (Estimated based on analogy)	Chemtura, 2006	No study details reported in an MSDS; estimated based on analogy to a similar compound to a component of Firemaster 550 (commercial mixture containing TBB and TBPH); it is not certain if this component contains TBPH.
Dermal Irritation		**LOW: TBPH is a slight skin irritant in rabbits. Experimental data reported mild irritation from components of a commercial mixture.**		
	Dermal Irritation	Slight skin irritant in rabbits	ACC, 2004	Study details reported in a secondary source. Test material was RC9927; FR-

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
				45B; CASRN 26040-51-7 (Purity > 95%).
		No skin irritation was reported in rabbits for a similar compound to an unspecified component of the commercial mixture. (Estimated based on analogy)	Chemtura, 2006	No study details reported in an MSDS; estimated based on analogy to a similar compound to a component of Firemaster 550 (commercial mixture containing TBB and TBPH); it is not certain if this component contains TBPH.
		An unspecified component of the commercial mixture was reported to be a slight skin irritant in rabbits. (Estimated)	Chemtura, 2006	No study details reported in an MSDS; estimated based on one component of Firemaster 550 (commercial mixture containing TBB and TBPH); it is not certain if this component contains TBPH.
		The commercial mixture Firemaster BZ 54 is a mild skin irritant. (Estimated)	Chemtura, 2013	Limited study details reported in an MSDS; Test substance: Firemaster BZ 54 (commercial mixture of TBB and TBPH) with a larger constituent of TBB; it is not clear which component or components of the mixture are driving the reported effects.
Endocrine Activity		**One study indicated that TBPH does not cause changes in estrogenic and androgenic activity in yeast reporter-gene assays. Increased serum thyroxine (T4) levels were reported in the serum of dams following oral administration to FM500 (mixture of 50% sum total of TBB and TBPH); other components of the mixture are TPP and IPTPP. It is unclear which component or components of the mixture are driving the endocrine activity effects.**		
		Potential for adrenal effects following long-term exposure to BZ-54 HP (Estimated)	Chemtura, 2008	No study details reported in an MSDS; Estimated based on BZ-54 HP (commercial mixture containing TBB and TBPH); it is not clear which component is driving repeated dose effects.

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PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	Negative for estrogenic and androgenic activity in yeast reporter-gene assays (Beta-galactosidase assay and bioluminescent estrogen and androgen screens using *Saccharomyces cerevisiae*).	Ezechias et al., 2012	Test substance purity: 99.5%
	Pregnant Wistar rats were administered 0, 0.1 or 1 mg/kg-day of FM550 in the diet during gestation and through lactation (GD8 - PND 21); Increased serum thyroxine (T4) levels (increase of 65%) in the high dose dams compared to controls was reported. There was no significant change in triiodothyronine (T3) levels in dam serum. There was no reported statistically significant change in T4 or T3 levels in pup serum on PND 21 when compared to controls. (Estimated)	Patisaul et al., 2013	Estimated based on data for FM550 mixture; non guideline study; the test substance identified as FM550 is a mixture made up of TBB, TBPH (sum total of TBB and TBPH is approximately 50%), TPP and IPTPP; it is not clear which component or components of the mixture are driving the reported endocrine activity effects.
	Reproductive/developmental toxicity screen in rats orally administered 0, 25, 100, 400 mg/kg-day of a similar compound to an unspecified component of a commercial mixture. Reduced number of successful pregnancies and viable offspring at doses of 100 and 400 mg/kg-day; histopathological effects reported in	Chemtura, 2006	Limited study details reported in an MSDS; estimated based on analogy to a similar compound to a component of Firemaster 550 (commercial mixture containing TBB and TBPH); it is not certain if this component contains TBPH; study conducted according to OECD 422.

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		thymus and male reproductive organs (testes and epididymides) at 400 mg/kg-day; histopathological effects in female reproductive organs and adrenals at doses of 25 mg/kg-day. NOAEL: Not established LOAEL: 25 mg/kg-day (lowest dose tested) (Estimated based on analogy)		
Immunotoxicity		**No data located. There is potential for immunotoxicity based on the structural alert for polyhalogenated aromatic hydrocarbons and professional judgment.**		
	Immune System Effects	Potential for thymus effects following long-term exposure to BZ-54 HP (Estimated)	Chemtura, 2008	No study details reported in an MSDS; Estimated based on BZ-54 HP (commercial mixture containing TBB and TBPH); it is not clear which component is driving repeated dose effects.
		Potential for immunotoxicity based on the structural alert for polyhalogenated aromatic hydrocarbons (Estimated)	Professional judgment	Estimated based on a structural alert for polyhalogenated aromatic hydrocarbons and professional judgment.
ECOTOXICITY				
ECOSAR Class		Esters		
Acute Aquatic Toxicity		**LOW: Based on an estimated Log Kow of 12 and the fact that the experimental effect levels in fish, daphnia, and algae were above the estimated water solubility (1.98 E-9 mg/L), NES are predicted for this endpoint.**		
Fish LC_{50}		Fish 96-hour LD_{50} = No effects at saturation (NES) (Experimental)	Submitted confidential study	Study details reported in a submitted confidential study.

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PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	Oncorhynchus mykiss rainbow trout 96-hour LC_{50} >12 mg/L (Estimated)	Chemtura, 2006, 2013	No study details reported in an MSDS; estimated based on one component of Firemaster 550 and for Firemaster BZ-54 (commercial mixtures containing TBB and TBPH); Based on log K_{ow} of 12 and the reported effect level was above the estimated water solubility (1.983×10^{-9} mg/L), NES are predicted for this endpoint.
	Oncorhynchus mykiss rainbow trout 96-hour LC_{50} = 1.6 mg/L (Estimated by analogy)	Chemtura, 2006	No study details reported in an MSDS; estimated based on analogy to a similar compound to a component of Firemaster 550 (commercial mixture containing TBB and TBPH); it is not certain if this component contains TBPH. Based on log K_{ow} of 12 and the reported effect level was above the estimated water solubility (1.983×10^{-9} mg/L), NES are predicted for this endpoint.
	Fathead minnow 96-hour LC_{50} = 10.8 mg/L (Estimated by analogy)	Chemtura, 2006	No study details reported in an MSDS; estimated based on analogy to a similar compound to a component of Firemaster 550 (commercial mixture containing TBB and TBPH); it is not certain if this component contains TBPH. Based on log K_{ow} of 12 and the reported effect level was above the estimated water solubility (1.983×10^{-9} mg/L), NES are predicted for this endpoint.
	Fish 96-hour LC_{50} < 0.001 mg/L (Estimated)	ECOSAR v1.11	NES: The estimated log K_{ow} of 12 for this chemical exceeds the SAR

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PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	ECOSAR: Esters		limitation for log K_{ow} of 5.0; NES are predicted for these endpoints.
	Fish 96-hour LC_{50} < 0.001 mg/L (Estimated) ECOSAR: Neutral organics	ECOSAR v1.11	NES: The estimated log K_{ow} of 12 for this chemical exceeds the SAR limitation for log K_{ow} of 5.0; NES are predicted for these endpoints. Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.
Daphnid LC_{50}	*Daphnia magna* 48- hour EC_{50}= 0.30 mg/L (immobility) (Experimental)	ACC, 2004	Study details reported in a secondary source. Test material was RC9927; FR-45B; CASRN 26040-51-7 (Purity > 95%). Based on an estimated log K_{ow} of 12 and the fact that the experimental effect levels in Daphnia were above the estimated water solubility (1.983×10^{-9} mg/L), NES are predicted for this endpoint.
	Daphnia magna 48-hour LC_{50} = 2.44 mg/L (Estimated by analogy)	Chemtura, 2006	No study details reported in an MSDS; estimated based on analogy to a similar compound to a component of Firemaster 550 (commercial mixture containing TBB and TBPH); it is not certain if this component contains TBPH. Based on log K_{ow} of 12 and the reported effect level was above the estimated water solubility (1.983×10^{-9} mg/L), NES are predicted for this

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PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
			endpoint.
	Daphnia magna 48-hour EC_{50} = 0.42 mg/L (Estimated)	Submitted confidential study; Chemtura, 2006, 2013	Study details reported in an unpublished study submitted to EPA. Limited study details were also reported in an MSDS; estimated based on one component of Firemaster 550 and for Firemaster BZ-54 (commercial mixture containing TBB and TBPH); Based on log K_{ow} of 12 and the reported effect level was above the estimated water solubility (1.983×10^{-9} mg/L), NES are predicted for this endpoint.
	Daphnia magna 24-hour EC_{50} = 1.2 mg/L (Estimated)	Submitted confidential study	Study details reported in an unpublished study submitted to EPA; Limited study details were also reported in an MSDS; estimated based on one component of Firemaster 550 and for Firemaster BZ-54 (commercial mixtures containing TBB and TBPH); Based on log K_{ow} of 12 and the reported effect level was above the estimated water solubility.
	Daphnia 48-hour LC_{50} < 0.001 mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	NES: The estimated log K_{ow} of 12 for this chemical exceeds the SAR limitation for log K_{ow} of 5.0; NES are predicted for these endpoints.
	Daphnid 48-hour LC_{50} < 0.001 mg/L (Estimated) ECOSAR: Neutral organics	ECOSAR v1.11	NES: The estimated log K_{ow} of 12 for this chemical exceeds the SAR limitation for log K_{ow} of 5.0; NES are predicted for these endpoints. Narcosis classes (neutral organics) are

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PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
			provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.
Green Algae EC_{50}	Green algae 96-hour LC_{50} = No effects at saturation (NES) (Experimental)	Submitted confidential study	Study details reported in an unpublished study submitted to EPA.
	Green algae 96-hour < 0.001mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	NES: The estimated log K_{ow} of 12 for this chemical exceeds the SAR limitation for log K_{ow} of 6.4; NES are predicted for these endpoints.
	Green algae 96-hour EC_{50} < 0.001 mg/L (Estimated) ECOSAR: Neutral organics	ECOSAR v1.11	NES: The estimated log K_{ow} of 12 for this chemical exceeds the SAR limitation for log K_{ow} of 6.4; NES are predicted for these endpoints. Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.
	Selenastrum capricornutum 96-hour EC_{50} >5.1 mg/L (Estimated)	Chemtura, 2006, 2013	No study details reported in an MSDS; estimated based on one component of Firemaster 550 and for Firemaster BZ-54 (commercial mixture containing TBB and TBPH); based on log K_{ow} of 12 and the reported effect level was above the estimated water solubility (0.000011 mg/L), NES are predicted

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PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
			for this endpoint.
Chronic Aquatic Toxicity	**LOW: Based on estimated chronic toxicity values for fish, daphnid, and algae that suggest no effects at saturation (NES). An experimental effect level for an analog in algae was above the estimated water solubility (1.98 E-9 mg/L) also suggesting NES.**		
Fish ChV	Fish ChV < 0.001 mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	NES: The estimated log K_{ow} of 12 for this chemical exceeds the SAR limitation for log K_{ow} of 8.0; NES are predicted for these endpoints.
	Fish ChV < 0.001 mg/L (Estimated) ECOSAR: Neutral organics	ECOSAR v1.11	NES: The estimated log K_{ow} of 12 for this chemical exceeds the SAR limitation for log K_{ow} of 8.0; NES are predicted for these endpoints. Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.
Daphnid ChV	Daphnia ChV < 0.001 mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	NES: The estimated log K_{ow} of 12 for this chemical exceeds the SAR limitation for log K_{ow} of 8.0; NES are predicted for these endpoints.
	Daphnid ChV < 0.001 mg/L (Estimated) ECOSAR: Neutral organics	ECOSAR v1.11	NES: The estimated log K_{ow} of 12 for this chemical exceeds the SAR limitation for log K_{ow} of 8.0; NES are predicted for these endpoints. Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use

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PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
			the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.
Green Algae ChV	Green algae 72-hour NOAEC = 0.31 mg/L 96-hour NOAEC = 1.3 mg/L (Estimated by analogy)	Chemtura, 2006	No study details reported in an MSDS; estimated based on analogy to a similar compound to a component of Firemaster 550 (commercial mixture containing TBB and TBPH); it is not certain if this component contains TBPH. Based on log K_{ow} of 12 and the reported effect level was above the estimated water solubility (1.983×10^{-9} mg/L), NES are predicted for this endpoint.
	Green algae ChV < 0.001 mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	NES: The estimated log K_{ow} of 12 for this chemical exceeds the SAR limitation for log K_{ow} of 8.0; NES are predicted for these endpoints.
	Green algae ChV < 0.001 mg/L (Estimated) ECOSAR: Neutral organics	ECOSAR v1.11	NES: The estimated log K_{ow} of 12 for this chemical exceeds the SAR limitation for log K_{ow} of 8.0; NES are predicted for these endpoints. Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
ENVIRONMENTAL FATE				
Transport		**Level III fugacity models incorporating available physical and chemical property data indicate that at steady state, TBPH is expected to be found primarily in soil and to a lesser extent, water. Hydrolysis of TBPH is not expected to occur at a significant rate at environmentally-relevant pH conditions. TBPH is expected to have low mobility in soil based on its measured K_{oc} value. Leaching of TBPH through soil to groundwater is not expected to be an important transport mechanism. Estimated volatilization half-lives indicate that it will be non-volatile from surface water. In the atmosphere, TBPH is expected to exist in the particulate phase, based on its estimated vapor pressure. Particulates will be removed from air by wet or dry deposition.**		
	Henry's Law Constant (atm-m^3/mole)	$3x10^{-7}$ (Estimated)	EPI v4.11	Estimated by the HENRYWIN Group SAR Method with no measured chemical property inputs.
	Sediment/Soil Adsorption/Desorption - K_{oc}	>28,840 (Measured)	Submitted confidential study	Limited study details available; the degree of precision reported is atypical for this type of study and expected to be beyond the capabilities of known test methods.
		>30,000 (Estimated)	EPI v4.11	Cutoff value for non-mobile compounds.
	Level III Fugacity Model	Air = 0.2% Water = 12% Soil = 88% Sediment = 0.01% (Estimated)	EPI v4.11	This estimation was obtained using the Level III Fugacity model based on the equal emissions distribution assumption with no measured chemical property inputs.

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Persistence		**HIGH: The primary removal processes of TBPH produce persistent metabolites and degradation products resulting in a high persistence designation. TBPH was reported to have a half-life of 3.5 days in water and 8.5 days in sediment in a confidential shake flask die-away test. In two closed bottle tests <4 or 2% of theoretical oxygen demand in a Closed Bottle test was reported after 28 days. TBPH has an estimated half-life of 120 days in soil where it is mainly expected to partition. TBPH is not expected to undergo hydrolysis at appreciable rates. Hydrolysis rates are expected to be pH-dependent and may be limited the by low water solubility of this compound. TBPH has the potential to undergo photodegradation, in an experimental study, half-lives of 147 to 220 minutes were obtained in the presence of organic solvents. The vapor phase reaction half-life of TBPH with atmospheric hydroxyl radicals is estimated at <1 day, although it is expected to exist primarily in the particulate phase in air.**		
Water	**Aerobic Biodegradation**	Passes Ready Test: No Test method: OECD TG 301D: Closed Bottle Test <4% ThOD after 10 days (Measured)	Health & Environmental Horizons Ltd, 2003	Adequate guideline study.
		Passes Ready Test: No Test method: OECD TG 301B: CO_2 Evolution Test 2% degradation as measured by CO_2 production after 28 days using the modified Sturm (OECD 301B) test (Measured)	ACC, 2004	Adequate guideline studies.
		Study results: 50%/8.5 days Test method: Shake Flask Performed in water with suspended sediment (Measured)	Submitted confidential study	Adequate guideline study. Although limited experimental data were available, the anticipated degradation product, mono(2-ethylhexyl) tetrabromophthalate, is anticipated to be resistant to degradation under the test conditions.
		Study results: 50%/3.5 days	Submitted confidential study	Adequate guideline study. Although

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PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
		Test method: Die-Away Shake flask die away test (Measured)		limited experimental data were available, the anticipated degradation product, mono(2-ethylhexyl) tetrabromophthalate, is anticipated to be resistant to degradation under the test conditions.
		Weeks (Primary Survey Model) Months (Ultimate Survey Model) (Estimated for degradation product)	EPI v4.11	Estimated for the degradation product mono(2-ethylhexyl) tetrabromophthalate.
	Volatilization Half-life for Model River	210 days (Estimated)	EPI v4.11	Based on the magnitude of the estimated Henry's Law constant.
	Volatilization Half-life for Model Lake	>1 year (Estimated)	EPI v4.11	Based on the magnitude of the estimated Henry's Law constant.
Soil	**Aerobic Biodegradation**			No data located.
	Anaerobic Biodegradation	Not probable	EPI v4.11; Holliger et al., 2004	The estimated value addresses the potential for ultimate biodegradation. However, there is potential for primary anaerobic biodegradation of haloaromatic compounds by reductive dehalogenation.
	Soil Biodegradation with Product Identification			No data located.
	Sediment/Water Biodegradation			No data located.
Air	**Atmospheric Half-life**	0.5 days Based on a 12-hour day. (Estimated)	EPI v4.11	
Reactivity	**Photolysis**	Half-life = 220 min. in methanol Half-life = 169 min. in tetrahydrofuran Half-life = 147 min. in toluene Di and tribrominated analogues of TBPH (most of which were also	Davis and Stapleton, 2009	The half-life and rate data are not relevant to removal rates in the environment as the test substance was dissolved in organic solvents. However, the results demonstrate the potential for some debromination.

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		missing both alkane branches) were identified by electron capture negative ion/mass spectrometry ECNI/MS as the most dominant photodegradation products (Measured)		
	Hydrolysis	Half-life of 29 days at pH 7; 3 days at pH 8 (Estimated)	EPI v4.11	Hydrolysis rates are expected to be pH-dependent and may be limited the by low water solubility of this compound.
		50%/>1 year at pH 4, 7, and 9 (Measured)	Submitted confidential study	Limited study details. Data indicate the resistance of the material to hydrolysis under environmental conditions.
Environmental Half-life		Aquatic mesocosm study; a controlled source of TBPH was applied and analyzed by GC-MS over the course of the study TBPH was detected in both the particulate and sediment compartment samples (Measured)	de Jourdan et al., 2013	This field study provides data about the partitioning and fate/persistence of this compound under environmental conditions.
		120 days in soil (Estimated)	PBT Profiler	Half-life estimated for the predominant compartment (soil), as determined by EPI methodology.
Bioaccumulation		**HIGH: The bioaccumulation hazard designation is estimated based on TBPH monitoring data reporting detections in many different species including those higher on the food chain. In addition, a stable metabolite and degradation product of TBPH is expected to have a moderate bioaccumulation designation based on an estimated BAF value. Although the experimental BAF is low, the persistence of TBPH and its detection in many species from different habitats and trophic levels indicates potential for a high bioaccumulation designation in aquatic or terrestrial species.**		
	Fish BCF	6.2 Reported as a range: 1.7 - 6.2 (Measured)	Submitted confidential study	Adequate guideline study.
		56 (Estimated for metabolite)	EPI v4.11	Estimations run for mono(2-

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PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
				ethylhexyl) tetrabromophthalate, with a SMILES: O=C(OCC(CC)CCCC)c(c(c(c(c1Br)Br)Br)C(=O)O)c1Br.
	Other BCF			No data located.
	BAF	2.4 (Estimated)	EPI v4.11	
		Fish were orally exposed to commercial flame retardant formulations including Firemaster BZ-54®, containing TBPH, for 56 days and depurated (e.g., fed clean food) for 22 days; homogenized fish tissues were extracted and analyzed on day 0 and day 56 using gas chromatography electron-capture negative ion mass spectrometry (GC/ECNI-MS). 2,3,4,5-tetrabromo-ethylhexylbenzoate (TBB) and TBPH, were detected in tissues at approximately 1% of daily dosage along with brominated metabolites (Measured)	Bearr et al., 2010	BAFs were not calculated. Non guideline study indicates that absorption of this compound can occur in fish following dietary exposure.
		TBPH was detected in liver tissues in rat dams. The pregnant rats were administered 0, 0.1 or 1 mg/kg-day of FM550 by oral gavage across gestation and through lactation (GD8 - PND 21). (Measured)	Patisaul et al., 2013	BAFs were not calculated. Non guideline study indicates that absorption of this compound can occur in rats through oral exposure; the test substance identified as FM550 is a mixture made up of TBPH, TBB (CASRN 183658-27-7), IPTPP (CASRN 68937-41-7) and TPP (CASRN 115-86-6).

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		169 Upper trophic Log BAF = 2.23 Mid trophic Log BAF = 3.17 Lower trophic Log BAF = 3.78 (Estimated for metabolite)	EPI v4.11	Estimations run for mono(2-ethylhexyl) tetrabromophthalate, with a SMILES: O=C(OCC(CC)CCCC)c(c(c(c(c1Br)Br)Br)C(=O)O)c1Br.
	Metabolism in Fish			No data located.
ENVIRONMENTAL MONITORING AND BIOMONITORING				
Environmental Monitoring		TBPH was detected in particle-phase air samples collected from the Canadian High Arctic, near the shores of the Great Lakes, Thailand, and the Tibetan Plateau. TBPH was detected in the marine atmosphere from the East Indian Archipelago toward the Indian Ocean and further toward Antarctica. TBPH was detected in seawater from the European Arctic. TBPH was detected in sediment samples from the Yadkin River in North Carolina. TBPH was detected in dust from Belgian, Canada, Kuwait, New Zealand, Pakistan, Sweden, Eastern Romania, United States and airplanes (Stapleton et al., 2008; Harju et al., 2009; Ali et al., 2011, 2012, 2013; Moller et al., 2011, 2012; Covaci et al., 2012; Dodson et al., 2012; EFSA, 2012; LaGuardia et al., 2012; Ma et al., 2012; Sahlstrom et al., 2012; Shoeib et al., 2012; Xiao et al., 2012; Allen et al., 2013).		
Ecological Biomonitoring		TBPH was detected in bivalve (*Corbicula fluminea*); finless porpoise; gastropod (*Elimia proxima*); fish; ring-billed gulls; cod liver oil supplement; Elvers; humpback dolphin (Hoh et al., 2009; Lam et al., 2009; EFSA, 2012; Gentes et al., 2012; LaGuardia et al., 2012; Sagerup et al., 2010; Suhring et al., 2013).		
Human Biomonitoring		This compound was detected human serum samples. This chemical was not included in the NHANES biomonitoring report (CDC, 2013; He et al., 2013).		

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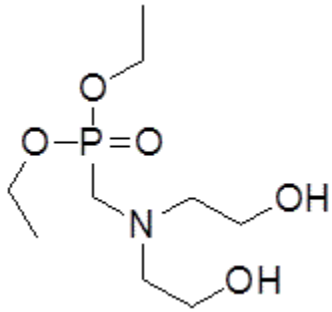
Diethyl bis(2-hydroxyethyl)aminomethylphosphonate

Screening Level Toxicology Hazard Summary

This table contains hazard information for each chemical; evaluation of risk considers both hazard and exposure. Variations in end-of-life processes or degradation and combustion by-products are discussed in the report but not addressed directly in the hazard profiles. The caveats listed below must be taken into account when interpreting the information in the table.

VL = Very Low hazard L = Low hazard M = Moderate hazard H = High hazard VH = Very High hazard – Endpoints in colored text (VL, L, M, H, and VH) were assigned based on empirical data. Endpoints in black italics *(VL, L, M, H,* and *VH*) were assigned using values from estimation software and professional judgment [(Quantitative) Structure Activity Relationships "(Q)SAR"].

Chemical	CASRN	Human Health Effects											Aquatic Toxicity		Environmental Fate	
		Acute Toxicity	Carcinogenicity	Genotoxicity	Reproductive	Developmental	Neurological	Repeated Dose	Skin Sensitization	Respiratory Sensitization	Eye Irritation	Dermal Irritation	Acute	Chronic	Persistence	Bioaccumulation
Diethyl bis(2-hydroxyethyl)aminomethylphosphonate	2781-11-5	L	*M*	M	L	L	*M*	*M*	*M*		L	VL	M	*L*	H	*L*



CASRN: 2781-11-5

MW: 255.25

MF: $C_9H_{22}NO_5P$

Physical Forms: Liquid
Neat: Liquid

Use: Flame retardant

SMILES: O=P(OCC)(OCC)CN(CCO)CCO

Synonyms: Diethyl bis(2-hydroxyethyl)aminomethylphosphonate; Phosphonic acid, ((bis(2-hydroxyethyl)amino)methyl)-, diethyl ester; Diethyl ((N,N-bis(2-hydroxyethyl)amino)methyl)phosphonate; O,O-Diethyl N,N-bis(2-hydroxyethyl)aminomethyl phosphonate
Tradenames: Fyrol 6; LEVAGARD 4090 N; ADEKA FC 450

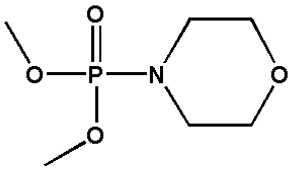
Chemical Considerations: The substance is a discrete chemical, but is sold at 70-90% purity. The substance, Phosphonic acid, P-[[bis(2-hydroxyethyl)amino]methyl]-, diethyl ester, reacts into the polymer during curing. The major impurities are most likely residual starting materials diethylphosphite, diethanolamine and formaldehyde. EPI v4.11 was employed to estimate physical/chemical and environmental fate values due to an absence of experimental data (Supresta, 2006).

Polymeric: No
Oligomeric: Not applicable

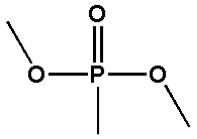
Metabolites, Degradates and Transformation Products: Hydrolysis products are diethylphosphite (762-04-9) and the diethanolamine/formaldehyde reaction product (72624-00-1); this latter substance can further degrade to form diethanolamine (111-42-2) and formaldehyde (50-00-0) (Sturtz et al., 1977; Professional judgment).

Analog: Phosphonic acid, 4-morpholinyl-, dimethyl ester (DMMPA; CASRN 597-25-1), phosphonic acid, P-methyl-, dimethyl ester (DMMP; CASRN 756-79-6) and phosphonic acid, dimethyl ester (DMP; CASRN 868-85-9)
Endpoint(s) using analog values: Carcinogenicity

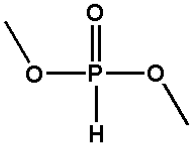
Analog Structure:



Phosphonic acid, 4-morpholinyl-, dimethyl ester (CASRN 597-25-1)



Phosphonic acid, P-methyl-, dimethyl ester (CASRN 756-79-6)



Phosphonic acid, dimethyl ester (CASRN 868-85-9)

Structural Alerts: Organophosphates, Neurotoxicity; Amines, Kidney Toxicity (EPA, 2012).
Risk Phrases: Not classified by Annex VI Regulation (EC) No 1272/2008 (ESIS, 2012).
Hazard and Risk Assessments: Hazard Characterization by EPA in September 2009 (EPA, 2009).

Diethyl bis(2-hydroxyethyl)aminomethylphosphonate CASRN 2781-11-5			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
PHYSICAL/CHEMICAL PROPERTIES			
Melting Point (°C)	-43 (Measured)	LANXESS, 2012	Nonguideline study, sufficient details were not available to assess the quality of this study.
Boiling Point (°C)	>170 Decomposes Results from a thermo gravimetric (TG) study run from 100-700°C. (Measured)	Kettrup et al., 1990	Adequate, value obtained from peer-reviewed primary source. The study showed that vaporization and decomposition occur simultaneously, and that 88% degradation had taken place by 700°C.
	>300 (Estimated)	EPI v4.11; EPA, 1999	Cutoff value for high boiling compounds according to HPV assessment guidance; decomposition likely occurs before the boiling point is reached.
	196 OECD 103 and EPA OPPTS 830.7220 test guidelines (Measured)	Supresta, 2006; Professional judgment	Adequate, decomposition occurs upon boiling as described in additional sources, above. The data are for the commercial mixture, reported as 85% purity. It is possible that this measured boiling point reflects vaporization of these impurities as well as vaporization of the test substance.
Vapor Pressure (mm Hg)	$3.3x10^{-7}$ at 25°C (Estimated)	EPI v4.11	
	0.43 at 20°C OECD 104 test guideline study employing the Isoteniscopic method. (Measured)	Supresta, 2006; Professional judgment	Inadequate, the data is for the commercial mixture, which is reported to have only 70-90% purity. The results are likely due to volatile impurities in the substance.
Water Solubility (mg/L)	900,000 (Measured) OECD 105 test guideline study, flask method.	Supresta, 2006	Adequate, guideline study. The data are for the commercial mixture, reported as 70-90% purity.

Diethyl bis(2-hydroxyethyl)aminomethylphosphonate CASRN 2781-11-5			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	1,000,000 (Estimated)	EPI v4.11	The estimated value is close to the measured value of 900,000 mg/L.
Log K_{ow}	-0.72 OECD 105 test guideline study. (Measured)	Supresta, 2006	Adequate, guideline study. The data are for the commercial mixture, with 70-90% purity.
Flammability (Flash Point)	86.5 EG A 9/DIN EN ISO 2719 method (Measured)	LANXESS, 2012	Nonguideline study, sufficient details were not available to assess the quality of this study.
	Not flammable (Estimated)	Professional judgment	No experimental data located; based on its use as a flame retardant.
Explosivity	Not expected to form explosive mixtures with air. (Estimated)	Professional judgment	No experimental data located; based on its use as a flame retardant.
Pyrolysis			No data located.
pH	8 (Measured)	LANXESS, 2012	Nonguideline study, sufficient details were not available to assess the quality of this study, which was carried out on a 10% solution in water.
pK_a	pK_b for nitrogen = 5.2 (Estimated)	ACE, 2013	Adequate, indicates that in solution this substance is a weak base.
	pK_b for nitrogen = 5.6 (Estimated)	HSDB, 2005	Adequate, indicates that in solution this substance is a weak base. Value obtained from peer-reviewed secondary source.
HUMAN HEALTH EFFECTS			
Toxicokinetics	**No data were located**		
Dermal Absorption *in vitro*			No data located.
Absorption, Distribution, Metabolism & Excretion — **Oral, Dermal or Inhaled**			No data located.
Absorption, Distribution, Metabolism & Excretion — **Other**			No data located.

Diethyl bis(2-hydroxyethyl)aminomethylphosphonate CASRN 2781-11-5				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Acute Mammalian Toxicity		**LOW: Based on an oral LD_{50} > 5000 mg/kg bw in rats and a dermal LD_{50} > 2,000 mg/kg bw in rabbits. No data were located for the inhalation route of exposure.**		
Acute Lethality	**Oral**	Rat 14-day oral LD_{50} >5,000 mg/kg bw Test conditions: 10 rats per sex; gavage (in corn oil) at 5,000 mg/kg bw; 14-day observation Results: clinical signs; all animals appeared normal by day 2	Supresta, 2006; EPA, 2009	Adequate; guideline study (EPA guidelines for pesticide registration; Fed. Reg. 43:163, 37336-37402 [1978]; OECD [1981]) Summarized in reliable secondary sources; Test substance: Fyrol 6; purity not specified.
	Dermal	Rabbit 14-day dermal LD_{50} >2,000 mg/kg bw Test conditions: 5 rabbits per sex; 24-hour dermal application at 2,000 mg/kg bw; 14-day observation Results: Clinical signs, dermal irritation; no deaths; all animals appeared normal by day 2	Supresta, 2006; EPA, 2009	Adequate; guideline study (EPA guidelines for pesticide registration; Fed. Reg. 43:163, 37336-37402 [1978]; OECD [1981]) Summarized in reliable secondary sources. Test substance: Fyrol 6; purity not specified.
	Inhalation			No data located.
Carcinogenicity		**MODERATE: Data for three structurally similar analogs indicate evidence of carcinogenicity in laboratory animals. Rats exposed orally to DMP, DMMP or DMMPA had increased incidence of lung tumors, leukemia, or kidney tumors but mice exposed orally to DMP or DMMPA did not have increased tumor incidence. While there is no evidence to indicate this compound is a suspected human carcinogen, the evidence of carcinogenicity in laboratory animals for the analogs and the uncertainty based on lack of studies on this compound warrants a Moderate hazard designation.**		
	OncoLogic Results			No data located.
	Carcinogenicity (Rat and Mouse)	Rats (F344) were orally administered 0, 100, 200 mg/kg-day (male) and 0, 50, and 100 mg/kg-day (female) of the analog DMP for 103 weeks. There is evidence of carcinogenicity in males following exposure (increased incidence of squamous	OECD SIDS, 2004	Estimated based on analogy to phosphonic acid, dimethyl ester (CASRN 868-85-9); data reported in a secondary source.

Diethyl bis(2-hydroxyethyl)aminomethylphosphonate CASRN 2781-11-5				
PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
		cell carcinoma in lung and alveolar/bronchial cell adenoma or carcinoma) Equivocal evidence was reported for female rats. (Estimated by analogy)		
		Mice (B6C3F1) were orally administered 0, 100, 200 mg/kg-day of the analog DMP. There was no evidence of carcinogenicity in male or female mice. (Estimated by analogy)	OECD SIDS, 2004	Estimated based on analogy to phosphonic acid, dimethyl ester (CASRN 868-85-9); data reported in a secondary source.
		IARC classification: The analog DMP "is not classifiable as to its carcinogenicity to humans (group 3)". (Estimated by analogy)	IARC, 1999	Estimated based on analogy to phosphonic acid, dimethyl ester (CASRN 868-85-9); IARC classification; estimated based on analogy to phosphonic acid, dimethyl ester (CASRN 868-85-9); data reported in a secondary source.
	Combined Chronic Toxicity/Carcinogenicity	In a 2-year toxicology and carcinogenicity study, F344/N rats were orally administered the analog DMMPA at a dose of 0, 150, 300, 600 mg/kg-day for 103 weeks. There was some evidence of carcinogenicity for male and female rats (increased incidence of mononuclear cell leukemia). (Estimated by analogy)	NTP, 1986	Estimated based on analogy to Phosphonic acid, 4-morpholinyl-, dimethyl ester (CASRN 597-25-1).

Diethyl bis(2-hydroxyethyl)aminomethylphosphonate CASRN 2781-11-5				
PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
		In a 2-year toxicology and carcinogenicity study, B6C3F1 mice were orally administered the analog DMMPA at a dose of 0, 150, 300, 600 mg/kg-day for 103 weeks. There was no evidence of carcinogenicity for male or female rats. (Estimated by analogy)	NTP, 1986	Estimated based on analogy to Phosphonic acid, 4-morpholinyl-, dimethyl ester (CASRN 597-25-1).

Diethyl bis(2-hydroxyethyl)aminomethylphosphonate CASRN 2781-11-5				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		In a 2-year toxicology and carcinogenicity study, F344/N rats were orally administered the analog Fyrol DMMP at a dose of 0, 500, or 1,000 mg/kg-day for 2 years. There was some evidence of carcinogenic activity in male rats (increased incidences of tubular cell hyperplasia, tubular cell adenocarcinomas, hyperplasia of the transitional cell epithelium, and transitional cell papillomas of the kidney). There was also increased incidence of mononuclear cell leukemia in male rats at the highest dose. No evidence of carcinogenic activity for female rats was reported. (Estimated by analogy)	NTP, 1987	Estimated based on analogy to phosphonic acid, P-methyl-, dimethyl ester (CASRN 756-79-6).
	Other			No data located.
Genotoxicity		**MODERATE: Based on weight of evidence from multiple studies. Diethyl bis(2-hydroxyethyl)aminomethylphosphonate produced chromosomal aberrations and gene mutations in mammalian cells *in vitro*. In contrast, negative results were obtained in gene mutation tests in bacteria and no cell transformation was evident in mammalian cells. No *in vivo* studies were located.**		
	Gene Mutation *in vitro*	Positive; Fyrol 6 (purity not specified) was weakly mutagenic to mouse lymphoma cell line (L5178Y) with and without metabolic activation	Supresta, 2006; EPA, 2009	Adequate studies summarized in reliable secondary sources.

Diethyl bis(2-hydroxyethyl)aminomethylphosphonate CASRN 2781-11-5				
PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
		Negative; Fyrol 6 (purity not specified) was not mutagenic in S. cerevisiae strain D4 with or without metabolic activation	Supresta, 2006; EPA, 2009	Adequate study summarized in reliable secondary sources.
		Negative; Fyrol 6 (purity not specified) was not mutagenic in S. typhimurium strains TA98, TA100, TA1535, TA1537, TA1538 with or without metabolic activation	Supresta, 2006; EPA, 2009	Adequate study summarized in reliable secondary sources.
	Gene Mutation *in vivo*			No data located.
	Chromosomal Aberrations *in vitro*	Positive; Fyrol 6 (purity not specified) caused increased chromosomal aberrations in mouse lymphoma cells (L5178Y) with and without metabolic activation	Supresta, 2006; EPA, 2009	Adequate study summarized in reliable secondary sources.
	Chromosomal Aberrations *in vivo*			No data located.
	DNA Damage and Repair			No data located.
	Other	Negative; Fyrol 6 (purity not specified) did not cause cell transformation in BALB/3T3 cells with or without metabolic activation	Supresta, 2006	Adequate study summarized in reliable secondary sources.

Diethyl bis(2-hydroxyethyl)aminomethylphosphonate CASRN 2781-11-5				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Reproductive Effects		**LOW: Based on a NOAEL of 750 mg/kg-day (LOAEL not established) in a combined reproductive/developmental toxicity screen in rats. No significant reproductive effects were observed.**		
	Reproduction/Developmental Toxicity Screen	Combined reproductive/developmental toxicity screen in Sprague-Dawley rats (12/sex/dose) Fyrol 6 (purity 85%) administered by gavage at 50, 250, or 750 mg/kg-day for 2 weeks prior to mating, during mating, gestation, lactation (females) Results: No effects on clinical signs, mortality, parental body weights, food consumption, reproductive or developmental indices, histopathology. Systemic toxicity: NOAEL: 750 mg/kg-day (highest dose tested) LOAEL: Not established Reproductive toxicity: NOAEL: 750 mg/kg-day (highest dose tested) LOAEL: Not established	Supresta, 2006; EPA, 2009	Adequate; guideline study (OECD 421) summarized in reliable secondary sources; True NOAELs may be > 750 mg/kg-day; No LOAELs were established in the study.
	Combined Repeated Dose with Reproduction/ Developmental Toxicity Screen			No data located.
	Reproduction and Fertility Effects			No data located.
	Other			No data located.

Diethyl bis(2-hydroxyethyl)aminomethylphosphonate CASRN 2781-11-5				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Developmental Effects		**LOW: Based on a NOAEL of 750 mg/kg-day (LOAEL not established) in a combined reproductive/developmental toxicity screen in rats. No significant developmental effects were observed.**		
	Reproduction/ Developmental Toxicity Screen	Combined reproductive/developmental toxicity screen in Sprague-Dawley rats (12/sex/dose) Fyrol 6 (purity 85%) administered by gavage at 50, 250, or 750 mg/kg-day for 2 weeks prior to mating, during mating, gestation, lactation (females) Results: No effects on clinical signs, mortality, parental body weights, food consumption, reproductive or developmental indices, histopathology. Maternal toxicity: NOAEL: 750 mg/kg-day (highest dose tested) LOAEL: Not established Developmental toxicity: NOAEL: 750 mg/kg-day (highest dose tested) LOAEL: Not established	Supresta, 2006; EPA, 2009	Adequate; guideline study (OECD 421) summarized in reliable secondary sources; true NOAELs may be > 750 mg/kg-day; No LOAELs were established in this study.
	Combined Repeated Dose with Reproduction/ Developmental Toxicity Screen			No data located.
	Prenatal Development			No data located.
	Postnatal Development			No data located.
	Prenatal and Postnatal Development			No data located.

Diethyl bis(2-hydroxyethyl)aminomethylphosphonate CASRN 2781-11-5				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Developmental Neurotoxicity			No data located.
	Other			No data located.
Neurotoxicity		**MODERATE: There is potential for neurotoxicity based on a structural alert for organophosphates. No experimental data was located.**		
	Neurotoxicity Screening Battery (Adult)	Potential for neurotoxicity based on a structural alert for organophosphates (Estimated)	Professional judgment	Estimated based on a structural alert for organophosphates and professional judgment.
	Other			No data located.
Repeated Dose Effects		**MODERATE: There is potential for kidney effects based on a structural alert for amines. No adverse effects were reported in a 13-week oral gavage study in rats at doses as high as 500 mg/kg-day (highest dose tested); however, only quantitative data for liver and kidney weight, and cross-sectional area of liver cells were reported. The experimental data are insufficient to rule out kidney toxicity; therefore, a conservative approach was applied and an estimated Moderate hazard was designated.**		
		Potential for kidney toxicity based on a structural alert for amines (Estimated)	Professional judgment	Estimated based on a structural alert for amines and professional judgment.
		Sprague-Dawley rats (22/sex/dose) administered Fyrol 6 (purity 90.7%) by gavage (in corn oil) at 0, 20, 100, or 500 mg/kg-day for 13 weeks. Results: No Fyrol 6 treatment-related adverse effects; increased liver weight, hepatocellular hypertrophy, eosinophilia of centrilobular hepatocytes considered adaptive effect in absence of histopathological evidence of hepatic necrosis or clinical evidence of liver dysfunction. NOAEL: 500 mg/kg-day (highest dose tested) LOAEL: Not established	Supresta, 2006; EPA, 2009	Study summarized in reliable secondary sources; only quantitative data was reported and only reported data for liver and kidney weight, and cross-sectional area of liver cells; no LOAEL was identified in the study.

Diethyl bis(2-hydroxyethyl)aminomethylphosphonate CASRN 2781-11-5				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Skin Sensitization		**MODERATE: There is uncertain potential for skin sensitization due to lack of data; Skin sensitization cannot be ruled out. A moderate hazard designation is applied conservatively.**		
	Skin Sensitization	There is uncertain potential for skin sensitization due to lack of data. (Estimated)	Professional judgment	No data located.
Respiratory Sensitization		**No data were located**		
	Respiratory Sensitization			No data located.
Eye Irritation		**LOW: Diethyl bis(2-hydroxyethyl)aminomethylphosphonate produced mild irritation in rabbits which cleared within 72-hours post-instillation.**		
	Eye Irritation	Rabbit (9 of mixed sex); mild conjunctival irritation at 0.01 mL in 6 rabbits with unwashed eyes at 24 hours postinstillation, no effects in 3 rabbits with washed eyes; irritation cleared by 72-hours postinstillation.	Supresta, 2006; EPA, 2009	Guideline study (EPA guidelines for pesticide registration; Fed. Reg. 43:163, 37336-37402 [1978]; OECD [1981]) summarized in secondary sources; Test substance: Fyrol 6; purity not specified.
Dermal Irritation		**VERY LOW: Diethyl bis(2-hydroxyethyl)aminomethylphosphonate was not irritating to rabbit skin.**		
	Dermal Irritation	Rabbit (6 of mixed sex); nonirritating when applied at 0.5 mL for 4 hours and observed at 4 and 48 hours post-administration.	Supresta, 2006; EPA, 2009	Study that followed DOT Fed. Reg. Title 49, Part 173 Appendix II (10/01/1977) summarized in secondary sources. Test substance: Fyrol 6; purity not specified.
Endocrine Activity		**No data were located**		
				No data located.
Immunotoxicity		**No data were located**		
	Immune System Effects			No data located.

Diethyl bis(2-hydroxyethyl)aminomethylphosphonate CASRN 2781-11-5			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
ECOTOXICITY			
ECOSAR Class			
Acute Aquatic Toxicity	**MODERATE: Based on an experimental acute aquatic toxicity value of > 86 mg/L in daphnia. Estimated values for fish, daphnia and green algae indicated a Low hazard.**		
Fish LC_{50}	*Oncorhynchus mykiss* (rainbow trout; aka *Salmo gairdneri*) 96-hr LC_{50} > 10,000 mg/L. Test substance: Fyrol 6; purity not given Static test; Test substance concentrations: 1,000, 1,800, 3,200, 5,600, 10,000 mg/L (nominal); There was 20% mortality at 3200 mg/L but none at higher concentrations. (Experimental)	Supresta, 2006; EPA, 2009	Guideline study (OECD 203) according to reliable secondary sources. Purity not given, but apparently in the range of 70-90% based on reported purity of batches used for selected physical-chemical properties endpoints.
	Freshwater fish 96-hour LC_{50} > 100 mg/L (Estimated) ECOSAR: Aliphatic amines	ECOSAR v1.11	
	Freshwater fish 96-hour LC_{50} > 100 mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	Estimate for the Esters class was provided for comparative purposes. See Section 5.5.1.
Daphnid LC_{50}	*Daphnia magna* (water flea) 48-hour EC_{50} > 86 mg/L Test substance: Fyrol 6; purity 84.5% Flow-through test Test substance concentrations: 63, 125, 250, 500, and 1,000 mg/L (nominal); 936 mg/L (measured at nominal of 1,000 mg/L) (Experimental)	Supresta, 2006; EPA, 2009	Guideline study (OECD 202; EPA OPPTS 850.1010) according to reliable secondary sources.
	Daphnia magna 48-hour LC_{50} > 100	ECOSAR v1.11	

Diethyl bis(2-hydroxyethyl)aminomethylphosphonate CASRN 2781-11-5			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	mg/L (Estimated) ECOSAR: Aliphatic amines		
	Daphnia magna 48-hour LC_{50} > 100 mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	Estimate for the Esters class was provided for comparative purposes. See Section 5.5.1.
Green Algae EC_{50}	Green algae (*Pseudokirchneriella subcapitata*) 96-hour EC_{50} >86 mg/L; Test substance: Fyrol 6; purity 84.5% Static test Test substance concentrations: 7.5, 15, 30, 60, and 120 mg/L (nominal); 86 mg/L (measured at 120 mg/L nominal) (Experimental)	Supresta, 2006; EPA, 2009	Study details reported in a secondary source.
	Green algae 96-hour EC_{50} > 100 mg/L (Estimated) ECOSAR: Aliphatic amines	ECOSAR v1.11	
	Green algae 96-hour EC_{50} > 100 mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	Estimate for the Esters class was provided for comparative purposes. See Section 5.5.1.

Diethyl bis(2-hydroxyethyl)aminomethylphosphonate CASRN 2781-11-5			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
Chronic Aquatic Toxicity	**LOW: Based a NOEC of 86 mg/L in green algae and estimated values for fish, daphnia and algae.**		
Fish ChV	Freshwater fish ChV ≥ 417 mg/L (Estimated)	Professional judgment	An ACR of 24 was derived for the phosphate ester class based on experimental data for Tris (p-t-butylphenyl) phosphate (TBPP). The acute-to-chronic ratio was applied to available experimental acute fish data for Diethyl bis(2-hydroxyethyl)aminomethylphosphonate (ChV >10,000 mg/L /24 = 417 mg/L)
	Freshwater fish ChV > 10 mg/L (Estimated) ECOSAR: Aliphatic amines	ECOSAR v1.11	
	Freshwater fish ChV > 10 mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	Estimate for the Esters class was provided for comparative purposes. See Section 5.5.1.
Daphnid ChV	Daphnia magna ChV > 10 mg/L (Estimated) ECOSAR: Aliphatic amines	ECOSAR v1.11	
	Daphnia magna ChV > 10 mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	Estimate for the Esters class was provided for comparative purposes. See Section 5.5.1.
Green Algae ChV	Green algae (*Pseudokirchneriella subcapitata*) 96-hour NOEC = 86 mg/L (Experimental)	Supresta, 2006	Study details reported in a secondary source.
	Green algae ChV > 10 mg/L (Estimated) ECOSAR: Aliphatic amines	ECOSAR v1.11	
	Green algae ChV > 10 mg/L	ECOSAR v1.11	Estimate for the Esters class was provided

Diethyl bis(2-hydroxyethyl)aminomethylphosphonate CASRN 2781-11-5				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		(Estimated) ECOSAR: Esters		for comparative purposes. See Section 5.5.1.
ENVIRONMENTAL FATE				
Transport		**Level III fugacity models incorporating available physical and chemical property data indicate that at steady state, diethyl bis(2-hydroxyethyl)aminomethylphosphonate is expected to be found primarily in soil and to a lesser extent, water. Diethyl bis(2-hydroxyethyl)aminomethylphosphonate is expected to exist in both neutral and cationic forms at environmentally-relevant pH, based on the estimated pK_b values. The neutral form of diethyl bis(2-hydroxyethyl)aminomethylphosphonate is expected to have high mobility in soil based on its estimated Koc. The cationic form may have less mobility, as cations bind more strongly to organic carbon and clay due to their positive charge. Estimated volatilization half-lives indicate that the substance will be nonvolatile from surface water. In the atmosphere, diethyl bis(2-hydroxyethyl)aminomethylphosphonate is expected to exist in both vapor and particulate phases, based on its estimated vapor pressure. Particulates will be removed from air by wet or dry deposition. Vapor-phase diethyl bis(2-hydroxyethyl)aminomethylphosphonate will be susceptible to atmospheric degradation processes.**		
	Henry's Law Constant (atm-m^3/mole)	$<10^{-8}$ (Estimated)	EPI v4.11; Professional judgment	Cutoff value for non-volatile compounds.
	Sediment/Soil Adsorption/Desorption - K_{oc}	10 (Estimated)	EPI v4.11	
	Level III Fugacity Model	Air = 0% Water = 35% Soil = 65% Sediment = 0% (Estimated)	EPI v4.11	

Diethyl bis(2-hydroxyethyl)aminomethylphosphonate CASRN 2781-11-5				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Persistence		**HIGH: Experimental studies on the commercial product, which is estimated to contain approximately 85% diethyl bis(2-hydroxyethyl)aminomethylphosphonate, determined the substance to be not readily biodegradable using a modified Sturm test (OECD TG 301B), as only 15-19% biodegradation occurred over 28 days using activated sewage sludge as the inoculum. Diethyl bis(2-hydroxyethyl)aminomethylphosphonate undergoes hydrolysis under alkaline conditions, with a half-life of 14 hours at pH 9; it is relatively stable to hydrolysis under neutral and acidic conditions, with half-lives of 26 days at pH 7 and 179 days at pH 4. Diethyl bis(2-hydroxyethyl)aminomethylphosphonate is not expected to be susceptible to direct photolysis by sunlight, since it does not absorb light at wavelengths >290 nm. The atmospheric half-life of vapor phase diethyl bis(2-hydroxyethyl)aminomethylphosphonate is estimated to be 0.9 hours, although it is expected to exist primarily in the particulate phase in air.**		
Water	**Aerobic Biodegradation**	Passes Ready Test: No Test method: OECD TG 301B: Modified Sturm test 19% degradation over 28 days for 20 mg/L substance; 15% degradation over 28 days for 10 mg/L substance. Purity of test substance not reported, but is most likely ca. 85%. Activated sludge from municipal sewage treatment plant employed. (Measured)	Supresta, 2006	Adequate, guideline study.
		Days-weeks (Primary survey model) Weeks-Months (Ultimate survey model) (Estimated)		
	Volatilization Half-life for Model River	>1 year (Estimated)	EPI v4.11	
	Volatilization Half-life for Model Lake	>1 year (Estimated)	EPI v4.11	
Soil	**Aerobic Biodegradation**			No data located.
	Anaerobic Biodegradation	Probable (Anaerobic-methanogenic biodegradation probability model)		

Diethyl bis(2-hydroxyethyl)aminomethylphosphonate CASRN 2781-11-5				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Soil Biodegradation with Product Identification			No data located.
	Sediment/Water Biodegradation			No data located.
Air	**Atmospheric Half-life**	0.075 days (Estimated)	EPI v4.11	
Reactivity	**Photolysis**	Not a significant fate process (Estimated)	Professional judgment; Mill, 2000	The substance does not contain functional groups that would be expected to absorb light at wavelengths >290 nm.
	Hydrolysis	Half-life at pH 4 = 179 days; Half-life at pH 7 = 26 days; Half-life at pH 9 = 14 hours, All values at 25°C as measured using the OECD 111 test guideline and EPA OPPTS 835.2100 test method (Measured)	Supresta, 2006	Adequate, valid guideline study. The purity of the substance was reported to be 85%.
Environmental Half-life				No data located.
Bioaccumulation		**LOW: Both the estimated BCF and BAF for fish are less than 100.**		
	Fish BCF	3.2 (Estimated)	EPI v4.11	
	Other BCF			No data located.
	BAF	1 (Estimated)	EPI v4.11	
	Metabolism in Fish			No data located.
ENVIRONMENTAL MONITORING AND BIOMONITORING				
Environmental Monitoring		No data located.		
Ecological Biomonitoring		No data located.		
Human Biomonitoring		No data located.		

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Screening Level Toxicology Hazard Summary

This table contains hazard information for each chemical; evaluation of risk considers both hazard and exposure. Variations in end-of-life processes or degradation and combustion by-products are discussed in the report but not addressed directly in the hazard profiles. The caveats listed below must be taken into account when interpreting the information in the table.

VL = Very Low hazard L = Low hazard M = Moderate hazard H = High hazard VH = Very High hazard – Endpoints in colored text (VL, L, M, H, and VH) were assigned based on empirical data. Endpoints in black italics *(VL, L, M, H,* and *VH*) were assigned using values from estimation software and professional judgment [(Quantitative) Structure Activity Relationships "(Q)SAR"].

* Each hazard designation for a mixture is based upon the component with the highest hazard, whether it is an experimental or estimated value.

Chemical	CASRN	Human Health Effects											Aquatic Toxicity		Environmental Fate	
		Acute Toxicity	Carcinogenicity	Genotoxicity	Reproductive	Developmental	Neurological	Repeated Dose	Skin Sensitization	Respiratory Sensitization	Eye Irritation	Dermal Irritation	Acute	Chronic	Persistence	Bioaccumulation
Emerald Innovation™ NH-1*	Confidential	H	*M*	L	*M*	L	M	H	M		M	M	VH	VH	*M*	*H*
Confidential C	Confidential	H	*M*	L	*M*	VL	M	L	M		M	M	H	H	L	L
Confidential D	Confidential	L	*M*	L	L	L	L	H	L		L	VL	VH	VH	L	M
Confidential E	Confidential	L	*M*	L	L	L	M	M	M		VL	M	VH	VH	*M*	*H*

	CASRN: Confidential
	MW: Confidential
	MF: Confidential
	Physical Forms: Liquid **Neat:**
	Use: Flame retardant
SMILES: Confidential	
Synonyms: Emerald Innovation™ NH-1; Halogen-free flame retardant	
Chemical Considerations: This alternative is a mixture. EPI v4.11 was used to estimate physical/chemical and environmental fate values due to an absence of experimental data. Measured values from experimental studies were incorporated into the estimations.	
Polymeric: No **Oligomeric:** Not applicable	
Metabolites, Degradates and Transformation Products: None identified; although there is potential for other confidential substances to be formed (Professional judgment).	
Analog: Not applicable **Endpoint(s) using analog values:** Not applicable	**Analog Structure:** Not applicable
Structural Alerts: Organophosphates; Neurotoxicity (EPA, 2012).	
Risk Phrases: One component is listed as R50/53: Very toxic to aquatic organisms. May cause long-term adverse effects in the aquatic environment (OECD-SIDS, 2002).	
Hazard and Risk Assessments: None identified.	

Emerald Innovation™ NH-1			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
PHYSICAL/CHEMICAL PROPERTIES			
Melting Point (°C)	**Confidential C**: -70 (Measured)	Confidential study (as cited in ATSDR, 2012)	Reported in peer reviewed secondary sources.
	Confidential D: 50.5 (Measured)	Lide, 2008	Reported in a primary source.
	Confidential D: 49 Reported as 49-50°C (Measured)	EC, 2000	Reported in a secondary source; consistent with value reported in primary source.
Boiling Point (°C)	**Confidential C:** 200 at 4 mmHg Reported as 200-230°C at 5.0-5.3 hPa (Measured)	Confidential study	Reported in a peer reviewed secondary source at a reduced pressure.
	Confidential C: 215 at 4 mmHg Reported as 215-228°C at 4 mmHg (Measured)	ATSDR, 2012	Reported in a peer reviewed secondary source.
	Confidential C: 225 at 4 mmHg Reported as 225-228°C at 4 mmHg (Measured)	Confidential study	Secondary source. No study details provided.
	Confidential D and E: >300 (Estimated)	EPI v4.11; EPA, 1999	Cutoff value for high boiling point compounds according to HPV assessment guidance.
	Confidential D: 245 Reported at 11 mm Hg (Measured)	O'Neil et al., 2006	Reported in a primary source.
	Confidential D: 220 Reported at 5 mm Hg (Measured)	EC, 2000	Reported in a secondary source; consistent with value reported in primary source.
Vapor Pressure (mm Hg)	**Confidential C:** 0.03 at 150°C (Measured)	ATSDR, 2012	Reported in a peer reviewed secondary source.
	Confidential C: 2.17×10^{-7} at 25°C Reported as 2.8×10^{-7} hPa at 25°C (Measured)	Confidential study	Reported in secondary source. No study details were provided.
	Confidential C: 0.01 at 20°C	Confidential study	Secondary source. No study details

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PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	(Measured)		provided.
	Confidential D: $6.28x10^{-6}$ at 25°C (Extrapolated)	Confidential study	Reported in a secondary source.
	Confidential D: $1.5x10^{-6}$ (Measured)	EC, 2000	Reported in a secondary source.
	Confidential E: $2.1x10^{-8}$ at 25°C (Estimated)	EPI v4.11	
Water Solubility (mg/L)	**Confidential C:** 1,100 (Measured) Reported as 1.1 g/L at 25°C	ATSDR, 2012	Reported in a peer reviewed secondary source.
	Confidential C: 1,100 (Measured) Reported as 1.1-1.3 g/L at 20°C	Confidential study	Reported in peer reviewed secondary source.
	Confidential D: 1.9 (Measured) Reported at 25°C	Confidential study	Reported in a secondary source.
	Confidential D: 0.75 (Measured) OECD Guideline 105	EC, 2000	Guideline study reported in a secondary source.
	Confidential E: $7.7x10^{-7}$ (Estimated)	EPA, 1999; EPI v4.11	Estimated value is less than the cutoff value, <0.001 mg/L, for insoluble compounds according to HPV assessment guidance.
	Confidential D: 0.025 (Measured)	EC, 2000	Reported in a secondary source; not consistent with other measured values.
Log K_{ow}	**Confidential C:** 3.75 (Measured)	HSDB, 2003; ATSDR, 2012; PhysProp, 2012	Valid guideline study. Reported in peer reviewed secondary sources.
	Confidential C: 3.65 Reported as Kow = 4,500 (Measured)	Confidential study	Secondary source. No study details provided.
	Confidential D: 4.59 (Measured)	Hansch et al., 1995	Reported in a primary source.
	Confidential D: 4.76 (Measured)	OECD-SIDS, 2002	Reported in a secondary source; consistent with value reported in primary source.

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PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	Confidential E: 11 (Estimated)	EPI v4.11; EPA, 1999	Estimated value is greater than the cutoff value, >10, according to methodology based on HPV assessment guidance.
Flammability (Flash Point)	Flash Point: 258°C Cleveland Open Cup method (Measured)	Chemtura, 2013	Reported in the product literature for commercial mixture.
Explosivity	**Confidential C, D & E:** Not expected to form explosive mixtures with air (Estimated)	Professional judgment	No experimental data located; based on its use as a flame retardant.
Pyrolysis			No data located.
pH	**Confidential C:** Neutral for 1 g/L water at 20°C (Measured)	Confidential study	Reported in peer reviewed secondary source.
	Confidential D & E: Not applicable (Estimated)	Professional judgment	Does not contain functional groups that are expected to ionize under environmental conditions.
pK_a	**Confidential D & E:** Not applicable (Estimated)	Professional judgment	Does not contain functional groups that are expected to ionize under environmental conditions.

Emerald Innovation™ NH-1				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
HUMAN HEALTH EFFECTS				
Toxicokinetics		**Confidential C was found to absorb into the hepatic portal circulation following dietary exposure; metabolism is likely to occur in the liver. Confidential D is hydrolyzed in the liver to produce a primary metabolite. Confidential D can be detected in human breast milk.**		
Dermal Absorption *in vitro*				No data located.
Absorption, Distribution, Metabolism & Excretion	**Oral, Dermal or Inhaled**	**Confidential C:** Rats were fed diets containing 03, 0.3 or 3.0% Confidential C for 5 or 14 weeks or 0.25 or 0.5 ml/kg for 18 weeks. Confidential C was absorbed into the hepatic portal circulation. The site of metabolism is likely to be the liver, which was the only target organ for toxicity in this study	ECHA, 2013	Sufficient study details in a secondary source.
		Confidential D: Pregnant rats were administered 0, 0.1 or 1 mg/kg-day of confidential product in the diet across gestation and through lactation (GD8 - PND 21) Components of a confidential product were detected in adipose, liver, and muscle tissues in Dams at PND 21 with the highest concentration in the adipose tissue (768 ng/g w.w. in high dose, 29.6 ng/g w.w. in low dose, <7.0 ng/g w.w. in controls). The primary metabolite was also detected in liver tissue of dams on PND 21.	Confidential study	Non guideline study indicates that absorption of this compound can occur in rats through oral exposure; the test substance is confidential product.
		Confidential D: Confidential D is hydrolyzed in rat liver homogenate to produce metabolites.	OECD-SIDS, 2002; ECHA, 2012	Reported in a secondary source.

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Other	**Confidential D:** Confidential D concentrations in milk were analyzed in a human cohort study conducted between 1997 and 2007. Median concentration across all subjects was 8.5 ng/g (min-max values: 3.2 - 11 ng/g).	ECHA, 2012	Limited study details reported in a secondary source.
Acute Mammalian Toxicity		**HIGH: Based on a 4-hour inhalation LC_{50} < 5.03 mg/L in rats following exposure to Confidential C. The LC_{50} value of 5.03 mg/L is in the Moderate hazard criteria range, the actual LC_{50} could possibly be < 1.0 mg/L; therefore, a conservative hazard designation is assigned. Confidential C is of LOW concern for acute toxicity via the oral and dermal routes of exposure. Acute toxicity is LOW for Confidential D and E.**		
Acute Lethality	**Oral**	**Confidential C:** Rat oral LD_{50} >2,000 mg/kg	ECHA, 2013	Sufficient study details in secondary source. Conducted in accordance with OECD Guideline 401.
		Confidential C: Rat oral LD_{50} = 3,000 mg/kg	Confidential study	No study details reported in a secondary source.
		Confidential C: Guinea pig oral LD_{50} = 3,000 mg/kg	ECETOC, 1992	No study details reported in a secondary source.
		Confidential C: Rat oral LD_{50} = 4,700 mg/kg	Confidential study	No study details reported in a secondary source.
		Confidential C: Rat oral LD_{50} = 9,490 mg/kg	ECETOC, 1992	No study details reported in a secondary source.
		Confidential D: Rat, mouse, oral LD_{50} >5,000 mg/kg	OECD-SIDS, 2002	Reported in a secondary source.
		Confidential D: Rat oral LD_{50} >6,400 mg/kg	ATSDR, 2009	Reported in a secondary source.
		Confidential D: Rat oral LD_{50} >20,000 mg/kg	OECD-SIDS, 2002	Study reported in a secondary source.
		Confidential D: Rat oral LD_{50} = 10,800 mg/kg	OECD-SIDS, 2002	Study reported in a secondary source; number of animals not reported.
		Confidential D: Rat oral LD_{50} =	OECD-SIDS, 2002	Study reported in a secondary source.

Emerald Innovation™ NH-1				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		3,500 mg/kg		Dose range and number of animals is not provided.
		Confidential E: Rabbit dermal LD_{50} >2,000 mg/kg	ECHA, 2013	Adequate study reported in a secondary source. Four studies; test substance is confidential product.
		Confidential E: Rat or LD_{50} 4,700 mg/kg (females); >5,000 mg/kg (males)	ECHA, 2013	Adequate study reported in a secondary source. Test substance is confidential product.
		Confidential E: Rat oral LD_{50} >5,000 mg/kg	ECHA, 2013	Adequate study reported in a secondary source. Three studies; test substance is confidential product.
		Confidential E: Rat oral LD_{50} = 20,000 mg/kg	Confidential study	Adequate primary source. Test substance is confidential product.
		Confidential E: Rat oral LD_{50} > 30 ml/kg (~32,490 mg/kg based on a density of 1.083 g/cm^3)	Confidential study	Adequate primary source.
	Dermal	**Confidential C:** Rabbit dermal LD_{50} >2 mL/kg (~2,040 mg/kg bw)	ECHA, 2013	Sufficient details in a secondary source. Equivalent or similar to OECD Guideline 402.
		Confidential C: Rabbit dermal LD_{50} >4,640 mg/kg	ECHA, 2013	Sufficient details reported in a secondary source. No information on substance purity.
		Confidential C: Rabbit dermal LD_{50} >5,000 mg/kg	ECHA, 2013	Sufficient details reported in a secondary source.
		Confidential C: Rabbit dermal LD_{50} >10,000 mg/kg	Confidential study	No details reported in a secondary source.
		Confidential D: Rabbit dermal LD_{50} >7,900 mg/kg	ATSDR, 2009	Reported in a secondary source.
		Confidential D: Rabbit dermal LD_{50} >10,000 mg/kg	OECD-SIDS, 2002	Reported in a secondary source.
		Confidential E: Rabbit dermal LD_{50}	Confidential study	Adequate primary source. Test

Emerald Innovation™ NH-1				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		> 10,000 mg/kg		substance is confidential product.
		Confidential E: Rabbit dermal LD_{50} >10 ml/kg (~10,830 mg/kg based on a density of 1.083 g/cm^3)	Confidential study	Adequate primary source.
	Inhalation	**Confidential C:** Rat 4-hour inhalation LC_{50} <5.03 mg/L During the first 4-hours post exposure 2/5 female rats died. During the 14-day observation period 4/5 males and all female rats died.	ECHA, 2013	Sufficient details reported in a secondary source. However, only a single concentration was tested; test substance was in aerosol form.
		Confidential C: Rat 4-hour inhalation LC_{50} >0.52 mg/L.	ECHA, 2013	Sufficient details reported in a secondary source. However, only a single concentration was tested.
		Confidential C: Rat 4-hour inhalation LC_{50} >4.43 mg/L.	ECHA, 2013	Sufficient details reported in a secondary source. No data on test substance purity.
		Confidential C: Rat 4-hour nose-only inhalation LC_{50} >6.4 mg/L	ECHA, 2013	Sufficient details reported in a secondary source. Conducted in accordance with OECD Guideline 403. No data on test purity.
		Confidential D: Rat 1-hour LC_{50} > 200 mg/L	OECD-SIDS, 2002; ATSDR, 2009	Reported in a secondary source. Insufficient exposure time (1 hour), no data on method or GLP.
		Confidential E: Rat 6-hour inhalation (vapor) LC_{50} >0.4 mg/L	ECHA, 2013	Adequate study reported in a secondary source. Test material is a confidential product.
		Confidential E: Rat 1-hour inhalation LC_{50} >200 mg/L	Confidential study	Adequate primary source. Test material is defined as confidential product.
Carcinogenicity		**MODERATE: There is uncertainty due to lack of data for Confidential C and E. Carcinogenic effects cannot be ruled out. OncoLogic modeling indicates a marginal to low potential for carcinogenicity for Confidential D. No long-term carcinogenicity assays were found.**		

Emerald Innovation™ NH-1				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	OncoLogic Results	**Confidential D:** Marginal; likely to have equivocal carcinogenic activity.	OncoLogic, 2008	No data located.
	Carcinogenicity (Rat and Mouse)	**Confidential D:** Mouse lung adenoma test: Male A/St mice (20/group) received i.p. injections of either 20 mg/kg (18/6 weeks); 40 mg/kg (3/1 week); or 80 mg/kg. No significant increase in incidence of adenoma compared to negative controls, and positive control (urethane) produced 19.6 tumors/mouse with 100% survival.	OECD-SIDS, 2002	No data located.
	Combined Chronic Toxicity/Carcinogenicity			No data located.
	Other			No data located.
Genotoxicity		**LOW: Based on negative results for *in vitro* and *in vivo* studies.**		
	Gene Mutation *in vitro*	**Confidential C:** Negative, HGPRT assay in Chinese hamster ovary (CHO) cells, with and without metabolic activation.	ECHA, 2013; Confidential study	Limited data reported in a secondary source. Study report was not available although data have been peer-reviewed in reference work. No information available regarding use of positive controls.
		Confidential C: Negative, mouse lymphoma L5178Y cells with and without metabolic activation. Positive controls responded as expected.	ECHA, 2013	Sufficient details reported in a secondary source. Conducted in accordance with OECD Guideline 476.
		Confidential C: Negative, *Salmonella typhimurium* strains TA1535, TA1537, TA98 and TA100 with and without metabolic activation. Positive controls responded as expected.	Confidential study	Sufficient details in a secondary source.

Emerald Innovation™ NH-1				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		Confidential C: Negative, *Salmonella typhimurium* strains TA98 and TA100 with and without metabolic activation. Positive controls responded as expected.	Confidential study	Sufficient study details reported in a primary source.
		Confidential C: Negative, *Salmonella typhimurium* strains TA98, TA100, TA1535, TA1537, TA1538 with and without metabolic activation. Positive controls responded as expected.	ECHA, 2013	Sufficient details in summaries of three similar studies reported in a secondary source. No data on test substance purity.
		Confidential C: Negative, *Salmonella typhimurium* strains TA1535, TA1537, TA98 and TA100 with and without metabolic activation.	ECHA, 2013	Adequate study reported in a secondary source. Study protocol in line with Guideline for gene point mutation assay in bacterial cells.
		Confidential C: Negative, *Salmonella typhimurium* strains TA98, TA100, TA1535, TA1537, TA1538 with and without metabolic activation. Cytotoxicity was evident in strain TA100 at >/= 0.29 microliters per plate.	ECHA, 2013	Adequate study reported in a secondary source. The test method is comparable to current protocols using bacterial strains standard at the date in which the study was conducted.
		Confidential C: Negative, *E. coli* strain pol A+ and pol A- with and without metabolic activation. No cytotoxicity, tested up to precipitating concentrations. Positive controls responded as expected.	ECHA, 2013	Sufficient study details reported in a secondary source. Acceptable scientific method. No data on test substance purity.
		Confidential D: Negative, Ames assay in *Salmonella typhimurium* strains TA98, TA100, TA1537, TA1538 with and without metabolic	ATSDR, 2009; ECHA, 2013	Reported in a secondary source.

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		activation		
		Confidential D: Negative, forward mutation assay in mouse lymphoma L5178Y cells	OECD-SIDS, 2002; ECHA, 2013	Reported in a secondary source.
		Confidential E: Negative, cell transformation assay in BALB/3T3 cells without metabolic activation. Test concentrations: 0.00125, 0.00250, 0.005, 0.01 and 0.02 µl/ml	ECHA, 2013	Adequate study reported in a secondary source. Test material is defined as confidential product.
		Confidential E: Negative, mouse lymphoma L5178Y cells with and without metabolic activation. Test concentrations: 0.013, 0.025, 0.038, 0.05, and 0.1 µl/ml	ECHA, 2013	Adequate study reported in a secondary source. Test material is defined as confidential product.
		Confidential E: Negative, mouse lymphoma L5178Y cells with and without metabolic activation. Test concentrations: 0.975, 15.6, 31.3, 62.5, and 125 nl/ml. The concentration of 125 nl/ml was highly toxic and insufficient survivors were obtained at 250 nl/ml to perform the assay.	ECHA, 2013	Adequate study reported in a secondary source. Test material is defined as confidential product.
		Confidential E: Negative, *Salmonella typhimurium* strains TA1535, TA1537, TA1538, TA98 and TA100 and *Saccharomyces cerevisiae* D4 with and without metabolic activation. Test concentrations: 0.01, 0.1, 1.0, 5.0, and 10 µl/plate	ECHA, 2013	Adequate study reported in a secondary source. Test material is defined as confidential product.
	Gene Mutation *in vivo*			No data located.

Emerald Innovation™ NH-1				
PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
	Chromosomal Aberrations *in vitro*	**Confidential D:** Negative in chromosome aberration test in Chinese hamster V79 cells; with and without metabolic activation.	ECHA, 2013	Reported in a secondary source.
		Confidential E: Negative, sister chromatid exchanges (SCEs) and chromosome aberrations in mouse lymphoma L5178Y cells with and without metabolic activation. Test concentrations: - S9 mix: 0.000625, 0.00125, 0.00250, 0.00500 and 0.01000 µl/ml; +S9 mix: 0.00125, 0.00250, 0.00500, 0.01000 and 0.02000 µl/ml	ECHA, 2013	Adequate study reported in a secondary source. Test material is defined as confidential product.
	Chromosomal Aberrations *in vivo*	**Confidential C:** Negative, micronucleus assay in NMRI mice (5/sex/dose) administered Confidential C via oral gavage at a dose of 1,800 mg/kg. Positive controls responded as expected.	ECHA, 2013	Sufficient details reported in a secondary source. Conducted in accordance with OECD Guideline 474. No data on test substance purity.
	DNA Damage and Repair	**Confidential C:** Negative, DNA damage and/or repair assay in Syrian hamster kidney cells with and without metabolic activation. Positive controls responded as expected.	ECHA, 2013	Sufficient details reported in a secondary source. No data on purity of test substance.
		Confidential D: Negative, unscheduled DNA synthesis in hamster fibroblast cells	OECD-SIDS, 2002	Reported in a secondary source.
	Other	**Confidential D:** Negative, mitotic gene conversion assay in *Saccharomyces cerevisiae* with and without activation	OECD-SIDS, 2002	Reported in a secondary source.

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Reproductive Effects		**MODERATE: No adverse effects were observed on fetal viability, post-implantation loss, total implantations or the incidence of fetal malformations at doses up to 1,500 mg/kg-day (LOAEL not established) following gestational oral exposure to Confidential C in rats. Although no reproductive effects were observed in this study, there is a lack of data on reproductive parameters as measured in fertility or multigenerational studies and no data were available for other routes of exposure. It is uncertain if effects would occur in more definitive studies or via other routes; a Moderate hazard has been designated based on this uncertainty. Reproductive toxicity is LOW for Confidential D and E.**		
	Reproduction/Developmental Toxicity Screen	**Confidential C:** Confidential C was administered by gavage in corn oil to three groups of 25 mated Charles River CD female rats at dose levels of 0 (corn oil), 250, 500 or 1,500 mg/kg-day on days 6 to 15 of gestation. The treatment had no effect at any dose level on fetal resorption, fetal viability, post-implantation loss, total implantations or the incidence of fetal malformations. NOAEL: 1,500 mg/kg-day (highest dose tested) LOAEL: Not established	Confidential study	Sufficient details reported in a secondary source.

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PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
	Combined Repeated Dose with Reproduction/ Developmental Toxicity Screen	**Confidential D:** Reproductive/developmental dietary study; Confidential D was administered in the diet for 91 days at concentrations of 0, 0.25, 0.50, 0.75, or 1.0% (~0, 166, 341, 516 or 690 mg/kg-day, respectively). At the completion of this study, females were mated with males from the same group. All remained on the same diet as in the subchronic study until day 20 of gestation when dams were sacrificed. No signs of parental toxicity, no reproductive effects (number pregnant, corpora lutea, implantations, implantation efficiency, resorptions). NOAEL: 690 mg/kg-day (highest dose tested) LOAEL: Not established	OECD-SIDS, 2002; ATSDR, 2009	Reported in a secondary source.
	Reproduction and Fertility Effects	**Confidential D:** Rabbits, dermal (clipped, intact), 5x/week, 3 weeks, 50% solution in ethanol; no effect on the reproductive organs reported up to the highest dose tested (1,000 mg/kg-day) NOAEL: 1,000 mg/kg-day (highest dose tested)	OECD-SIDS, 2002	Reported in a secondary source. Organs examined by histopathology; there were no effects at the highest dose tested; dermal repeated-dose study.
		Confidential E: Sprague-Dawley rats (12/sex/dose) were orally gavaged with 50, 250, 1,000 mg/kg-day	ECHA, 2013	Adequate study reported in a secondary source. Test material is defined as confidential product.

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PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
		Confidential E. Exposure was 2 weeks prior to mating, during mating period (up to 2 weeks, males and females) and during gestation, lactation and until post-partum day 4 (females). No mortality or overt signs of parental toxicity. No effect was seen on body weight and food consumption. Gross necropsy and organ weight data and histopathology of the reproductive organs revealed no adverse findings. Mean litter size and mean number of live pups was comparable between the treatment groups. No effects on litter weights. Percent post-implantation loss was higher in 250 and 1,000 mg/kg-day groups (not statistically significant). Subsequently, a statistically significant increase in the absolute number of stillbirths in the 250 and 1,000 mg/kg-day groups was noted. However, overall a similar number of pup deaths were observed across all groups. Overall, pup survival from day 0 to 4 was lower in the 250 mg/kg-day group (due to 10 deaths in one litter), higher in the 50 mg/kg-day group and approximately the same as control in the 1,000 mg/kg-day group. NOAEL: 1,000 mg/kg-day (highest dose tested)		

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		LOAEL: Not established		
	Other	**Confidential D:** Men living in homes with higher amounts of Confidential D in house dust had reduced sperm count and altered hormone levels related to fertility and thyroid function. Each interquartile range (IQR) Confidential D increase in house dust samples was associated with a 19% decrease in sperm concentrations and a 10% increase in prolactin levels.	Confidential study	The actual exposure to Confidential D is unknown; it is not known if Confidential D or other substances found in the household dust caused or contributed to the reported toxicity.

Emerald Innovation™ NH-1				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Developmental Effects		**LOW: Based on a rat oral reproductive/developmental NOAEL = 690 mg/kg-day for fetal effects (highest dose tested) following exposure to Confidential D. Developmental toxicity is also LOW for Confidential E (based on a NOAEL and LOAEL of 400 and 1,000 mg/kg-day, respectively) and VERY LOW for Confidential C (based on a NOAEL of 2,000 mg/kg-day). There were no data located for the developmental neurotoxicity endpoint. Decreased cholinesterase activity in pregnant lab animals has been shown to have a negative impact on fetal brain development. As a result, there is uncertain potential for developmental neurotoxicity for this substance.**		
	Reproduction/ Developmental Toxicity Screen	**Confidential D:** Reproductive/developmental dietary study; Confidential D was administered in the diet for 91 days at concentrations of 0, 0.25, 0.50, 0.75, or 1.0% (~0, 166, 341, 516 or 690 mg/kg-day, respectively). At the completion of this study, females were mated with males from the same group. All remained on the same diet as in the subchronic study until day 20 of gestation when dams were sacrifice. No effects on fetal endpoints (viability, early or late deaths, fetal weight, length or distribution) or skeletal anomalies. Developmental effects: NOAEL: 690 mg/kg-day (highest dose tested) LOAEL: Not established	OECD-SIDS, 2002; ATSDR, 2009; ECHA, 2012	A LOAEL was not identified; there were no effects at the highest dose tested.
	Combined Repeated Dose with Reproduction/ Developmental Toxicity Screen			No data located.

Emerald Innovation™ NH-1				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Prenatal Development	**Confidential C:** In a range-finding developmental toxicity study, Confidential C was administered by gavage in corn oil to groups of 5 mated Charles River CD female rats at dose levels of 0, 25, 250, 500 1,000, and 2,000 mg/kg-day on days 6 to 15 of gestation. At doses up to 1,000 mg/kg-day, all rats survived. Two animals died or were sacrificed in the high dose group. Maternal toxicity (reduced righting reflex, hypoactivity, lethargy, ataxia and stained anogenital haircoat) was observed in the animals receiving 500 mg/kg-day or greater. Maternal weight gain was normal in animals receiving 1,000 mg/kg-day or less. The treatment had no effect at any dose level on fetal resorption, fetal viability, postimplantation loss and total implantations. Maternal Toxicity: NOAEL: 250 mg/kg-day LOAEL: 500 mg/kg-day Developmental toxicity: NOAEL: 2,000 mg/kg-day (highest dose tested) LOAEL: Not established	ECHA, 2013	Adequate study reported in a secondary source. Conforms to Guidelines for a range finding teratology study, but some data missing. No data on when sacrifices were conducted. No data on whether fetal examinations were conducted.
		Confidential C: In a developmental toxicity study, Confidential C was	ECHA, 2013; Confidential study	Sufficient study details reported in secondary sources. No data on test

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PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
		administered by gavage in corn oil to three groups of 25 mated Charles River CD female rats at dose levels of 250, 500 and 1,500 mg/kg-day on days 6 to 15 of gestation. Sacrifices were conducted on Gd 20. Maternal weight gain was depressed only in the high-dose group. The treatment had no effect at any dose level on fetal resorption, fetal viability, postimplantation loss, total implantations or incidence of fetal malformations. Maternal Toxicity: NOAEL: 500 mg/kg-day LOAEL: 1,500 mg/kg-day Developmental toxicity: NOAEL: 1,500 mg/kg-day (highest dose tested) LOAEL: Not established		substance purity in secondary sources.
		Confidential D: Pregnant Wistar rats were administered 0, 0.1 or 1 mg/kg-day of the confidential analog in the diet during gestation and through lactation (GD8 - PND 21); Maternal toxicity: Increased serum thyroxine (T4) levels in the high dose dams compared to controls was reported. There was no significant change in triiodothyronine (T3) levels in dam serum. Decreased hepatic	Confidential study	Estimated based on data for confidential mixture; non guideline study.

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PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
		carboxylesterease activity was also reported in dams in the high dose group. Developmental toxicity: female offspring in the high dose group displayed a significantly earlier vaginal opening when compared to controls. A statistically significant increase in weight was reported in both males and females in the high dose group at PND 120. This effect persisted through PND 180 to PND 220 with high dose males and females having significantly higher weights than same sex controls. A dose-dependent decrease in the number of rats to enter with open arms, (indicating anxiety), was reported in both male and female offspring. Increased blood glucose levels were reported in male offspring in the high-dose group compared to controls. There was no statistically significant difference in heart weight of male or female offspring. Left ventricular (LV) free wall thickness was significantly increased in male offspring in the high dose group; there were no changes in LV thickness in females at any dose. Maternal Toxicity: NOAEL: 0.1 mg/kg-day LOAEL: 1 mg/kg-day		

Emerald Innovation™ NH-1				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		Developmental toxicity: NOAEL: 0.1 mg/kg-day LOAEL: 1 mg/kg-day (based on early vaginal opening in females, increased weight in males and females, decreased open arm behavior, increased blood glucose levels in males and increased LV thickness in males)		
		Confidential E: Sprague-Dawley rats (7 females/group) were administered Confidential E via oral gavage at doses on 100, 400, 1,000 mg/kg-day on GD 6-20. Reduced food consumption on GD 6-9 (1,000 mg/kg-day). Increased body weight gain (400 and 1,000 mg/kg-day). Increased absolute and relative liver weight in all treatment groups (not considered by study authors to be treatment-related). Embryo- or feto-toxicity as indicated by a reduction in fetal body weight (1,000 mg/kg-day). Craniofacial malformations in 3 fetuses (1,000 mg/kg-day). Increased maternal body weight gain was reported on GD0-6 for the 100 and 400 mg/kg-day dose groups and on GD16-21 for the 400 mg/kg-day dose group; absolute and relative liver weights were increased in all treatment groups.	ECHA, 2013	Adequate study reported in a secondary source. Test material is defined as confidential product.

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PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
		Maternal toxicity: NOAEL: Not established LOAEL: 100 mg/kg-day (lowest dose tested) Developmental toxicity: NOAEL: 400 mg/kg-day LOAEL: 1,000 mg/kg-day		
		Confidential E: Charles River rats (25 females) were administered Confidential E via oral gavage at doses of 0, 300, 1,000, 3,000 mg/kg-day once daily on GD 6-19. Clinical signs of toxicity in all groups, including controls. Decrease in mean number of early resorptions and mean postimplantation loss (mid dose), which was attributed by study authors to a random occurrence. Slight increase in number of litters with malformations (high dose), but was not considered biologically significant by study authors (single incidences). NOAEL (maternal and developmental): 3,000 mg/kg-day (highest dose tested) LOAEL: Not established	ECHA, 2013	Adequate study reported in a secondary source. Test material is defined as confidential product.
		Confidential E: Charles River rats (5 females/group) were administered Confidential E at doses of 250, 500,	ECHA, 2013	Adequate study reported in a secondary source. Test material is defined as confidential product.

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		1,000, 2,500, 5,000 mg/kg-day once daily on GD 6-19. No mortality or behavioral effects were observed. Anogenital staining and/or matting in all treatment groups. Red and/or brown matter around the nose, mouth and forelimbs (5,000 mg/kg-day). Slight reduction in body weight gain (1,000 and 2,500 mg/kg-day); severe reduction in mean maternal body weight gain (5,000 mg/kg-day). Increase in postimplantation loss, decrease in viable fetuses (5,000 mg/kg-day). Maternal toxicity: NOAEL: 2,500 mg/kg-day LOAEL: 5,000 mg/kg-day Developmental toxicity: NOAEL: 5,000 mg/kg-day LOAEL: Not established		
	Postnatal Development			No data located.
	Prenatal and Postnatal Development			No data located.
	Developmental Neurotoxicity	**Confidential C:** There were no data located for the developmental neurotoxicity endpoint. As a result, there is uncertain potential for developmental neurotoxicity for this substance.	Professional judgment	No data located.

Emerald Innovation™ NH-1				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		Confidential D: There were no data located for the developmental neurotoxicity endpoint. Decreased cholinesterase activity in pregnant lab animals has been shown to have a negative impact on fetal brain development. As a result, there is uncertain potential for developmental neurotoxicity for this substance.	Professional judgment	No data located.
		Confidential E: Uncertain concern for developmental neurotoxicity based on the potential for Cholinesterase (ChE) inhibition in dams that may result in alterations of fetal neurodevelopment. (Estimated)	Professional judgment	Estimated based on a structural alert for organophosphates for the neurotoxicity endpoint.
	Other			No data located.
Neurotoxicity		**MODERATE: Neurotoxic effects following exposure to Confidential C included morphological changes to the sciatic nerve, reduction in caudal nerve response and increases in absolute and relative refractory periods at a dose of 255 mg/kg-day in rats (lowest dose tested). These studies indicated that there is some potential for neurotoxicity at higher doses. In addition, there is potential for neurotoxic effects based on a structural alert. A NOAEL and LOAEL of ~ 10 and ~ 100 mg/kg-day, respectively were established in rabbits following dermal exposure to Confidential E. Adverse effects included decreased brain cholinesterase. The potential for neurotoxic effects following exposure to Confidential D is LOW.**		
	Neurotoxicity Screening Battery (Adult)	**Confidential C:** Sprague-Dawley rats (12/sex/dose), received Confidential C daily via oral gavage at doses of 0.25 or 0.50 g/kg-day for 18 weeks. (255 or 510 mg/kg-day). Adverse neurological signs were evident in almost all exposed rats in the second half of the study. Nerve conduction	ECHA, 2013; Confidential study	Sufficient study details study reported in a secondary source. Study limited by not establishing a NOAEL.

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PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
		measurements were made with all rats at the end of the 6th, 12th, and 18th week. No differences in body weights throughout the study. Breathing difficulty and ataxia were observed. Tremors at high dose. Significantly reduced conduction velocity in the caudal nerve in both treatment groups. Increased absolute (18 weeks) and relative refractory periods (12 and 18 weeks). Morphological changes (axonal degeneration and demyelination) in both treated groups, with a greater incidence in the high dose animals. Both myelinated and unmyelinated nerves were adversely affected. The gradual development of neurotoxicity after several weeks of treatment confirms the progressive nature of this form of toxicity, and suggests that repeated exposure is necessary to elicit a neurotoxic response. NOAEL: Not established LOAEL: 255 mg/kg-day		

Emerald Innovation™ NH-1				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		Confidential D: 4-month dietary study, 10 rats/dose, 0.25, 0.5, 0.75 or 1% test concentration (161, 345, 517 or 711 mg/kg-day, respectively), no neurobehavioral effects (open field, accelerating rotarod, forelimb grip strength and negative geotaxis examinations). NOAEL: 711 mg/kg-day (highest dose tested) LOAEL: Not established	ATSDR, 2009	Reported in a secondary source.
		Confidential C: Single oral administration of Confidential C to rats (1,000 – 3,200 mg/kg for females, 1,000 – 9,000 mg/kg for males) (20/sex/group). Three weeks after administration, measurements of nerve conduction velocity (NCV), relative refractory period (RRP) and absolute refractory period (ARP) were conducted in the caudal nerve. Dose related reductions in caudal NCV in both sexes and a significant increase in refractory period (both RRP and ARP) recorded in the two highest dosed male groups. No morphological changes in the sciatic nerves of low dose rats. At higher doses some changes were recorded, including sciatic nerve section degenerative changes in some myelinated and unmyelinated fibers.	ECHA, 2013; Confidential study	Sufficient study details reported in secondary sources.

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PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
		NOAEL: 1,500 mg/kg LOAEL: 3,200 mg/kg for males and 1750 mg/kg for females		
		Confidential C: Sprague-Dawley rats (20/sex/group) administered Confidential C in the diet at concentrations of 0, 300, 3,000 and 10,000 ppm (approximately 20.4, 204, or 612 mg/kg-day) for 18-weeks followed by an 8-week recovery period. No effect on bodyweight; no gross signs of neurotoxicity; no significant alterations in NCV, ARP, or RRP except for significant reductions in NCV in high-dose females; no microscopic morphological changes in central and peripheral nervous tissues. NOAEL: 204 mg/kg-day LOAEL: 612 mg/kg-day	ECHA, 2013	Sufficient study details reported in a secondary source.
		Confidential E: White leghorn hens were administered Confidential E via oral gavage at an oral dose of 11,700 mg/kg-day for 6 weeks. Significant inhibition of plasma cholinesterase was found, but no significant inhibition of brain neurotoxic esterase. NOAEL: ≥ 11,700 mg/kg-day	ECHA, 2013	Adequate study reported in a secondary source. Test material is defined as confidential product.

Emerald Innovation™ NH-1				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		LOAEL: Not established		
		Confidential E: White leghorn chickens were administered Confidential E via oral gavage at an oral dose of 0, 240, 300, 360 and 420 mg/kg-day for 5 consecutive days and were observed for 30 days. No behavioral signs of delayed neurotoxicity were observed. Gross pathological examination revealed no lesions attributable to ingestion of the test substance. NOAEL: >420 mg/kg-day LOAEL: Not established	Confidential study	Adequate primary source. Test material is defined as confidential product.
		Confidential E: White leghorn hens were administered Confidential E via oral gavage at a single dose of 11,830 mg/kg. No adverse effects. NOAEL: 11,830 mg/kg LOAEL: Not established	ECHA, 2013	Adequate study reported in a secondary source. Test material is defined as confidential product.
	Other	**Confidential C:** There is potential for neurotoxic effects based on a structural alert for organophosphates. (Estimated)	Professional judgment	Estimated based on a structural alert and professional judgment.
		Confidential C: In a 14-day gavage study in rats (20/sex/group), at doses of 0.8 and 1.12 ml/kg-day (814 and 1142 mg/kg-day) for females and at 0.8 and 2.24 ml/kg-day (814 and 2285 mg/kg-day) for males, no clinical signs of neurotoxicity were reported.	ECHA, 2013; Confidential study	Sufficient study details in secondary source.

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		Significant reduction in caudal nerve conduction velocity was observed in high dose females and dose-related increases of refractory (relative and absolute) periods were also observed in all animals immediately after cessation of exposure. After 15 days recovery increases in ARP and RRP remained only in high dose females. NOAEL: 814 mg/kg-day LOAEL: 1,142 mg/kg-day (based on electrophysiological changes still present after the recovery period)		
		Confidential C: Twenty hens were tested with two doses of 5,000 mg/kg Confidential C administered in a gelatin capsule or dermally 21-days apart and were killed 21 days after the second dose. Esterase inhibition studies (NTE, brain AChE and plasma BuChE) were conducted following a single oral dose of Confidential C to groups of 5 hens. Positive and negative controls were also evaluated for comparison. All 20 hens dosed with 2 x 5,000 mg/kg Confidential C survived. No treatment-related findings of neurotoxicity were observed in Confidential C-treated hens dosed orally or dermally. NTE activity in the brain following Confidential C	ECHA, 2013; Confidential study	Sufficient study details reported in secondary sources.

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		exposure was within normal limits; brain AChE was inhibited by 45% with no evidence of associated clinical signs or cholinergic toxicity and plasma BuChE activity was also inhibited. Exposure to Confidential C does not induce delayed neurotoxicity in hens and no neurologic deficits nor histopathological changes characteristic of OPIDN were observed. NOAEL: >5,000 mg/kg LOAEL: Not established		
		Confidential D: There is potential for neurotoxic effects based on a structural alert for organophosphates (Estimated)	Professional judgment	Estimated based on a structural alert for organophosphates and professional judgment.
		Confidential D: Two female hens/dose in delayed neurotoxicity test, gavage, 2,000, 3,000, 5,000, 8,000, or 12,500 mg/kg, no signs of toxicity in-life or at necropsy NOAEL ≥12,500 mg/kg; highest dose tested LOAEL: Not established	OECD-SIDS, 2002	Reported in a secondary source. No data on test substance purity.
		Confidential D: Several acute oral studies in hens, administered doses up to 12,500 mg/kg, generally found no signs of paralysis, histopathological changes in examined nerve tissues, or	OECD-SIDS, 2002	Reported in a secondary source. No data on test substance purity.

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		behavior immediately after or during observation periods of up to 36 days. However, blood cholinesterase was decreased by up to 87% in studies where it was measured. NOAEL: ≥12,500 mg/kg; highest dose tested LOAEL: Not established		
		Confidential E: Rabbits (10/sex/dose) were dermally exposed to Confidential E at doses of 0, 10, 100, and 1,000 mg/kg 6 hours/ days, 5 days/week for 23 days. No treatment-related deaths. Edema, atonia, desquamation and fissuring. Increased mean terminal blood urea nitrogen values (high dose). Dose response depression of RBC and brain cholinesterase (mid and high dose). No effect on body weights, hematology and clinical chemistry data, organ weights and organ/body weight ratios. No treatment-related gross or microscopic changes. NOAEL: ≈ 10 mg/kg-day; LOAEL: ≈ 100 mg/kg-day	ECHA, 2013	Adequate study reported in a secondary source. Test material is defined as confidential product.
		Confidential E: There is potential for neurotoxic effects based on a structural alert for organophosphates (Estimated)	Professional judgment	Estimated based on a structural alert and professional judgment.

Emerald Innovation™ NH-1				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Repeated Dose Effects		**HIGH: Based on weight of evidence including reduced body weight in male rats administered Confidential D in the diet for 28-days. The NOAEL of 23.5 mg/kg-day and the LOAEL of 161.4 mg/kg-day span across the High and Moderate hazard designation ranges (DfE criteria are for 90-day repeated dose studies; criteria values are tripled for chemicals evaluated in 28-day studies making the High hazard range < 30 mg/kg-day and the Moderate hazard range between 30 and 300 mg/kg-day). Repeated dose toxicity is of MODERATE concern for Confidential E (based on a NOAEL and LOAEL of ≈ 10 and ≈ 100 mg/kg-day, respectively in a dermal study in rabbits) and of LOW concern for Confidential C (based on a NOAEL and LOAEL value of 100 mg/kg-day and > 200 mg/kg-day, respectively, in rats following oral exposure).**		
		Confidential C: Sprague Dawley rats (10/sex/dose) were administered Confidential C via oral gavage at doses of 0, 1, 10 and 100 mg/kg once per day for 14 days. Confidential C did not have any effect on body weight gain or organ weights in either sex or at any dose level. There were no treatment-related hematological abnormalities or gross/microscopic changes detected in major tissues and organs following dosing with Confidential C. NOAEL: ≥ 100 mg/kg-day (highest dose tested) LOAEL: Not established	ECHA, 2013; Confidential study	Sufficient study details reported in secondary sources. Study limited by inability to establish a LOAEL.
		Confidential C: In a 4-week study, Sprague-Dawley rats were fed diets containing 0, 500, 2,000, 7,500 or 15,000 mg Confidential C/kg (approximately 25, 100, 375, or 750 mg/kg-bw/day). No signs of toxicity were in males; slight decrease in body weight and food consumption in	Confidential study	Limited study details in secondary sources.

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PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
		females (7,500 or 15,000 mg/kg). No compound-related changes were observed at necropsy. Toxicity in males: NOAEL: >750 mg/kg-day (highest dose tested) LOAEL: Not established Toxicity in females: NOAEL: 100 mg/kg-day LOAEL: 375 mg/kg-day		
		Confidential C: Sprague Dawley rats (12/sex/dose) were administered Confidential C via oral gavage at doses of 0.25 and 0.5 mL/kg (255 and 510 mg/kg-day, based on a density of 1.018 g/cm^3), 5 days/week for 18 weeks. Reduced activity in all rats, clinical signs of toxicity (difficulties in breathing, piloerection, lacrimation, increased urination) at high dose. No hematological changes. Dose-related decrease in red cell AChE and reduction in GPT (high dose only). Significant increase in both liver and kidney weights (high dose females), a significant increase in liver weight in low dose females and similar increase for high dose males when expressed as percent body weight. Cardiac lesions (males in both treated groups).	ECHA, 2013; Confidential study	Sufficient study details in secondary sources. Limitations include inability to determine a NOAEL.

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PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
		NOAEL: Not established LOAEL: 0.25 mL/kg (255 mg/kg-day) based on increased liver weight in females and decrease in red blood cell AChE plus cardiac lesions in males		
		Confidential C: Confidential C was administered to four groups of Sprague-Dawley rats (20/sex/group) at target dietary concentrations of 0, 300, 3,000 and 10,000 ppm for 18-weeks. Dietary analyses verified the following average inclusion rates of Confidential C in the diets: 280 ppm (low); 3,000 ppm (intermediate); 9,900 ppm (high dose). No ophthalmic lesions attributable to Confidential C. All treatment group rats gained weight. Reduced food consumption during the first week in high and intermediate dose groups. Throughout the remaining period all treatment groups consumed amounts of diet similar to the controls. Hematological and clinical chemistry parameters were equivalent in dosed and control rats with the following exceptions: increased platelet counts (10,000 ppm both sexes) and increased serum gamma glutamyl transpeptidase and a depressed plasma cholinesterase in the 3,000 and 10,000	ECHA, 2013; Confidential study	Sufficient study details reported in secondary sources. Conducted in accordance with OECD Guideline 408.

Emerald Innovation™ NH-1				
PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
		ppm groups. Increased liver weight (absolute and relative) at the high dose (10,000 ppm). Microscopic examination revealed mild periportal hepatocellular hypertrophy and periportal vacuolization in males only at 3,000 and 10,000 ppm. NOAEL: 300 ppm Confidential C in the diet (equivalent to approximately 20.4 mg/kg-day), for both sexes LOAEL: 3,000 ppm (approximately 204 mg/kg-bw/day) for periportal vacuolization and hypertrophy in males		
		Confidential C: New Zealand white rabbits (6/sex/dose) were dermally exposed to Confidential C at doses of 0, 10, 100 or 1,000 mg/kg-day, 5 days/week for 21 days. There were no deaths and no adverse clinical signs of toxicity were observed in treated rabbits. No adverse systemic toxicity was observed following dosing at 1,000 mg/kg-day. Local irritation (minimal to moderate erythema, edema, atonia and desquamation) occurred in a dose-related manner and severity and increased with time. Microscopic observations of treated skin from high dose animals included squamous cell hyperplasia, hyperkeratosis, hair	ECHA, 2013; Confidential study	Sufficient study details reported in secondary sources. Conducted in accordance with OECD Guideline 410.

Emerald Innovation™ NH-1				
PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
		follicles distended with keratin and surface accumulation of keratin and erosions/ulcers. No such observations were seen in control males and only infrequently in control females. A no effect level (NOEL) for skin irritation was not established in this study, but irritation at the low dose was minimal. NOAEL: 1,000 mg/kg-day (for systemic toxicity; highest dose tested) LOAEL: Not established		
		Confidential C: Wistar rats (15/sex/group) were fed a diet containing 0.03, 0.3 or 3.0% Confidential C for 5 or 14 weeks. Body weight gain was suppressed in all rats in the top dose groups (3.0%). Serum cholinesterase activity was significantly decreased in both sexes in the 0.3 and 3.0% groups and serum gamma glutamyl transferase was significantly increased in both sexes in the top dose group after both 5 and 14-weeks of exposure. Serum amylase levels were also increased in males (0.3 and 3.0 % groups) and in females (3%). Absolute and relative liver weights in both sexes were significantly increased in the top dose group (3.0%) after both 5 and 14-weeks of treatment. Histopathological	ECHA, 2013; Confidential study	English abstract only provides qualitative data; therefore, magnitude of the effects described cannot be ascertained. NOAEL and LOAEL derived by the authors are unreliable.

Emerald Innovation™ NH-1				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		examination showed that only male rats in the top dose group (3.0%) exhibited moderate periportal hepatocyte swelling after 14-weeks. NOEL: 0.03 % diet (male rat: 20 mg/kg-day; female rat: 22 mg/kg-day) LOAEL: 0.3% (~210 mg/kg-day for males and 250 mg/kg-day for females)		
		Confidential D: 28-day repeated dose dietary study, rats were fed test substance at concentrations of 0, 250, 1,000 and 4,000 ppm. Effects on body weights were observed. NOAEL (male): 250 ppm (23.5 mg/kg-day) LOAEL (male): 1,000 ppm (161.4 mg/kg-day)	ECHA, 2012	Reported in secondary source. DfE criteria are for 90-day repeated dose studies. Criteria values are tripled for chemicals evaluated in 28-day studies.
		Confidential D: 35-day repeated-dose oral (dietary) study, 5 male rats/group, test compound concentrations of 0, 0.5, and 5.0% (~0, 350, and 3,500 mg/kg-day, respectively), with a 0.1% (~70 mg/kg-day) dose replacing the high dose group after 3 days. Slight reduction in body weight gain and increase in liver weight in 350 mg/kg-day dose group. NOAEL: 70 mg/kg-day	OECD-SIDS, 2002	Reported in a secondary source. Limited study details provided.

Emerald Innovation™ NH-1				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		LOAEL: 350 mg/kg-day		
		Confidential D: 4-month repeated-dose dietary study, Sprague-Dawley rats (10 rats/dose) were fed 0.25, 0.5, 0.75 or 1% test concentration (161, 345, 517 or 711 mg/kg-day, respectively). Reduced body weight gain (11%) at 345 mg/kg-day. NOAEL: 161 mg/kg-day LOAEL: 345 mg/kg-day	OECD-SIDS, 2002; ATSDR, 2009	Reported in a secondary source.
		Confidential D: 21-day repeated-dose dermal study, rabbits (10/sex/group) were exposed to test compound concentrations of 0, 100, and 1,000 mg/kg-day. No mortality, clinical symptoms, or changes in body weight, hematology, clinical chemistry, necropsy, organ weights and histopathology reported; only decreased acetyl cholinesterase levels in plasma, erythrocytes and brain were reported and not considered to be of toxicological relevance as there was no clinical or histological correlation. NOAEL: 1,000 mg/kg-day; highest dose tested LOAEL: Not established	OECD-SIDS, 2002	Reported in a secondary source. Treatment period only 21 days.
		Confidential D: In a 3-month study, rats were orally gavaged with test substances at 0, 380 and 1,900 mg/kg-	ATSDR, 2009	Limited study details reported in a secondary source. Primary source is an abstract with few experimental

Emerald Innovation™ NH-1				
PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
		day. No toxic effects were observed. NOEL: 1,900 mg/kg-day; highest dose tested LOEL: Not established		details.
		Confidential E: Rabbits (10/sex/dose) were dermally exposed to Confidential E at doses of 0, 10, 100, and 1,000 mg/kg 6 hours/ days, 5 days/week for 23 days. No treatment-related deaths. Edema, atonia, desquamation and fissuring. Increased mean terminal blood urea nitrogen values (high dose). Dose response depression of RBC and brain cholinesterase (mid and high dose). No effect on body weights, hematology and clinical chemistry data, organ weights and organ/body weight ratios. No treatment-related gross or microscopic changes. NOAEL: ≈ 10 mg/kg-day; LOAEL: ≈ 100 mg/kg-day	ECHA, 2013	Adequate study reported in a secondary source. Test material is defined as confidential product.
		Confidential E: Rabbits (10/sex/dose) were dermally exposed to Confidential E at doses of 100 and 1,000 mg/kg 6 hours/ days, 5 days/week for 3 weeks. No deaths. No clinical signs of toxicity. The test material was mildly	ECHA, 2013	Adequate study reported in a secondary source. Test material is defined as confidential product.

Emerald Innovation™ NH-1				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		to moderately irritating to the skin. A dose-correlated body weight effect was noted. Significant inhibition of plasma, erythrocyte and brain cholinesterase activity. No significant gross or microscopic pathologic alterations except for the local skin lesions. LOAEL: ≈ 100 mg/kg-day NOAEL: 1,000 mg/kg-day		
		Confidential E: Male and female rats (15/sex/group) were fed Confidential E in the diet at doses of 100, 300, 1,000 ppm (7.5, 21.4, 71.6 mg/kg-day, males; 9.0, 26.5, 86.2 mg/kg-day, females) for 90 days. No adverse effects related to test article treatment in any of the dosage groups. NOAEL: 1,000 ppm (71.6 mg/kg-day for males, 86.2 mg/kg-day for females; highest dose tested) LOAEL: Not established	ECHA, 2013	Adequate study reported in a secondary source. Test material is defined as confidential product.
		Confidential E: Confidential E was administered to Sprague-Dawley rats (20/sex/dose) at concentrations of 0, 100, 400 and 1,600 ppm by diet for 90 days. **Confidential E:** No treatment related mortality and clinical signs.	ECHA, 2013	Adequate study reported in a secondary source. Test material is defined as confidential product.

Emerald Innovation™ NH-1				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		Statistically significant differences in hematology and clinical chemistry values and in red blood cell, plasma and brain cholinesterase activities between control and treated animals were minimal, inconsistent and considered not to be of biological significance. A biologically significant increase in liver and adrenal weights (only females) was noted in the high-dose groups, but this was not regarded as a toxic and therefore not an adverse effect. NOAEL: 1,600 ppm (107.5 mg/kg-day for males and 124.8 mg/kg-day for females; highest dose tested) LOAEL: Not established		
		Confidential E: Sprague-Dawley rats (10/sex/dose) were fed Confidential E in the diet at doses of 0, 250, 500, 750, 1,000 and 2,000 mg/kg-day for 1 month. No deaths or toxicologically significant clinical signs. Hepatic enlargement and mahogany red livers at all doses (significant at ≥500 mg/kg-day). Rounding of hepatic edges and diffuse green-tan discoloration of kidneys (≥500 mg/kg-day).	ECHA, 2013	Adequate study reported in a secondary source. Test material is defined as confidential product.

Emerald Innovation™ NH-1				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		NOAEL: 250 mg/kg-day LOAEL: ≥500 mg/kg-day		
		Confidential E: Charles River rats (15/sex/dose) were exposed via whole-body inhalation to Confidential E aerosol at concentrations of 0, 10.1 or 101.1 mg/m^3 (0, 0.0101, or 0.1011 mg/L), or 6 hours/day, 5 days/week for a total of 62 exposures over 90 days. No deaths attributed to test material. Ruffed, discolored fur and ptosis (both doses); rhinitis, sneezing, wheezing and hemorrhagic conjunctivitis (high dose). No difference in body weights, hematology parameters, clinical chemistry values and urinalysis parameters. Gross necropsy showed no adverse effects. Increased liver weight in high-dose males. No treatment related histopathological effects. NOAEL: 101.1 mg/m^3 (0.1011 mg/L) LOAEL: Not established	ECHA, 2013	Adequate study reported in a secondary source. Test material is defined as confidential product.

Emerald Innovation™ NH-1				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Skin Sensitization		**MODERATE: Confidential C and E produced positive responses in a local lymph node assays in mice but did not produce sensitization in a modified Buehler test in guinea pigs or in repeated patch tests in human volunteers. Confidential D was not a skin sensitizer in guinea pigs.**		
	Skin Sensitization	**Confidential C:** Sensitizing, mouse local lymph node assay (LLNA). The test item solutions were applied on the dorsal surface of ears of experimental animals (25 µL/ear) for three consecutive days. A significant lymphoproliferative response was noted.	ECHA, 2013	Sufficient study details reported in a secondary source. Conducted according to OECD Guideline 429.
		Confidential C: Not sensitizing, guinea pigs, modified Buehler test There were no signs of irritation at any of the test sites during induction or at challenge. No data provided regarding positive controls.	ECHA, 2013	The lack of positive controls diminishes reliability of the results.
		Confidential C: Not sensitizing, repeated human insult patch test in 209 volunteers. 3-week induction period, 4 applications of 0.2 mL per week for 24 hours to occluded skin. During the fourth week, 4 similar applications were made to previously untreated sites. There was no dermal reaction to challenge applications.	Confidential study	Sufficient information reported in a secondary source.
		Confidential D: Several human case studies have reported allergic dermatitis; 15 of 23,192 (0.065%) human volunteers patch tested from 1950 to 1962 had positive reactions to cellulose acetate film containing 7-	OECD-SIDS, 2002	Reported in a secondary source. Limited study details provided; patch testes conducted with mixtures; unclear which component of mixture caused low incidence of sensitization.

Emerald Innovation™ NH-1				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		10% Confidential D and 3-4% phthalic esters		
		Confidential D: A confidential skin sensitization study with negative results in guinea pigs	Submitted confidential study	Reported in a confidential study.
		Confidential D: None of the patients tested in two separate studies of 343 and 174 patients, respectively, had sensitization reactions to triphenyl phosphate	OECD-SIDS, 2002	Reported in a secondary source. Limited study details provided.
		Confidential D: Not sensitizing, guinea pig maximization test	OECD-SIDS, 2002	Study reported in a secondary source; conducted according to OECD Guide-line 406.
		Confidential E: Sensitizing, Mouse local lymph node assay (LLNA).	ECHA, 2013	Adequate study reported in a secondary source. Test material is defined as confidential product.
		Confidential E: Not sensitizing, patch test, human volunteers	ECHA, 2013	Adequate study reported in a secondary source. Test material is defined as confidential product.
Respiratory Sensitization		**No data were located.**		
	Respiratory Sensitization			No data located.

Emerald Innovation™ NH-1				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Eye Irritation		**MODERATE: Confidential C produced slight irritation in rabbits which persisted up to 72 hours in some animals. Confidential D is mildly irritating to the eyes with effects clearing within 72 hours. Confidential E did not produce eye irritation in rabbits.**		
	Eye Irritation	**Confidential C:** Slightly irritating, rabbits. Undiluted 0.1 mL was applied; the eye was washed 24 hours later. One hour up to 72 hours, the treated conjunctiva showed beefy-red blood vessels and slight to moderate swelling. From 24 to 48 hours, the iris of one animal was reddened. Diffuse translucent areas of the cornea were observed one hour after administration in two animals, persisting to72 hours in one animal. Clear colorless discharge was observed in all animals, persisting to 48 hours in one animal. All signs of irritation had resolved at 7 days.	ECHA, 2013	Sufficient study details reported in a secondary source. Conducted in accordance with OECD Guideline 405.
		Confidential C: Slightly irritating, rabbits (3/sex). Undiluted 0.1 mL was applied. All dosed rabbits displayed excessive blinking and rubbing on instillation. No corneal opacity or iritis. Conjunctival redness, chemosis and discharge in all rabbits at 1-h post-exposure and redness persisted in 1/6 rabbits through 48-h. Slight to obvious swelling with partial eversion of the eyelids and slight discharge was observed in all rabbits at 1-h post-	ECHA, 2013	Sufficient study details reported in a secondary source.

Emerald Innovation™ NH-1				
PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
		instillation. All ocular lesions had resolved at 72-h.		
		Confidential C: Slightly irritating, rabbits (3/sex). **Confidential C:** No corneal opacity. Iritis (grade 1) in one female rabbit. Conjunctival irritation (grade 1 or 2) in all test animals at 1hour post-instillation, in 4 rabbits at 24 hours, persisting to 72 hours in one rabbit.	ECHA, 2013	Sufficient study details reported in a secondary source.
		Confidential C: Slightly irritating, rabbits. Undiluted 0.1 mL was applied. 3/6 rabbits exhibited moderate conjunctival erythema and iritis which resolved within 48-h.	ECHA, 2013	Limited study details reported in a secondary source.
		Confidential C: In four studies Confidential C was non-irritating to the eyes of albino rabbits.	Confidential study	No details provided in a secondary source.
		Confidential D: Not irritating, rabbits	OECD-SIDS, 2002	Study reported in a secondary source; conducted according to OECD Guide-line 405.
		Confidential D: Mild irritation in rabbit eyes, clearing within 72 hours	OECD-SIDS, 2002	Study reported in a secondary source
		Confidential E: Not irritating, rabbits	Confidential study	Adequate primary source. Test material is defined as confidential product.
		Confidential E: Not irritating, rabbits; No irritation in the washed and unwashed eyes after 24, 48, 72 hours and 4 days.	ECHA, 2013	Adequate study reported in a secondary source. Test material is defined as confidential product.

Emerald Innovation™ NH-1				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		Confidential E: Not irritating, rabbits; No irritation in the washed and unwashed eyes after 1 hour or up to 4 days.	ECHA, 2013	Adequate study reported in a secondary source. Test material is defined as confidential product.
		Confidential E: Not irritating, rabbits; No irritation in the washed and unwashed eyes after 24, 48, 72 hours and 4 and 7 days.	ECHA, 2013	Adequate study reported in a secondary source. Two studies, test material is a confidential product.
Dermal Irritation		**MODERATE: Based on weight of evidence. Confidential C produced moderate irritation in rabbits which persisted up to 72 hours in some animals. Confidential E initially produced moderate to severe irritation in rabbits with mild to moderate irritation and erythema persisting 72 hours post-administration. Confidential D is not a skin irritant in rabbits.**		
	Dermal Irritation	**Confidential C:** Moderately irritating, three rabbits. Undiluted 0.5 mL applied for 4 hours; semi occlusive. Well-defined to severe erythema up to 72 hours in 2 rabbits. Same rabbits showed very slight to slight edema, with roughness and scaling of the skin up to 7 days. All effects were reversible within 14 days.	ECHA, 2013	Sufficient details reported in a secondary source. Conducted in accordance with OECD Guideline 404.
		Confidential C: Moderately irritating, six rabbits. Undiluted 0.5 mL was applied. Erythema was more severe in abraded than intact sites at both 24- and 72-hours. Effects were not fully reversible within 72-hours.	ECHA, 2013	Sufficient study details reported in a secondary source.
		Confidential C: Slightly irritating, six rabbits	ECHA, 2013	Sufficient study details reported in a secondary source.

Emerald Innovation™ NH-1				
PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
		Undiluted 0.5 mL was applied to intact skin of rabbits under occlusion for 4-hour induced a slight transient irritation response.		
		Confidential C: Slightly irritating, six rabbits. Undiluted 0.5 mL applied for 2 hours; occlusive. At 24-hour post exposure rabbits had slight erythema at the intact site with incidence and severity of irritation increasing at 72-hour to well-defined erythema. At the abraded sites, the incidence and severity of irritation remained the same over both time periods. No edema or corrosive effect was observed in any treated rabbit at any site. Effects were no fully reversible within 72 hours.	ECHA, 2013	Sufficient study details reported in a secondary source.
		Confidential C: Irritating, rabbits (6/sex/group), 21-day dermal study. Rabbits received 10, 100, or 1,000 mg/kg on unabraded skin followed by occlusion for 6 hours. Slight to moderate erythema. Microscopic observations showed squamous cell hyperplasia, hyperkeratosis, hair follicles distended with keratin and surface accumulation of keratin and cellular debris, erosions ulcers, acute/subacute inflammation and congestion and hemorrhages in various combinations. Dose-related effects with increasing severity over	Confidential study	Sufficient study details reported in a secondary source.

Emerald Innovation™ NH-1				
PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
		time.		
		Confidential C: Not irritating, six rabbits. Undiluted 0.5 mL applied for 24 hours; occlusive. Irritation consisted of very slight erythema (scores of 0.33 at 24-hour and 0.17 at 72-h).	ECHA, 2013	Sufficient study details reported in a secondary source.
		Confidential D: Not irritating, rabbits; semi-occlusive or occlusive conditions for 4, 24 or 72 hours	OECD-SIDS, 2002	Study reported in secondary source; conducted according to OECD Guide-line 404
		Confidential D: Non-irritant, rabbit	ATSDR, 2009	Reported in a secondary source.
		Confidential E: Irritating, rabbits; Moderate to severe erythema in intact and abraded skin of 6 rabbits after 4 hours. By 24 hours, irritation decreased to mild erythema in two rabbits. At 72 hours, 5 rabbits had mild to moderate erythema and irritation cleared in 1 rabbit.	ECHA, 2013	Adequate study reported in a secondary source. Test material is defined as confidential product.
		Confidential E: Irritating, rabbits; Mild erythema and edema 24 hours after exposure (4 rabbits). At the 72 hour observation, irritation decreased and included mild erythema in one of the six rabbits. Primary Irritant Score = 0.46.	ECHA, 2013	Adequate study reported in a secondary source. Test material is defined as confidential product.
		Confidential E: Not irritating, rabbits	Confidential study	Adequate primary source. Test material is defined as confidential product.
		Confidential E: Not irritating, rabbits; No effects in intact and abraded skin	ECHA, 2013	Adequate study reported in a secondary source. Test material is defined as confidential product.

Emerald Innovation™ NH-1				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		following a 24 hour exposure.		
		Confidential E: Not irritating, rabbits; Mild erythema was noted at the 24 hour observation period in 2/6 animals. All scores were 0 by 72 hours.	ECHA, 2013	Adequate study reported in a secondary source. Test material is defined as confidential product.
Endocrine Activity		**Confidential C is listed in one study in the top 20 EOCs (endocrine disrupting chemicals) in U.S. stream waters. It inhibited the luciferase expression induced by dihydrotestosterone and 17ß-estradiol and increased both 17 beta-estradiol (E2) and testosterone (T) concentrations in H295R cells. Confidential C was negative for estrogenic activity in a yeast two-hybrid assay and did not act as an estrogen receptor agonist or adversely affect sex hormones of zebrafish.** **Confidential D was found to be inactive in estrogen-receptor binding assays; however, it was shown to be a moderate androgen-receptor (AR) binder in a competitive binding assay. Confidential D was shown to inhibit human AR in the absence of agonist and to inhibit testosterone-induced AR activity. In addition, Confidential D significantly impaired reproduction in zebrafish and was correlated with decreased sperm count and altered hormone levels in men. Increased serum thyroxine (T4) levels were reported in the serum of dams following oral administration to a confidential product containing Confidential D; other components of the mixture were not identified. It is unclear which component or components of the mixture are driving the endocrine activity effects.** **No data were available for Confidential E. By analogy, rats exposed to a mixture containing Confidential E had significantly prolonged diestrus, hypertrophy and cholesteryl lipidosis of adrenocortical and ovarian interstitial cells and minimal degeneration in the adrenal cortex and ovary. No effect on the testes was noted.**		
		Confidential C: Ranked as a top 20 EOC (endocrine disrupting chemical) in U.S. stream water	Confidential study	
		Confidential C: Confidential C inhibited the luciferase expression induced by dihydrotestosterone (10^{-9} M). The IC_{50} value was 4.7×10^{-5} - 6.0×10^{-4} M. Confidential C also	Confidential study	Adequate primary source; Japanese with English abstract.

Emerald Innovation™ NH-1			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	inhibited the luciferase expression induced by 17ß-estradiol (3 x 10^{-10} M). The IC_{50} value was 3.3 x 10^{-5} - 2.3 x 10^{-4} M.		
	Confidential C: Endocrine disrupting potential investigated using human cell lines as well as zebrafish (*Danio rerio*). Sex hormone synthesis and steroidogenic gene transcriptions were measured using H295R cells. With MVLN cells, estrogen receptor binding activities of OPFRs were evaluated. In zebrafish, sex hormones and related gene transcriptions were determined for each sex after 14 days of exposure. Confidential C increased both 17 beta-estradiol (E2) and testosterone (T) concentrations in H295R cells. In MVLN cells. Transcription of SULT1E1 and SULT2A1 genes was down-regulated when the cells were exposed to 10 mg/L Confidential C. Confidential C did not act as an estrogen receptor agonist and had no adverse effects on sex hormones of zebrafish.	Confidential study	Adequate primary source.
	Confidential C: Negative for estrogenic activity in a yeast two-hybrid assay. REC10 (M) = >1 x 10^{-4} (concentration showing 10% relative activity of 10^{-7} M 17 beta-estradiol)	Confidential study	Adequate primary source.
	Confidential D: 21-day reproduction	Confidential study	Adequate primary source.

Emerald Innovation™ NH-1			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	study in zebrafish. Significant decrease in fecundity, significant increases of plasma 17B-estradiol (E2) concentrations, vitellogenin (VTG) levels, and E2/testosterone (T) and E2/11-ketotestosterone (11-KT) ratios. Sex-dependent changes in transcriptional profiles of several genes of the hypothalamus-pituitary-gonad (HPG) axis.		
	Confidential D: Study conducted to determine effects of triaryl phosphates on mouse and human nuclear receptors. Mouse constitutively active receptor (CAR) was activated by 1.3-fold following exposure to Confidential D. Testosterone-induced AR-dependent activity was lowered by 30-40%.	Confidential study	Adequate primary source.
	Confidential D: Exposure to Confidential D in zebrafish resulted in severe pericardial edema and blocked looping of the atrium and ventricle. Confidential D-induced cardiotoxicity in zebrafish embryos is mediated through an AHR independent pathway.	Confidential study	Adequate primary source.
	Confidential D: In a luciferase reporter-gene assay using cultured cells, Confidential D inhibited the luciferase expression induced by dihydrotestosterone (10^{-9} M).	Confidential study	Primary source in Japanese with English abstract.

Emerald Innovation™ NH-1			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	IC_{50} for antiandrogenic activity = 0.000047 - 0.0006 M		
	Confidential D: Endocrine disrupting potential was investigated using human cells lines (H295R, MVLN) and zebrafish plasma. Confidential D was cytotoxic to H295R cells (showing <80% cell viability at ≥ 10 mg/L) and significantly increased E2 and T production. Transcription of CYP19A1 was significantly up-regulated and transcription of SULT1E1 gene was down-regulated. No binding affinity to E2 receptor in MVLN cells, but binding of E2 to ER was reduced in a dose-dependent manner. Plasma E2 was significantly increased in fish plasma and T and 11-KT were decreased (1 mg/L). Changes in transcription of steroidogenic genes and vitellogenin gene were observed.	Confidential study	Adequate, primary source.
	Confidential D: Men living in homes with higher amounts of Confidential D in house dust had reduced sperm count and altered hormone levels related to fertility and thyroid function. Each interquartile range (IQR) Confidential D increase in house dust samples was associated with a 19% decrease in sperm concentrations and a 10% increase in prolactin levels.	Confidential study	The actual exposure to Confidential D is unknown; it is not known if Confidential D or other substances found in the household dust caused or contributed to the reported toxicity.

Emerald Innovation™ NH-1			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	Confidential D: Pregnant Wistar rats were administered 0, 0.1 or 1 mg/kg-day of the analog confidential product in the diet during gestation and through lactation (GD8 - PND 21); Increased serum thyroxine (T4) levels (increase of 65%) in the high dose dams compared to controls was reported. There was no significant change in triiodothyronine (T3) levels in dam serum. There was no reported statistically significant change in T4 or T3 levels in pup serum on PND 21 when compared to controls.	Confidential study	Estimated based on experimental data for a confidential product.
	Confidential D: Inhibited AR activity in COS-1 cells transfected with human AR both in the absence of agonist, as well as inhibited testosterone-induced AR activity by 30 40%. (Measured)	ATSDR, 2009	Reported in a secondary source.
	Confidential D: Moderate binding in a competitive androgen-receptor (AR) binding assay using recombinant rat protein expressed in *Escherichia coli*.	ATSDR, 2009	Reported in a secondary source.
	Confidential D: Inactive in a binding assay with the rat uteri estrogen receptor from ovariectomized Sprague-Dawley rats	ATSDR, 2009	Reported in a secondary source
	Confidential E: In an oral study, male and female rats were administered Confidential E at doses of 0 or 1.7 g/kg-day (0 or 1700 mg/kg-day) via gavage in sesame oil	Confidential study	Estimated based on analogy. Data are for a confidential mixture.

Emerald Innovation™ NH-1			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	or 2.8 g/kg (2,800 mg/kg) neat Confidential E for 20, 40 and 60 days. Hypertrophy and cholesteryl lipidosis of adrenocortical and ovarian interstitial cells; minimal degeneration in the adrenal cortex and ovary. No decreased testicular weight or degeneration of seminiferous tubules. (Estimated by analogy)		
	Confidential E: In an oral study, groups of intact and ovariectomized female rats were administered Confidential E at doses of 0 or 1.7 g/kg-day (0 or 1,700 mg/kg-day) via oral gavage in sesame oil vehicle or as neat Confidential E for 20, 40 or 60 days. Cholesteryl lipidosis in AC and OI cells; elevated estradiol levels (14.5 times greater than controls). No effect on serum concentrations of androstenedione and corticosterone. Abnormal reproductive cycles in treated females that were significantly prolonged in diestrus. Increased liver weights (134% that of controls) and P-450 enzymes (3 times greater than controls) (Estimated by analogy)	Confidential study	Estimated based on analogy. Data are for a confidential mixture.

Emerald Innovation™ NH-1				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Immunotoxicity		**Confidential C produced weak inhibition of mouse lymphocyte mitogenesis for T-cells; no inhibition was observed in B-cells. Oral exposure of rats to Confidential D for 4 months and dermal exposure of rabbits for 3 weeks produced no effects on immune function parameters.**		
	Immune System Effects	**Confidential C:** Immunotoxicity evaluation using the mouse splenic lymphocyte mitogenesis test. No inhibition for lymphocyte mitogenesis in B-cells; weak inhibition for lymphocyte mitogenesis for T cells.	Confidential study	
		Confidential D: 120-day dietary study, rats, 0, 0.25, 0.5, 0.75, and 1% of Confidential D(~0, 161, 345, 517 and 711 mg/kg-day); initial, secondary, and tertiary immunizations with sheep red blood cells performed at 60, 81, and 102 days, respectively. No significant effects were reported on the weight and histopathology of the spleen, thymus and lymph nodes, and no significant changes to the humoral response were reported.	ATSDR, 2009	Reported in a secondary source.
		Confidential D: Rabbits, up to 1,000 mg/kg-day, applied 5 days/week for 3 weeks to intact or abraded skin had no gross or microscopic effects on the spleen, thymus, or lymph nodes.	ATSDR, 2009	Reported in a secondary source.

Emerald Innovation™ NH-1			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
ECOTOXICITY			
ECOSAR Class			
Acute Aquatic Toxicity	**VERY HIGH: Based on experimental fish 96-hour LC_{50} values < 1.0 mg/L for Confidential D and E and a 48-hour EC_{50} of 0.34 mg/L in daphnia for Confidential E. Acute aquatic toxicity is of HIGH concern for Confidential C based on an experimental 48-hour LC_{50} of 6.8 mg/L in fish.**		
Fish LC_{50}	**Confidential C:** Freshwater fish (*Oryzias latipes*) 48-hour LC_{50} = 6.8 mg/L (mortality 30°C), 27 mg/L (mortality 20°C) and 44 mg/L (mortality 10°C) Static conditions. The acute toxicity of Confidential C to the killifish is increased with an increase in temperature. (Experimental)	ECHA, 2013; Confidential study	Adequate study reported in Japanese with English summary and tables.
	Confidential C: Freshwater fish (*Carassius auratus*) 96-hour LC_{50} > 5 mg/L (Experimental)	Confidential study	Adequate study reported in a secondary source.
	Confidential C: Freshwater fish (*Pimephales promelas*) 96-hour LC_{50} = 11.2 mg/L Flow-through conditions; nominal concentrations of 6.29, 9.68, 14.9, 22.9 and 35.2 mg/L. (Experimental)	ECHA, 2013	Adequate study reported in a secondary source.
	Confidential C: Freshwater fish (*Pimephales promelas*) 96-hour LC_{50} = 16 mg/L (Experimental)	Confidential study	Adequate study reported in a secondary source

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PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	Confidential C: Freshwater fish (*Oncorhynchus mykiss*) 96-hour LC_{50} = 24 mg/L Nominal concentrations of 0 (control, dechlorinated tap water), 10, 18, 32, 56, 100 mg/L under static conditions (Experimental)	ECHA, 2013; Confidential study	Adequate study reported in a secondary source. No monitoring of physico-chemical conditions.
	Confidential C: Freshwater fish 96-hour LC_{50} = 5.06mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	Estimate for the Esters class was provided for comparative purposes. See Section 5.5.1.
	Confidential D: Freshwater fish (*Oncorhynchus mykiss*) 96-hour LC_{50} = 0.4 mg/L (Experimental)	OECD-SIDS, 2002	Reported in a secondary source.
	Confidential D: Freshwater fish (*Oncorhynchus mykiss*) 96-hour LC_{50} = 0.85 mg/L (Experimental)	OECD-SIDS, 2002	Reported in a secondary source. Guideline study.
	Confidential D: Freshwater fish (*Lepomis macrochirus*) 96-hour LC_{50} = 290 mg/L (Experimental)	OECD-SIDS, 2002	Limited study details reported in a secondary source. The study does not meet important criteria for standard methods (e.g., test substance concentration at solubility threshold in water).
	Confidential D: Fish 96-hour LC_{50} = 1.34mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	Estimate for the Esters class was provided for comparative purposes. See Section 5.5.1.
	Confidential E: Freshwater fish (*Ictalurus punctatus*) 96-hour LC_{50} = 0.8 mg/L (static);	ECHA, 2013	Adequate study reported in a secondary source. Test material is a confidential product.

Emerald Innovation™ NH-1			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	Nominal concentrations: 0.06, 0.12, 0.25, 0.5 and 1.0 mg/L (Experimental)		
	Confidential E: Freshwater fish (*Oncorhynchus mykiss*) 96-hour LC_{50} = 2 mg/L (static); 24-hour LC_{50} = 26 mg/L; 48-hour LC_{50} = 13 mg/L; **Confidential E:** 96-hour NOEC = 0.56 mg/L; nominal concentrations: 0.56, 0.75, 1.0, 1.4, 1.8, 2.4, 3.2, 4.2, 5.6, 7.5, 10, 14, 18, 24, 32 and 49 mg/L (Experimental)	ECHA, 2013	Adequate study reported in a secondary source. Test material is a confidential product.
	Confidential E: Freshwater fish (*Oncorhynchus mykiss*) 96-hour LC_{50} = 2 mg/L (static) (Experimental)	ECHA, 2013	Adequate study reported in a secondary source. Test material is a confidential product.
	Confidential E: Freshwater fish (*Pimephales promelas*) 96-hour LC_{50} = 2.3 mg/L (static) (Experimental)	ECHA, 2013	Adequate study reported in a secondary source. Test material is a confidential product.
	Confidential E: Freshwater fish (*Oncorhynchus mykiss*) 96-hour LC_{50}= 2.37 mg/L (static); 24-hour LC_{50} = 7.1 mg/L; 48-hour LC_{50}= 3.77 mg/L; 96-hour NOEC = 1 mg/L; nominal concentrations:1.0, 1.8, 3.2, 5.6 and 10.0 mg/L (Experimental)	ECHA, 2013	Adequate study reported in a secondary source. Test material is a confidential product.
	Confidential E: Saltwater fish (*Cyprinodon variegatus*)	ECHA, 2013	Adequate study reported in a secondary source. Test material is a

Emerald Innovation™ NH-1			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	96-hour LC_{50} = 3 mg/L (static); 96-hour NOEC = 1.8 mg/L; (Experimental)		confidential product.
	Confidential E: Freshwater fish (*Lepomis macrochirus*) 96-hour LC_{50} = 3.1 mg/L (static) (Experimental)	ECHA, 2013	Adequate study reported in a secondary source. Test material is a confidential product.
	Confidential E: Freshwater fish (*Pimephales promelas*) 96-hour LC_{50} = 3.4 mg/L (static) (Experimental)	ECHA, 2013	Adequate study reported in a secondary source. Test material is a confidential product.
	Confidential E: Freshwater fish (*Oncorhynchus mykiss*) 96-hour LC_{50} = 3.9 mg/L (flow-through); 24-hour LC_{50} = 10.4 mg/L; 48-hour LC_{50} = 4.9 mg/L; 72-hour LC_{50} = 4.2 mg/L; 96-hour NOEC = 2.5 mg/L (Experimental)	ECHA, 2013	Adequate study reported in a secondary source. Test material is a confidential product.
	Confidential E: Freshwater fish (*Oncorhynchus mykiss*) 96-hour LC_{50} = 5.4 mg/L (static) 24-hour LC_{50} = 30.3 mg/L; 48-hour LC_{50} = 15.2 mg/L; 96-hour NOEC = 3.2 mg/L; nominal concentrations:3.2, 5.6, 10.0, 18.0 and 32.0 mg/L (Experimental)	ECHA, 2013	Adequate study reported in a secondary source. Test material is a confidential product.
	Confidential E: Saltwater fish (*Cyprinodon variegatus*) 96-hour LC_{50} > 0.27 mg/L (semi-	ECHA, 2013	Adequate study reported in a secondary source. Test material is a confidential product.

Emerald Innovation™ NH-1			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	static); 96-hour NOEC = 0.27 mg/L; nominal concentrations: 0.13, 0.22, 0.36, 0.6 and 1.0 mg/L (Experimental)		
	Confidential E: Saltwater fish (*Cyprinodon variegatus*) 96-hour LC_{50} > 1.3 mg/L (semi-static); 96-hour NOEC = 1.3 mg/L nominal concentrations: 0.13, 0.22, 0.36, 0.60 and 1.0 mg/L measured (mean) concentrations: 0.19, 0.33, 0.38, 0.83 and 1.3 mg/L (Experimental)	ECHA, 2013	Adequate study reported in a secondary source. Test material is a confidential product.
	Confidential E: Freshwater fish 96-hour LC_{50} = < 0.001 mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	Estimate for the Esters class was provided for comparative purposes. See Section 5.5.1. NES: The log K_{ow} of 11 for this chemical exceeds the SAR limitation for the log K_{ow} of 5.0; NES are predicted for these endpoints.
Daphnid LC_{50}	**Confidential C:** *Daphnia magna* 48-hour EC_{50} = 53 mg/L 48-hour NOEC = 4.6 mg/L Nominal concentrations: 2.2, 4.6, 10, 22, 46 and 100 mg/L; Measured concentrations: 4.44-8.33-22.2-46.0-100 mg/L (initial) (Experimental)	ECHA, 2013	Adequate study reported in a secondary source. Conducted in accordance with OECD Guideline 202.
	Confidential C: *Daphnia magna* 48-	Confidential study	Adequate study reported in a

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PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	hour EC_{50} = 75 mg/L; 24-hour LC_{50} = 84 mg/L; NOEC = 32 mg/L (Experimental)		secondary source.
	Confidential C: *Daphnia magna* 48-hour LC_{50} = 8.73mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	Estimate for the Esters class was provided for comparative purposes. See Section 5.5.1.
	Confidential D: Daphnid 48-hour LC_{50} = 1.28 mg/L (Experimental)	Confidential study	Sufficient study details reported.
	Confidential D: Daphnid 48-hour EC_{50} = 1.35 mg/L Static (Experimental)	OECD-SIDS, 2002	Study reported in a secondary source; conducted according to US EPA 660/3-75-009.
	Confidential D: Daphnid 48-hour LC_{50} = 1.0 mg/L (Experimental)	Confidential study	Sufficient study details reported.
	Confidential D: Daphnid 48-hour LC_{50} = 2.11 mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	Estimate for the Esters class was provided for comparative purposes. See Section 5.5.1.
	Confidential E: *Daphnia magna* 48-hour EC_{50} = 0.34 mg/L (static) (Experimental)	ECHA, 2013	Adequate study reported in a secondary source. Test material is a confidential product.
	Confidential E: *Daphnia magna* 48-hour EC_{50} = 2.9 mg/L (static) Test concentrations not specified (Experimental)	ECHA, 2013	Adequate study reported in a secondary source. Test material is a confidential product.
	Confidential E: *Daphnia magna* 48-hour EC_{50} = 5 mg/L (static) Test concentrations not specified	ECHA, 2013	Adequate study reported in a secondary source. Test material is a confidential product.

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PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	(Experimental)		
	Confidential E: *Daphnia magna* 48-hour LC_{50} < 0.001 mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	Estimate for the Esters class was provided for comparative purposes. See Section 5.5.1. NES: The log K_{ow} of 11 for this chemical exceeds the SAR limitation for the log K_{ow} of 5.0; NES are predicted for these endpoints.
Green Algae EC_{50}	**Confidential C:** Green algae (*Pseudokirchneriella subcapitata*) 72-hour EC_{50} = 61 mg/L (growth rate); Static conditions; nominal concentrations: 0, 0.32, 1.0, 3.2, 10, 32, 100 mg/L (Experimental)	ECHA, 2013	Adequate study reported in a secondary source. Conducted in accordance with OECD Guideline 201.
	Confidential C: Green algae 96-hour EC_{50} = 2.82mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	Estimate for the Esters class was provided for comparative purposes. See Section 5.5.1.
	Confidential D: Green algae (*Selenastrum capricornutum*) 96-hour EC_{50} = 2.0 mg/L (Experimental)	OECD-SIDS, 2002	Reported in a secondary source.
	Confidential D: Green algae 96-hour EC_{50} = 2.0 mg/L (Experimental)	Confidential study	Sufficient study details reported.
	Confidential D: Green algae 96-hour EC_{50} = 0.60mg/L (Estimated)	ECOSAR v1.11	Estimate for the Esters class was provided for comparative purposes.

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PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	ECOSAR: Esters		See Section 5.5.1.
	Confidential E: Green algae (*Pseudokirchneriella subcapitata*) 96-hour EC_{50} = 2.6 mg/L (growth rate) (static) nominal concentrations: 0.6 mg/L, 1.0 mg/L, 3.2 mg/L, 5.6 mg/L and 10 mg/L (Experimental)	ECHA, 2013	Adequate study reported in a secondary source. Test material is a confidential product.
	Confidential E: Green algae 96-hour EC_{50} < 0.001 mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	Estimate for the Esters class was provided for comparative purposes. See Section 5.5.1. NES: The log K_{ow} of 11 for this chemical exceeds the SAR limitation for the log K_{ow} of 6.4; NES are predicted for these endpoints.
Chronic Aquatic Toxicity	**VERY HIGH: Based on an experimental fish 30-day LOEC = 0.037 mg/L for Confidential D and experimental data in fish and daphnia for Confidential E. Chronic aquatic toxicity is of HIGH concern for Confidential D and E based on experimental values for algae. A High concern is also indicated for Confidential C based on estimated ChV values for fish using the ECOSAR Esters class.**		
Fish ChV	**Confidential C:** Freshwater fish ChV = 0.26 mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	Estimate for the Esters class was provided for comparative purposes. See Section 5.5.1.
	Confidential D: Freshwater fish (*Oncorhynchus mykiss*) 30-day LOEC = 0.037 mg/L (Experimental)	ECHA, 2013	Reported in a secondary source.

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PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	Confidential D: Fish (*Pimephales promelas*) 30-day LOEC = 0.23 mg/L NOEC = 0.087 mg/L There were no changes in hatchability of eggs, mean total length, and average we weight of fry. There was reduced percentage survival of fry through 30 days post-exposure at 0.23 mg/L. Severe scoliosis was reported in several fry and erratic swimming was reported in all fry at 0.23 mg/L. (Experimental)	OECD-SIDS, 2002	Sufficient study details reported.
	Confidential D: Fish ChV = 0.06 mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	Estimate for the Esters class was provided for comparative purposes. See Section 5.5.1.
	Confidential E: Freshwater fish (*Pimephales promelas*) 90-day NOEC = 0.093 mg/L (flow-through); nominal concentrations: 0.06, 0.12, 0.25, 0.5 and 1.0 mg/L measured (mean) concentrations: 0.022, 0.040, 0.093, 0.194 and 0.496 mg/L (Experimental)	ECHA, 2013	Adequate study reported in a secondary source. Test material is a confidential product.

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PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	Confidential E: Freshwater fish (*Pimephales promelas*) 30-day NOEC (growth, reproduction) = 0.14 mg/L (flow-through); 30-day LOEC (reproduction) = 0.25 mg/L; 30-day NOEC (mortality) = 0.25 mg/L; measured concentrations: 0.06, 0.14, 0.25, 0.41, 1.34 mg/L (Experimental)	ECHA, 2013	Adequate study reported in a secondary source. Test material is a confidential product.
	Confidential E: Freshwater fish (*Pimephales promelas*) 30-day LC_{50} > 1 < 2 mg/L (flow-through); nominal concentrations: 0.125, 0.25, 0.5, 1.0 and 2.0 mg/L (Experimental)	ECHA, 2013	Adequate study reported in a secondary source. Test material is a confidential product.
	Confidential E: Freshwater fish ChV < 0.001 mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	Estimate for the Esters class was provided for comparative purposes. See Section 5.5.1. NES: The log K_{ow} of 11 for this chemical exceeds the SAR limitation for the log K_{ow} of 8.0; NES are predicted for these endpoints.
Daphnid ChV	**Confidential C:** *Daphnia magna* ChV = 3.61 mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	Estimate for the Esters class was provided for comparative purposes. See Section 5.5.1.

Emerald Innovation™ NH-1			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	Confidential D: Daphnid ChV = 0.69 mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	Estimate for the Esters class was provided for comparative purposes. See Section 5.5.1.
	Confidential E: *Daphnia magna* 21-day NOEC (reproduction) = 0.015 - 0.02 mg/L (flow-through); 21-day NOEC (mortality) = 0.03 - 0.06 mg/L; 21-day EC_{50} (immobilization) = 0.028 mg/L; 5 concentrations were used, but these are not specified in the report. (Experimental)	ECHA, 2013	Adequate study reported in a secondary source. Test material is a confidential product.
	Confidential E: *Daphnia magna* 21-day NOEC (mortality) = 0.03 - 0.07 mg/L (flow-through); 21-day NOEC (reproduction) > 0.026 mg/L; 21-day EC_{50} (immobilization) = 0.023 mg/L; 5 concentrations were used, but these are not specified in the report. (Experimental)	ECHA, 2013	Adequate study reported in a secondary source. Test material is a confidential product.
	Confidential E: *Daphnia magna* 21-day NOEC (reproduction) = 0.032 mg/L (flow-through); nominal concentrations: 0, 0.032, 0.096, 0.256, 0.352 mg/L) (Experimental)	ECHA, 2013	Adequate study reported in a secondary source. Test material is a confidential product.

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PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	Confidential E: *Daphnia magna* 21-day NOEC (reproduction/survival) = 0.0399 mg/L (Flow through); 21-day LOEC (reproduction/survival) = 0.0933 mg/L; 21-day NOEC (mortality) = 0.04 mg/L; nominal (t=0): 20.025, 0.075, 0.225, 0.675 and 1 mg/L measured (t=0) sediment pond: 0.068, 0.116, 0.411, 0.980 mg/L measured (t=2) sediment pond: 0.029, 0.059, 0.202, 0.504 and 0.789 mg/L (Experimental)	ECHA, 2013	Adequate study reported in a secondary source. Test material is a confidential product.
	Confidential E: *Daphnia magna* 21-day NOEC (mortality, reproduction) = 0.040 mg/L (flow-through); 21-day LOEC (mortality, reproduction) = 0.1 mg/L nominal concentrations: 0.01, 0.20, 0.40, 0.80, 0.16 mg/L (Experimental)	ECHA, 2013	Adequate study reported in a secondary source. Test material is a confidential product.
	Confidential E: *Daphnia magna* ChV < 0.001 mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	Estimate for the Esters class was provided for comparative purposes. See Section 5.5.1. NES: The log K_{ow} of 11 for this chemical exceeds the SAR limitation for the log K_{ow} of 8.0; NES are predicted for these endpoints.

Emerald Innovation™ NH-1			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
Green Algae ChV	**Confidential C:** Green algae (*Pseudokirchneriella subcapitata*) 72-hour NOEC = 4.6 mg/L Static conditions; nominal concentrations: 0, 0.32, 1.0, 3.2, 10, 32, 100 mg/L (Experimental)	ECHA, 2013	Adequate study reported in a secondary source. Conducted in accordance with OECD Guideline 201.
	Confidential C: Green algae ChV = 1.27 mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	Estimate for the Esters class was provided for comparative purposes. See Section 5.5.1.
	Confidential D: Green algae (*Scenedesmus subspicatus*) 72-hour LOEC = 0.5 - 5 mg/L NOEC = 0.25 - 2.5 mg/L (Experimental)	OECD-SIDS, 2002	Study reported in secondary source; conducted according to OECD guideline 201.
	Confidential D: Green algae ChV = 0.35 mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	Estimate for the Esters class was provided for comparative purposes. See Section 5.5.1.
	Confidential E: Green algae (*Pseudokirchneriella subcapitata*) 14-day LOEC (biomass) = 0.1 mg/L (static); 14-day EC_{100} (93% growth inhibition) = 10.0 mg/L nominal concentrations: 0.1 mg/L, 1 mg/L, 10.0 mg/L and 100 mg/L (Experimental)	ECHA, 2013	Adequate study reported in a secondary source. Test material is a confidential product.

Emerald Innovation™ NH-1				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		Confidential E: Green algae ChV < 0.001 mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	Estimate for the Esters class was provided for comparative purposes. See Section 5.5.1. NES: The log K_{ow} of 11 for this chemical exceeds the SAR limitation for the log K_{ow} of 8.0; NES are predicted for these endpoints.
ENVIRONMENTAL FATE				
Transport		**Level III fugacity models incorporating available physical and chemical property data indicate that at steady state, the components of this mixture are expected to be found primarily in soil and to a lesser extent, water. Confidential C and D are expected to have moderate mobility in soil, based on measured K_{oc} values in silty clay, loamy sand and silt loam and estimates. Confidential E is expected to have negligible mobility in soil. Leaching through soil to groundwater may occur, though it is not expected to be an important transport mechanism. Confidential D may volatilize from moist soil and water surfaces based on its Henry`s Law constant. Volatilization from dry surface is not expected based on its vapor pressure. In the atmosphere, Confidential D is expected to exist in both the vapor phase and particulate phase; Confidential C and E are expected to exist in the particulate phase. Particulates may be removed from air by wet or dry deposition.**		
	Henry's Law Constant (atm-m^3/mole)	**Confidential C:** <10^{-8} (Estimated)	EPI v4.11	Estimated using measured water solubility and vapor pressure values.
		Confidential D: 1.2x10^{-5} (Measured)	Confidential study	Reported in a primary source.
		Confidential E: 6.9x10^{-7} (Estimated)	EPI v4.11	Using HENRYWIN v3.20 Bond method results.
	Sediment/Soil Adsorption/Desorption - K_{oc}	**Confidential C:** 1,300 (Estimated)	EPI v4.11	MCI Method
		Confidential D: 2,514 Reported for silty clay. (Measured)	Confidential study	Reported in a primary source.
		Confidential D: 2,736 Reported for silt loam (Measured)	Confidential study	Reported in a primary source.
		Confidential D: 3,561 Reported for loamy sand. (Measured)	Confidential study	Reported in a primary source.

Emerald Innovation™ NH-1				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		Confidential E: >30,000 (Estimated)	EPI v4.11; EPA, 2005	Estimated value is greater than the cutoff value, >30,000, for non-mobile compounds.
	Level III Fugacity Model	**Confidential C:** Air = 0.1% Water = 22.4% Soil = 76.8% Sediment = 0.7% (Estimated)	EPI v4.11	
		Confidential D: Air = 0.7% Water = 14.5% Soil = 75.8% Sediment = 9.02% (Estimated)	EPI v4.11	Reported in a Level III Fugacity model. Experimental data is consistent with partitioning to sediment.
		Confidential E: Air = 0.2% Water = 11.3% Soil = 85.1% Sediment = 3.5% (Estimated)	EPI v4.11	

Emerald Innovation™ NH-1				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Persistence		**MODERATE: Based on primary and ultimate biodegradation data that suggest a half-life for ultimate degradation of ≥16 days and <60 days for Confidential E based on a close structural analog. Biodegradation studies for an analog to Confidential E reported 100% primary degradation after approximately 11 days in a river die-away study and 93% primary degradation after 9 weeks in a SCAS test using activated sludge inoculum under aerobic conditions. The analog to Confidential E was found to have primary half-lives of 4.2 and 8.4 days in pond and river sediment, respectively, and showed mineralization of 1.7-37.2% after 8 weeks in water-sediment microcosms. However, DfE criteria are based on ultimate biodegradation and the above results are consistent with a MODERATE designation. Other components of the commercial mixture were found to degrade more rapidly. Confidential C was found to be readily biodegradable with activated sludge inoculum and the modified Sturm test. Confidential D was found to be readily biodegradable in a Japanese MITI ready biodegradability test, OECD 301C and 93.8% removal of Confidential D as dissolved organic carbon (DOC) occurred over 20 days in an OECD 303A guideline study. The biodegradation results for Confidential C and D are consistent with a Low persistence designation. The mixture contains phosphate esters; these components are expected to be generally resistant to hydrolysis in neutral or acidic waters, but may be hydrolyzed slowly in alkaline waters. Photolysis is not expected to be an important fate process since this mixture does not contain compounds with functional groups that would be expected to absorb light in the environment.**		
Water	**Aerobic Biodegradation**	**Confidential C:** Passes Ready Test: Yes Test method: OECD TG 301B: CO_2 Evolution Test 87% degradation after 28 days (Measured)	Confidential study	Valid guideline study.
		Confidential C: Passes Ready Test: No Test method: OECD TG 301C: Modified MITI Test (I) 0% degradation after 4 weeks using an activated sludge inoculum. (Measured)	Confidential study	Valid guideline study.
		Confidential C: Study results:	Confidential study	Valid guideline study.

Emerald Innovation™ NH-1				
PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
		88%/28d Test method: 302A: Inherent - Modified SCAS Test Primary degradation (Measured)		
		Confidential C: Study results: 51%/28d Test method: Shake Flask Ultimate biodegradation (Measured)	Confidential study	Valid non-guideline study. Monsanto shake flask procedure.
		Confidential C: Study results: Test method: Die-Away Slight degradation (~0-10%) after 30 days using river water inoculum and four river die-away tests. During two river die-away tests from the same study, the test substance achieved 20% degradation after 30 days and 100% degradation after 22 days. (Measured)	Confidential study	Valid non-guideline study; study details could not be determined as the source paper was written in Japanese.
		Confidential C: Study results: 100%/14d Test method: Other 100% degradation after 14 days using river water inoculum after an acclimatization period of several days and a molybdenum blue colorimetric method. (Measured)	Confidential study	Reported in peer reviewed secondary source. Limited study details were provided.
		Confidential C: Study results: Test method: Other	Confidential study	Reported in peer reviewed secondary source. Limited study details were provided.

Emerald Innovation™ NH-1				
PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
		17.6 and 100% degradation after 14 days using seawater inoculum after an acclimatization period of several days and a molybdenum blue colorimetric method. (Measured)		
		Confidential D: Passes Ready Test: Yes Test method: OECD TG 301C: Modified MITI Test (I) 83-94% biodegradation after 28 days at 100 mg/L of test substance. (Measured)	OECD-SIDS, 2002	Reported in a guideline study.
		Confidential D: Study results: 100%/3 days Test method: Die-Away Reported as inherently biodegradable in a river water/river die-away test (Measured)	OECD-SIDS, 2002	Reported in a secondary source.
		Confidential E: Study results: 93%/9 weeks Test method: Biological Treatment Simulation SCAS test. 93% primary degradation after 9 weeks in domestic activated sludge at a test substance addition rate of 3 mg/L every 24 hours. (Estimated by analogy)	Confidential study	Nonguideline study for confidential analog.
		Confidential E: Study results: 100%/11 days Test method: Die-Away	Confidential study	Nonguideline study for confidential analog.

Emerald Innovation™ NH-1				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		Complete primary degradation occurred after about 11 days in a river water die-away study. (Estimated by analogy)		
	Volatilization Half-life for Model River	**Confidential C:** >1 year (Estimated)	EPI v4.11	
		Confidential D: 4 days (Estimated)	EPI v4.11	Reported in the volatilization from water model.
		Confidential E: 79 days (Estimated)	EPI v4.11	
	Volatilization Half-life for Model Lake	**Confidential C:** >1 year (Estimated)	EPI v4.11	
		Confidential D: 47 days (Estimated)	EPI v4.11	Reported in the volatilization from water model.
		Confidential E: >1 year (Estimated)	EPI v4.11	
Soil	**Aerobic Biodegradation**	**Confidential D:** Study results: 93.8%/20 days Test method: 303A: Activated Sludge Units - Simulation Test Removal as DOC, using initial concentration of 5 mg/L with activated sludge. Reported as inherently biodegradable. (Measured)	EC, 2000; OECD-SIDS, 2002	Reported in a guideline study.
		Confidential D: Study results: 77%/28 days Test method: Other Reported as ultimately biodegradable. Monsanto Shake Flask Procedure (precursor to Closed bottle test). (Measured)	OECD-SIDS, 2002	Reported in a secondary source.

Emerald Innovation™ NH-1				
PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
		Confidential D: Study results: 82%/28 days Test method: CO_2 Evolution Modified Sturm test. Reported as ultimately biodegradable. Measured in domestic, adapted activated sludge (Measured)	OECD-SIDS, 2002	Reported in a secondary source.
		Confidential D: Study results: 93%/49 days Test method: 302A: Inherent - Modified SCAS Test Reported as inherently biodegradable. (Measured)	OECD-SIDS, 2002	Reported in a guideline study.
	Anaerobic Biodegradation	**Confidential C & E:** Not probable (Anaerobic-methanogenic biodegradation probability model)	EPI v4.11	
		Confidential D: Study results: 89.7%/40 days Test method: CO_2 Evolution Test Primary degradation: 31.1% after 3 days, 89.7% after 40 days in river sediment. CO_2 evolution: 0.8% after 3 days, and 21.9% after 40 days. (Measured)	OECD-SIDS, 2002	Reported in a secondary source.
	Soil Biodegradation with Product Identification			No data located.
	Sediment/Water Biodegradation	**Confidential D:** 86.9%/40 days Primary degradation in river sediment. 43.3% after 3 days 86.9% after 40 days (Measured)	OECD-SIDS, 2002	Reported in a secondary source.
		Confidential E: Mineralization of the	Confidential study	Nonguideline study for confidential

Emerald Innovation™ NH-1				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		test substance (2 mg) ranged from 1.7 to 37.2% after 8 weeks in microcosms containing sediment and water from lacustrine, riverine, and estuarine ecosystems. The rate of degradation was related to the nutrient level and contaminant. (Estimated by analogy)		analog.
		Confidential E: 50%/4.2 days at 25°C in pond sediment; 50%/8.4 days at 25°C in river sediment. Test substance was subject to static river and pond sediment-water incubations in respirometer flasks at temperatures and redox conditions typical of aquatic environments. (Estimated by analogy)	Confidential study	Nonguideline study for confidential analog.
Air	**Atmospheric Half-life**	**Confidential C:** 0.08 days (Estimated)	EPI v4.11	
		Confidential D: 1 day (Estimated)	EPI v4.11	
		Confidential E: 0.43 days (Estimated)	EPI v4.11	
Reactivity	**Photolysis**	**Confidential C, D and E:** Not expected to be a significant fate process. (Estimated)	Mill, 2000; Professional judgment	This compound does not contain functional groups that would be expected to absorb light of wavelengths >290 nm.
		Confidential D: A 0.1 mg/L solution (with acetone) was exposed to a mercury lamp to examine the effect of UV light on the degradation of Confidential D. High pressure lamp (100W): 100%/20	EC, 2000	Reported in a secondary source under laboratory conditions.

Emerald Innovation™ NH-1				
PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
		minutes Low pressure lamp (15W): 100%/1 hour (Measured)		
	Hydrolysis	**Confidential C:** Phosphate esters, are generally resistant to hydrolysis in neutral or acidic waters, but may be hydrolyzed in alkaline waters. (Measured)	Confidential study; ATSDR, 2012	Reported in several secondary sources. No quantitative rate data were located.
		Confidential C: Half-lives: 95 days at pH 5, 6, 7, and 8 93 days at pH 9 75 days at pH 10 (Estimated)	EPI v4.11	
		Confidential D: 50%/>28 days Reported at 25°C; pH 5 (Measured)	EC, 2000; OECD-SIDS, 2002	Reported in a secondary source.
		Confidential D: 50%/19 days Reported at 25°C; pH 7 (Measured)	OECD-SIDS, 2002	Reported in a secondary source.
		Confidential D: 50%/3 days Reported at 25°C; pH 9 (Measured)	EC, 2000; OECD-SIDS, 2002	Reported in a secondary source.
		Confidential D: 50%/7.5 days Reported at pH 8.2 in river/lake water (Measured)	EC, 2000	Reported in a secondary source.
		Confidential D: 50%/1.3 days Reported at pH 9.5 in river/lake water (Measured)	EC, 2000	Reported in a secondary source.
		Confidential D: 100%/10 minutes at pH 13 (Measured)	ECHA, 2013	Reported in secondary source. Documentation of study details was not sufficient to assess its reliability.
		Confidential E: Half-lives: 460 years at pH 5; 46 years at pH 6; 4.6 years at pH 7;	EPI v4.11	

Emerald Innovation™ NH-1				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		170 days at pH 8; 17 days at pH 9; 1.7 days at pH 10 (Estimated)		
Environmental Half-life		**Confidential C:** 17 days (Estimated)	PBT Profiler	Half-life estimated for the predominant compartment, soil, as determined by EPI methodology.
		Confidential D: 75 days (Estimated)	PBT Profiler	Half-life estimated for the predominant compartment, soil, as determined by EPI and the PBT Profiler methodology.
		Confidential D: In loamy sand, observed half-lives of 37 days (aerobic) and 21 days (anaerobic) (Measured)	OECD-SIDS, 2002	Reported in a secondary source.
		Confidential E: 120 days (Estimated)	PBT Profiler	Half-life estimated for the predominant compartment, soil, as determined by EPI methodology.
Bioaccumulation		**HIGH: The bioaccumulation designation is based on an estimated BAF value for Confidential E; this value is >1,000. The estimated low BCF value is consistent with the limited water solubility estimates. The bioaccumulation designations for the other components, Confidential C and D, are LOW and MODERATE, respectively.**		
	Fish BCF	**Confidential C:** 4.1 Reported as <0.6 to 4.1 in Carp. Substance concentration: 0.2 mg/L. (Measured)	HSDB, 2003	Guideline study reported in a peer reviewed secondary source.
		Confidential C: <5.8 in Carp Substance concentration: 0.02 mg/L (Measured)	HSDB, 2003	Guideline study reported in a peer reviewed secondary source.
		Confidential D: 132-364 (Rainbow trout) (Measured)	Confidential study	Adequate.
		Confidential D: 271	EC, 2000	Reported in a secondary source.

Emerald Innovation™ NH-1				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		Rainbow trout (Measured)		
		Confidential D: 364 Reported as 132-364 in rainbow trout (Measured)	OECD-SIDS, 2002	Insufficient study details to assess the quality of the reported values.
		Confidential D: 193 Reported as 84-193 in Medaka (Measured)	EC, 2000	Reported in a secondary source.
		Confidential D: 160 Reported as 68-160 in Fathead minnow (Measured)	EC, 2000	Reported in a secondary source.
		Confidential D: 144 Medaka (Measured)	OECD-SIDS, 2002	Reported in a secondary source.
		Confidential D: 110 Goldfish (Measured)	OECD-SIDS, 2002	Reported in a secondary source.
		Confidential E: 37 (Estimated)	EPI v4.11	Estimated using the representative structure.
	Other BCF			No data located.
	BAF	**Confidential C:** 54 (Estimated)	EPI v4.11	
		Confidential D: 73 (Estimated)	EPI v4.11	
		Confidential E: 18,000 (Estimated)	EPI v4.11	Estimated using the representative structure.
	Metabolism in Fish			No data located.

Emerald Innovation™ NH-1			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
ENVIRONMENTAL MONITORING AND BIOMONITORING			
Environmental Monitoring	Confidential C was detected in river water, drinking water and wastewater effluent. It was detected in indoor air and dust in offices and homes. It has been detected globally in the atmosphere. It was detected in sediment samples. Confidential D has been detected in drinking water, household dust, sediment, river water, seawater, rainwater, snow, wastewater effluent, ambient air, and indoor air (Confidential references).		
Ecological Biomonitoring	Confidential C was detected in herring gull eggs and fish. Confidential D has been detected in fish tissues, bottlenose dolphin blubber (Confidential references).		
Human Biomonitoring	Confidential C has been detected in human adipose tissue. Confidential D was detected in human milk, adipose tissue and human plasma. Confidential C, D and E were not included in the NHANES biomonitoring report (CDC, 2013; Confidential references).		

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Expandable graphite

Screening Level Toxicology Hazard Summary

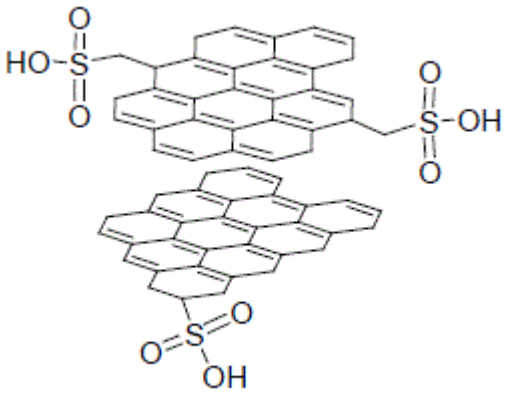
This table contains hazard information for each chemical; evaluation of risk considers both hazard and exposure. Variations in end-of-life processes or degradation and combustion by-products are discussed in the report but not addressed directly in the hazard profiles. The caveats listed below must be taken into account when interpreting the information in the table.

VL = Very Low hazard L = Low hazard M = Moderate hazard H = High hazard VH = Very High hazard – Endpoints in colored text (VL, L, M, H, and VH) were assigned based on empirical data. Endpoints in black italics *(VL, L, M, H,* and *VH*) were assigned using values from estimation software and professional judgment [(Quantitative) Structure Activity Relationships "(Q)SAR"].

♦ Expandable graphite commercial formulations are prepared using chemical washes which may be present in the final product as residues. The associated hazards vary depending on the specific wash chemicals used, and as a result, the hazards may change by manufacturer. One confidential wash has additional hazard concern as follows, based on experimental data: HIGH-Acute Toxicity, Eye Irritation, Dermal irritation. Other manufacturers may use a wash that contains chromic acid (CASRN 7738-94-5) with additional hazard concerns as follows, based on experimental data: HIGH-Acute Toxicity, Carcinogenicity, Genotoxicity, Reproductive, Repeated dose, Skin sensitization, Respiratory sensitization, Eye Irritation, Dermal irritation.

		Human Health Effects											Aquatic Toxicity**		Environmental Fate	
Chemical	CASRN	Acute Toxicity	Carcinogenicity	Genotoxicity	Reproductive	Developmental	Neurological	Repeated Dose	Skin Sensitization	Respiratory Sensitization	Eye Irritation	Dermal Irritation	Acute	Chronic	Persistence	Bioaccumulation
Expandable graphite	12777-87-6	L♦	*M*♦	L♦	*L*♦	*L*	*L*	*M*♦	*L*♦	♦	M♦	M♦	L♦	*M*♦	*H*	*L*

**Aquatic toxicity: EPA/DfE criteria are based in large part upon water column exposures which may not be adequate for poorly soluble substances such as many flame retardants that may partition to sediment and particulates.



Representative structure

CASRN: 12777-87-6

MW: >1,000 (Estimated)

MF: $[C]_n[SO_3H]_x$

Physical Forms: Solid
Neat:

Use: Flame retardant

SMILES: Not applicable

Synonyms: Sulfuric acid, compd. with graphite; Sulfuric acid, compd. With graphite (1:?); Expandable graphite; exfoliated graphite; sulfuric acid, compound with graphite; graphite hydrogen sulfate (CASRN 12689-13-3); graphite bisulfate (CASRN 12689-13-3); graphite intercalation compounds

Chemical Considerations: Expandable graphite is manufactured by a process where the carbon sheets of graphite are modified by oxidative chemical treatment. The oxidation of graphite causes an increase in the distance between graphite crystal lattice planes and an increase in the specific volume of the graphite particles by a factor of 200 to 400. There are different hazards that result from the specific wash chemicals used and, as a result, the hazards may change by manufacturer. Commercial expandable graphite products may contain 0.1-3.0% free silica or quartz (CASRN 14808-60-7) as residuals from graphite. Synthetic and natural graphite may be mixtures that contain deliberate additives such as cristobalite, clay, coal, and petroleum products. Also, natural graphite is usually found associated with impurities such as mica, iron oxide, granite and free silica in 2-25%. Expandable graphite is typically 85-98% carbon (CASRN 7782-42-5); the other components of the commercial products are the expansion agents (i.e., sulfuric acid CASRN 7664-93-9) and other formulation specific confidential additives. Nanoscale components are not expected to be present and were not included in this assessment. Expandable graphite particle sizes reported in product documentation are typically >200µm x 30 µm, outside of the nanoscale range (Jager et al., 2010; MSDS, 2012; AvTech Industries, 2013; GrafTech, 2013; IPCS, 2013; Professional judgment).

Polymeric: No
Oligomeric: Not applicable

Metabolites, Degradates and Transformation Products: Products of combustion are carbon dioxide; carbon monoxide; sulfuric acid; sulfur dioxide (MSDS, 2012).

Analog: Graphite (CASRN 7782-42-5) **Endpoint(s) using analog values:** Carcinogenicity	**Analog Structure:** Not applicable

Structural Alerts: Respirable, Poorly Soluble Particulates (EPA, 2012).

Risk Phrases: Not classified by Annex VI Regulation (EC) No 1272/2008 (ESIS, 2012).

Hazard and Risk Assessments: None identified

Expandable graphite CASRN 12777-87-6			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
PHYSICAL/CHEMICAL PROPERTIES			
Melting Point (°C)	4,489 (Estimated by analogy)	HSDB, 2009b	Reported for Graphite (CASRN 7782-42-5).
Boiling Point (°C)	3,825 sublimes (Estimated by analogy)	HSDB, 2009b	Reported for Graphite (CASRN 7782-42-5).
	Triple point: graphite-liquid-gas 4492°C at 101.325 kPa (Estimated by analogy)	HSDB, 2009a	Reported for Graphite (CASRN 7782-42-5).
Vapor Pressure (mm Hg)	$<10^{-8}$ at 25°C (Estimated)	EPA, 1999	Cutoff value for nonvolatile compounds according to HPV assessment guidance.
Water Solubility (mg/L)	<0.001 (Estimated by analogy) Graphite (CASRN 7782-42-5) is reported as insoluble in water	HSDB, 2009b	Cutoff value for non-soluble compounds.
	Soluble sulfur content in expandable natural graphite samples was determined by ICP-MS: 614, 635 and 641 mg/L; corresponds to 0.764, 0.755 and 0.789 % soluble sulfur respectively (Measured)	ECHA, 2013b	This nonguideline study provides supporting information about the solubility of the sulfur component of this sample.
	Using preliminary visual experiments the water solubility is <11 mg/L according to OECD Guideline 105 and EU Method A.6. The concentration of the test item was determined using ICP-OES method. (Measured)	ECHA, 2013b	It was not possible to determine the water solubility of the complete test item.
Log K_{ow}			No data located; this chemical is outside the estimation domain of EPI.
Flammability (Flash Point)			No data located.
Explosivity	Not expected to form explosive mixtures in air (Estimated)	Professional judgment	No experimental data located; based on its use as a flame retardant.

Expandable graphite CASRN 12777-87-6				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Pyrolysis				No data located.
pH		2 at 20°C; according to CIPAC Handbook Volume L, 2005; MT 191 Acidity or Alkalinity of Formulations (Measured)	ECHA, 2013b	Reported in a secondary source.
pK_a		Not applicable (Estimated)	Professional judgment	Not applicable; this substance contains compounds that are outside the estimation domain of SPARC.
HUMAN HEALTH EFFECTS				
Toxicokinetics		**No experimental data were located on the absorption, distribution, metabolism or excretion of expandable graphite. An IPCS reported that graphite (CASRN 7782-42-5) may be absorbed into the body following inhalation exposure; however, the report does not indicate what the data is based on and was not reported in any other source. Absorption is not expected for the oral and dermal routes of exposure based on analogy to graphite; nano-scale components are not expected to be present and data for the nanoscale graphite were not included in this assessment.**		
Dermal Absorption *in vitro*				No data located.
Absorption, Distribution, Metabolism & Excretion	**Oral, Dermal or Inhaled**	Graphite can be absorbed into the body via the inhalation route	IPCS, 2013	Very Limited data reported in a secondary source for Graphite (CASRN 7782-42-5), though there is no indication what the data is based on; this information was not reported in any other source.
	Other			No data located.

Expandable graphite CASRN 12777-87-6				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Acute Mammalian Toxicity		**LOW: Expandable graphite is not acutely toxic via the oral or dermal routes in rats. No adequate experimental data were located for the inhalation route; however, graphite dust may be irritating to the respiratory tract. Expandable graphite commercial formulations are prepared with chemical washes. There are variable hazards from the specific wash chemicals used and, as a result the hazards may change by manufacturer. A High hazard concern for acute toxicity is estimated for formulations containing one confidential wash and also for washes containing chromic acid (CASRN 7738-94-5).**		
Acute Lethality	**Oral**	Rat oral LD_{50} > 2,000 mg/kg bw All animals survived until the end of the study without showing any signs of toxicity.	ECHA, 2013b	Data are for Expandable Natural Graphite (sulfuric acid, compound with graphite), Purity > 93 %. Study was conducted according to OECD Guideline 423 and GLP.
	Dermal	Rat dermal LD_{50} > 2,000 mg/kg bw semi-occlusive conditions	ECHA, 2013b	Data are for Expandable Natural Graphite (sulfuric acid, compound with graphite), Purity > 93 %. Study was conducted according to OECD Guideline 402 and GLP.
	Inhalation	Graphite dust is irritating to the respiratory tract	REACH, 2006	Data are for Graphite (CASRN 7782-42-5); limited data reported in a secondary source.
		Inhalation LC_{50} = not determined; All attempts to generate an atmosphere using the test substance as received were unsuccessful.	ECHA, 2013b	Data are for Expandable Natural Graphite (sulfuric acid, compound with graphite), Purity > 93 %. Study was conducted according to OECD Guideline 403 and GLP. The overall results of the pre-test trials indicate that the physical properties of the test substance prevented the achievement of the required testing concentration.

Expandable graphite CASRN 12777-87-6				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Carcinogenicity		**MODERATE: No experimental data were located for expandable graphite. Graphite (CASRN 7782-42-5) is classified as a Group 1 carcinogen by IARC and a suspected carcinogen by NTP. These classifications are based on quartz as an impurity, and do not apply to graphite that is completely free of quartz. However, there is no evidence of graphite on the market in pure form. In order to remain conservative, a MODERATE hazard is designated by analogy to graphite. Expandable graphite commercial formulations are prepared with chemical washes. There are variable hazards from the specific wash chemicals used and, as a result the hazards may change by manufacturer. A High hazard concern for carcinogenicity is estimated for formulations containing chromic acid (CASRN 7738-94-5).**		
	OncoLogic Results			No data located.
	Carcinogenicity (Rat and Mouse)			No data located.
	Combined Chronic Toxicity/Carcinogenicity			No data located.
	Other	Graphite is classified as a Group 1 carcinogen and suspected carcinogen by IARC and NTP, respectively. The classifications are a result of quartz as an impurity, and do not apply to graphite that is completely free of quartz. However, there is no evidence of graphite on the market in pure form.	GrafTech, 2013	Data are for Graphite (CASRN 7782-42-5).

Expandable graphite CASRN 12777-87-6				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Genotoxicity		**LOW: Based on negative results in *in vitro* gene mutation and chromosomal aberration studies. The size of expandable graphite particles are much larger than the nanoscale graphite used in an *in vitro* micronucleus test in human bronchial epithelial cells using graphite nanofibers (95%; outer diameter 80-200 nm, inner diameter 30-50 nm, length 5-20 µm) which had positive results. Toxicity was most likely a result from the impurity quartz rather than from graphite itself. Expandable graphite commercial formulations are prepared with chemical washes. There are variable hazards from the specific wash chemicals used and, as a result the hazards may change by manufacturer. A High hazard concern for genotoxicity is estimated for formulations containing chromic acid (CASRN 7738-94-5).**		
	Gene Mutation *in vitro*	Negative, (*Salmonella typhimurium*) strains TA 98, TA 100, TA 1535, TA 1537 and TA 102 with and without metabolic activation	ECHA, 2013b	Data are for Expandable Natural Graphite (sulfuric acid, compound with graphite), Purity > 93 %. Study was conducted in accordance with OECD Guideline 471 and GLP
	Gene Mutation *in vivo*			No data located.
	Chromosomal Aberrations *in vitro*	Positive, *In vitro* micronucleus test in human bronchial epithelial BEAS 2B cells without metabolic activation; continuous treatment for 48 and 72 hours. Treatment for 24 hours produced negative results	CCRIS, 2013	Data are for Graphite (CASRN 7782-42-5); test material was graphite nanofibers (95%; outer diameter 80-200 nm, inner diameter 30-50 nm, length 5-20 µm)
		Negative, *in vitro* mammalian cell micronucleus test in human lymphocytes, with and without metabolic activation	ECHA, 2013b	Data are for Expandable Natural Graphite (sulfuric acid, compound with graphite), Purity > 93 %. Study was conducted in accordance with OECD Guidelines and GLP
	Chromosomal Aberrations *in vivo*			No data located.
	DNA Damage and Repair			No data located.
	Other			No data located.

Expandable graphite CASRN 12777-87-6				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Reproductive Effects		**LOW: No experimental data were located for expandable graphite. There were no adverse reproductive effects in rats at doses up to 1,159 mg/kg-day in an oral combined repeated dose reproduction/developmental toxicity screening study using graphite (CASRN 7782-42-5). Expandable graphite commercial formulations are prepared with chemical washes. There are variable hazards from the specific wash chemicals used and, as a result the hazards may change by manufacturer. A High hazard concern for reproductive toxicity is estimated for formulations containing chromic acid (CASRN 7738-94-5).**		
	Reproduction/Developmental Toxicity Screen			No data located.
	Combined Repeated Dose with Reproduction/ Developmental Toxicity Screen	In a combined repeated dose toxicity study with reproduction/developmental toxicity screening, male and female Wistar rats (10/sex/group) were fed expanded graphite powder in the diet at concentrations of 0, 91, 261, 813 mg/kg-day (for males), 0, 120, 343, 1,067 mg/kg-day (for females in premating period), 0, 106, 309, 930 mg/kg-day (for females during gestation) and 0, 111, 370, 1,159 mg/kg-day (for females during lactation). Mating was insufficient in all treatment groups and control; it was reported that the reason for insufficient mating was unclear. No adverse effects on precoital time or fertility, number of implantation sites or number of live born pups. No effect on litter size, pup survival, or pup body weight. Sporadically observed clinical findings in pups and controls (reduced size of testes and epidydimides) were not considered to be related to the test substance.	ECHA, 2013b	Data are for Expanded graphite powder (CASRN 7782-42-5). Study was conducted in accordance with OECD Guideline 422 and GLP.

Expandable graphite CASRN 12777-87-6				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		NOAEL (parental, reproductive and developmental): 12,000 mg/kg diet (target high limit, corresponding to 813 mg/kg-day for males and 1,067, 930 and 1,159 mg/kg-day for females during premating, gestation and lactation, respectively); highest doses tested LOAEL: Not established		
	Reproduction and Fertility Effects			No data located.
	Other			No data located.
Developmental Effects		**LOW: No experimental data were located for expandable graphite. There were no adverse developmental effects in rats at doses up to 1,159 mg/kg-day in an oral combined repeated dose reproduction/developmental toxicity screening study using graphite (CASRN 7782-42-5). Sporadically observed clinical findings in pups and controls (reduced size of testes and epidydimides) were not considered to be related to the test substance.**		
	Reproduction/ Developmental Toxicity Screen			No data located.

Expandable graphite CASRN 12777-87-6				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Combined Repeated Dose with Reproduction/ Developmental Toxicity Screen	In a combined repeated dose toxicity study with reproduction/developmental toxicity screening, male and female Wistar rats (10/sex/group) were fed expanded graphite powder in the diet at concentrations of 0, 91, 261, 813 mg/kg-day (for males), 0, 120, 343, 1,067 mg/kg-t/day (for females in premating period), 0, 106, 309, 930 mg/kg-day (for females during gestation) and 0, 111, 370, 1,159 mg/kg-day (for females during lactation). Mating was insufficient in all treatment groups and control; it was reported that the reason for insufficient mating was unclear. No adverse effects on precoital time or fertility, number of implantation sites or number of live born pups. No effect on litter size, pup survival, or pup body weight. Sporadically observed clinical findings in pups and controls (reduced size of testes and epidydimides) were not considered to be related to the test substance. NOAEL (parental, reproductive and developmental): 12,000 mg/kg-day diet (target high limit, corresponding to 813 mg/kg-day for males and 1,067, 930 and 1,159 mg/kg-day for females during premating, gestation and lactation, respectively); highest doses tested LOAEL: Not established	ECHA, 2013b	Data are for Expanded graphite powder (CASRN 7782-42-5). Study was conducted in accordance with OECD Guideline 422 and GLP.
	Prenatal Development			No data located.

Expandable graphite CASRN 12777-87-6				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Postnatal Development			No data located.
	Prenatal and Postnatal Development			No data located.
	Developmental Neurotoxicity			No data located.
	Other			No data located.
Neurotoxicity		**LOW: No experimental data were located for expandable graphite. There were no adverse neurological effects in rats at doses up to 1159 mg/kg-day in a combined repeated dose reproduction/developmental toxicity screening study using graphite (CASRN 7782-42-5). Functional Observational Battery tests were normal.**		
	Neurotoxicity Screening Battery (Adult)	In a combined repeated dose toxicity study with reproduction/developmental toxicity screening, male and female Wistar rats (10/sex/group) were fed expanded graphite powder in the diet at concentrations of 0, 91, 261, 813 mg/kg-day (for males), 0, 120, 343, 1067 mg/kg-day (for females in premating period), 0, 106, 309, 930 mg/kg-day (for females during gestation) and 0, 111, 370, 1159 mg/kg-day (for females during lactation). No effects on locomotor activity or any of the investigated endpoints of the Functional Observational Battery. NOAEL: 12,000 mg/kg-day diet (target high limit, corresponding to 813 mg/kg-day for males and 1067, 930 and 1159 mg/kg-day for females during premating, gestation and lactation, respectively); highest doses tested LOAEL: Not established	ECHA, 2013b	Data are for Expanded graphite powder (CASRN 7782-42-5). Study was conducted in accordance with OECD Guideline 422 and GLP.
	Other			No data located.

Expandable graphite CASRN 12777-87-6			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
Repeated Dose Effects	**MODERATE: No experimental data were located for expandable graphite. There were no adverse effects in rats at doses up to 1159 mg/kg-day in an oral combined repeated dose reproduction/developmental toxicity screening study using graphite (CASRN 7782-42-5). Repeated inhalation of graphite fumes or dust over a prolonged period of time may increase the risk of developing lung diseases. Prolonged and repeated overexposure to graphite dust can lead to pneumoconiosis and may increase the risks of developing respiratory cancer. It should be noted that the potential for fibrotic disease is a result of exposure to quartz as an impurity, and not to pure graphite.** **Expandable graphite commercial formulations are prepared with chemical washes. There are variable hazards from the specific wash chemicals used and, as a result the hazards may change by manufacturer. A High hazard concern for repeated dose toxicity is estimated for formulations containing chromic acid (CASRN 7738-94-5).**		

Expandable graphite CASRN 12777-87-6				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		In a combined repeated dose toxicity study with reproduction/developmental toxicity screening, male and female Wistar rats (10/sex/group) were fed expanded graphite powder in the diet at concentrations of 0, 91, 261, 813 mg/kg body weight/day (for males), 0, 120, 343, 1,067 mg/kg-day (for females in premating period), 0, 106, 309, 930 mg/kg-day (for females during gestation) and 0, 111, 370, 1,159 mg/kg-day (for females during lactation). No adverse effects on body weight gain or food consumption; no effect on hematology or clinical chemistry NOAEL (parental, reproductive and developmental): 12,000 mg/kg-day diet (target high limit, corresponding to 813 mg/kg-day for males and 1067, 930 and 1,159 mg/kg-day for females during premating, gestation and lactation, respectively); highest doses tested LOAEL: Not established	ECHA, 2013b	Data are for Expanded graphite powder (CASRN 7782-42-5). Study was conducted in accordance with OECD Guideline 422 and GLP.
		Male Wistar rats were exposed via inhalation (head/nose) to target concentrations of 0.5, 2.5, or 10 mg/m^3 graphene or graphite nanoplatelets 6 hours/day for 5 days. No adverse clinical signs or alterations in body weight. Increases in lavage markers indicative for inflammatory processes following exposure to 10 mg/m<SUP3< sup> graphene. The calculated volumetric load	Ma-Hock et al., 2013	Study details reported in a primary source; study conducted in accordance with OECD Guideline 412 and GLP

Expandable graphite CASRN 12777-87-6				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		did not correlate to toxicity, nor did the particle surface burden of the lung. No adverse effects following exposure to graphite nanoplatelets.		
		Repeated inhalation of fumes or dust over a prolonged period of time increases the risk of developing lung diseases. Prolonged and repeated overexposure to dust can lead to pneumoconiosis. Repeated exposure to high concentrations of dust may adversely affect the lungs and increase the risks of developing respiratory cancer.	REACH, 2006; GrafTech, 2013	Limited details in a secondary source. The potential for fibrotic disease is a result of exposure to quartz as an impurity, not graphite.
		There are over 600 cases of graphite pneumoconiosis reported in literature; 14 cases had relatively complete documentation as to details about dust exposure and only 1 completely documented case suggests that nearly pure graphite may cause pneumoconiosis.	HSDB, 2009b	Data are for Graphite (CASRN 7782-42-5). Study details reported in a secondary source
Skin Sensitization		**LOW: No experimental data for expandable graphite were located. Graphite (CASRN 7782-42-5) was not a dermal sensitizer in mice. Expandable graphite commercial formulations are prepared with chemical washes. There are variable hazards from the specific wash chemicals used and, as a result the hazards may change by manufacturer. A High hazard concern for skin sensitization is estimated for formulations containing chromic acid (CASRN 7738-94-5).**		
	Skin Sensitization	Not a skin sensitizer in mice. Test item: 0.5%, 1%, 2.5%, 5% and 10% graphite in acetone:olive oil (5:1). 10% graphite was the maximum achievable dose.	ECHA, 2013a	Data are for Expanded graphite powder (CASRN 7782-42-5). Study was conducted in accordance with OECD Guideline 429 and GLP.

Expandable graphite CASRN 12777-87-6				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Respiratory Sensitization		**No data were located; however, expandable graphite commercial formulations are prepared with chemical washes. There are variable hazards from the specific wash chemicals used and, as a result the hazards may change by manufacturer. A High hazard concern for respiratory sensitization is estimated for formulations containing chromic acid (CASRN 7738-94-5).**		
	Respiratory Sensitization			No data located.
Eye Irritation		**MODERATE: Expandable graphite produced slight irritation to rabbits, which was fully reversible within 6-10 days. Expandable graphite dust may cause irritation. Expandable graphite commercial formulations are prepared with chemical washes. There are variable hazards from the specific wash chemicals used and, as a result the hazards may change by manufacturer. A High hazard concern for eye irritation is estimated for formulations containing one confidential wash and also for washes containing chromic acid (CASRN 7738-94-5).**		
	Eye Irritation	Dust may irritate the eyes	REACH, 2006; GrafTech, 2013	Limited details in a secondary source
		Test substance was instilled into one eye for 24 hours. Slight irritation to rabbits which was fully reversible within 6-10 days. Conjunctival discharge, redness and chemosis, but no corrosive ocular effects.	ECHA, 2013b	Data are for Expandable Natural Graphite. Study was conducted according to OECD Guideline 405 and GLP.
Dermal Irritation		**MODERATE: Expandable graphite was not a primary skin irritant in rats; however graphite dust may irritate the skin causing eczema-like skin disorders. Prolonged contact with graphite may cause redness, irritation and dry skin. Expandable graphite commercial formulations are prepared with chemical washes. There are variable hazards from the specific wash chemicals used and, as a result the hazards may change by manufacturer. A High hazard concern for dermal irritation is estimated for formulations containing one confidential wash and also for washes containing chromic acid (CASRN 7738-94-5).**		
	Dermal Irritation	Dust may irritate skin. May cause eczema-like skin disorders (dermatitis). Prolonged skin contact may cause redness, irritation and dry skin.	REACH, 2006; GrafTech, 2013	Limited details in a secondary source.
		Test substance was applied to approximately 10% of total body surface of rats and was covered for 24 hours. Not	ECHA, 2013b	Data are for Expandable Natural Graphite. Study was conducted according to OECD Guideline 402

Expandable graphite CASRN 12777-87-6				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		a primary skin irritant in rats		and GLP.
Endocrine Activity		**No data were located**		
				No data located.
Immunotoxicity		**No experimental data were located for expandable graphite. Rats gavaged with graphite powder (CASRN 7782-42-5) suspended in physiological saline had a dose-dependent increase in LDH, ß-glucuronidase and total protein and Polymorphonuclear levels were 12.2% and 27.3% for the low and high dose, respectively. The inflammatory response was dose-related, with slight recovery after 14 days.**		
	Immune System Effects	Female Wistar rats (5/group) gavaged with 0.5 and 3 mg graphite suspended in 0.3 mL physiological saline. No mortalities or systemic effects. Dose-dependent increase in LDH, ß-glucuronidase and total protein. Polymorphonuclear levels were 12.2% and 27.3% on day 3 at the low- and high dose, respectively. Slight inflammatory effect at the low dose and moderate effect at the high dose. Slight recovery after 14 days; however, polymorphonuclear levels remained statistically increased.	ECHA, 2013a	Data are for Expanded graphite powder (CASRN 7782-42-5).
ECOTOXICITY				
ECOSAR Class				
Acute Aquatic Toxicity		**LOW: Based on experimental LD/LC_{50} values > 100 mg/L in fish daphnia and algae. It should be noted that expandable graphite may contain soluble surface acidity or alkalinity, which may be hazardous to aquatic organisms.**		
Fish LC_{50}		Freshwater fish (*Oncorhynchus mykiss*) 96-hour LC_{50} > 100 mg/L Static conditions; 100 mg/L test item (nominal concentration) (Experimental)	ECHA, 2013b	Data are for Expandable Natural Graphite (sulfuric acid, compound with graphite), Purity > 93 %. Study was conducted in accordance with OECD Guideline 203 and GLP
		Expandable graphite may contain soluble surface acidity or alkalinity, which is	MSDS, 2012	Limited details in an MSDS. Data for Expandable flake graphite, 85-

Expandable graphite CASRN 12777-87-6			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	expected to be hazardous to aquatic organisms. (Experimental)		98% carbon (CASRN 12777-87-6), manufactured by Ashbury Carbons.
Daphnid LC_{50}	Daphnia magna 48-hour EC_{50} > 100 mg/L Static conditions; 100 mg/L (nominal concentration) (Experimental)	ECHA, 2013b	Data are for Expandable Natural Graphite (sulfuric acid, compound with graphite), Purity > 93 %. Study was conducted in accordance with OECD Guideline 202 and GLP
Green Algae EC_{50}	Green algae (*Pseudokirchneriella subcapitata*) 72-hour EC_{50} > 100 mg/L Static conditions; 100 mg/L (nominal concentration) (Estimated by Analogy)	ECHA, 2013b	Data are for Expanded Graphite Powder. Study was conducted according to OECD Guideline 201 and GLP.
	Expandable graphite may contain soluble surface acidity or alkalinity, which is expected to be hazardous to aquatic organisms. (Experimental)	MSDS, 2012	Limited details in an MSDS. Data for Expandable flake graphite, 85-98% carbon (CASRN 12777-87-6), manufactured by Ashbury Carbons.
Chronic Aquatic Toxicity	**MODERATE: No data were located. Based on lack of data for this endpoint, chronic aquatic toxicity cannot be ruled out. It should be noted that expandable graphite may contain soluble surface acidity or alkalinity, which may be hazardous to aquatic organisms. This compound is not amenable to available estimation methods.**		
Fish ChV			No data located.
Daphnid ChV			No data located.
Green Algae ChV			No data located.

Expandable graphite CASRN 12777-87-6				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
ENVIRONMENTAL FATE				
Transport		**The transport evaluation is based on available analog data for graphite (CASRN 7782-42-5) and professional judgment. The negligible water solubility, and negligible vapor pressure of the naturally occurring, major component of this material would suggest that it will be relatively immobile in the environment.**		
	Henry's Law Constant (atm-m^3/mole)	$<10^{-8}$ (Estimated)	Professional judgment	Cutoff value for nonvolatile compounds based on professional judgment. No data located; this chemical is outside the estimation domain of EPI.
	Sediment/Soil Adsorption/Desorption - K_{oc}	>30,000 (Estimated)	Professional judgment; EPA, 2005	Cutoff value for nonmobile compounds.
	Level III Fugacity Model		Professional judgment	No data located; this chemical is outside the estimation domain of EPI.
Persistence		**HIGH: Expandable graphite is estimated to display high persistence in the environment. The major component of this chemical, graphite, is a naturally occurring material and is nonreactive under typical environmental conditions.**		
Water	**Aerobic Biodegradation**			No data located.
	Volatilization Half-life for Model River			No data located.
	Volatilization Half-life for Model Lake			No data located.
Soil	**Aerobic Biodegradation**			No data located.
	Anaerobic Biodegradation			No data located.
	Soil Biodegradation with Product Identification			No data located.
	Sediment/Water Biodegradation			No data located.
Air	**Atmospheric Half-life**	Not applicable (Estimated)	Professional judgment	No data located. Substance contains naturally occurring material that is

Expandable graphite CASRN 12777-87-6				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
				not amenable to atmospheric degradation processes. The negligible vapor pressure of the major component of this material suggests that partitioning to air is unlikely.
Reactivity	**Photolysis**	Not a significant fate process. (Estimated)	Professional judgment; Mill, 2000	No data located. The substance does not contain functional groups that would be expected to absorb light at environmentally significant wavelengths.
	Hydrolysis	Not a significant fate process. (Estimated)	Professional judgment	No data located; hydrolysis is not anticipated to be an environmental removal process due to the lack of functional groups that hydrolyze under environmental conditions.
Environmental Half-life				Not all input parameters for this model were available to run the estimation software (EPI).
Bioaccumulation		**LOW: This chemical is not expected to be bioaccumulative based on its negligible water solubility, large MW, large cross sectional diameter and professional judgment.**		
	Fish BCF	<100 (Estimated)	Professional judgment	This chemical has negligible water solubility. This chemical is a large solid which is unlikely to pass through biological membranes.
	Other BCF			No data located.
	BAF	<100 (Estimated)	Professional judgment	No data located; this chemical is outside the estimation domain of EPI.
	Metabolism in Fish			No data located.

Expandable graphite CASRN 12777-87-6			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
ENVIRONMENTAL MONITORING AND BIOMONITORING			
Environmental Monitoring	Graphite (CASRN 7782-42-5) is found as a naturally occurring material and is mined in open-pit and underground mines (HSDB, 2009b).		
Ecological Biomonitoring	No data located.		
Human Biomonitoring	No data located.		

AvTech Industries (2013) MSDS (Material Safety Data Sheet) FR Eco-Additive 20TM.

CCRIS (2013) Graphite Chemical Carcinogenesis Research Information System.

ECHA (2013a) Graphite. Registered substances. European Chemicals Agency. http://apps.echa.europa.eu/registered/data/dossiers/DISS-9e9d7f16-96ef-5932-e044-00144f67d031/AGGR-bbd4665b-6e31-46e4-8a3c-0c1308670910_DISS-9e9d7f16-96ef-5932-e044-00144f67d031.html#AGGR-bbd4665b-6e31-46e4-8a3c-0c1308670910.

ECHA (2013b) Sulphuric acid, compound with graphite. Registered substances. European Chemicals Agency. http://apps.echa.europa.eu/registered/data/dossiers/DISS-9e9fa19d-efcf-29ab-e044-00144f67d031/DISS-9e9fa19d-efcf-29ab-e044-00144f67d031_DISS-9e9fa19d-efcf-29ab-e044-00144f67d031.html.

EPA (1999) Determining the adequacy of existing data. Washington, DC: U.S. Environmental Protection Agency. http://www.epa.gov/hpv/pubs/general/datadeqfn.pdf.

EPA (2005) Pollution prevention (P2) framework. Washington, DC: U.S. Environmental Protection Agency, Office of Pollution Prevention and Toxics. http://www.epa.gov/opptintr/newchems/pubs/sustainable/p2frame-june05a2.pdf.

EPA (2012) TSCA New Chemicals Program (NCP) chemical categories. http://www.epa.gov/oppt/newchems/pubs/npcchemicalcategories.pdf.

ESIS (2012) European chemical Substances Information System. European Commission. http://esis.jrc.ec.europa.eu/.

GrafTech (2013) Material Safety Data Sheet GRAFGUARD.

HSDB (2009a) Carbon. Hazardous Substances Data Bank. National Library of Medicine. http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?HSDB.

HSDB (2009b) Graphite. Hazardous Substances Data Bank. National Library of Medicine. http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?HSDB.

IPCS (2013) Graphite (Natural).

Jager H, Frohs W, Banek M, et al. (2010) Carbon 4. Industrial carbons. Ullmann's encyclopedia of industrial chemistry. http://onlinelibrary.wiley.com/doi/10.1002/14356007.n05_n03/full#n05_n03-sec1-0012.

MSDS (2012) Expandable flake graphite. Material Safety Data Sheet.

Ma-Hock L, Strauss V, Treumann S, et al. (2013) Comparative inhalation toxicity of multi-wall carbon nanotubes, graphene, graphite nonoplatelets and low surface carbon black. Part and Fibre Toxicol 52(1):23-41.

Mill T (2000) Photoreactions in surface waters. In: Boethling R, Mackay D, eds. Handbook of Property Estimation Methods for Chemicals, Environmental Health Sciences. Boca Raton: Lewis Publishers, 355-381.

REACH (2006) Review of Annex IV of the regulation no. 1907/2006 (REACH) evaluation of existing entries Appendix 2.

Fyrol™ HF-5

Screening Level Toxicology Hazard Summary

This table contains hazard information for each chemical; evaluation of risk considers both hazard and exposure. Variations in end-of-life processes or degradation and combustion by-products are discussed in the report but not addressed directly in the hazard profiles. The caveats listed below must be taken into account when interpreting the information in the table.

VL = Very Low hazard L = Low hazard M = Moderate hazard H = High hazard VH = Very High hazard – Endpoints in colored text (VL, L, M, H, and VH) were assigned based on empirical data. Endpoints in black italics *(VL, L, M, H,* and *VH*) were assigned using values from estimation software and professional judgment [(Quantitative) Structure Activity Relationships "(Q)SAR"].

* Each hazard designation for a mixture is based upon the component with the highest hazard, whether it is an experimental or estimated value.
[d] This hazard designation would be assigned MODERATE for a potential for lung overloading if >5% of the particles are in the respirable range as a result of dust forming operations.
[§] Based on analogy to experimental data for a structurally similar compound.
[‡] The highest hazard designation of any of the oligomers with MW <1,000.
[∞] Based on experimental test data for a residual impurity reported to be present in this substance at levels up to 5% by weight.

Chemical	CASRN	Human Health Effects											Aquatic Toxicity		Environmental Fate	
		Acute Toxicity	Carcinogenicity	Genotoxicity	Reproductive	Developmental	Neurological	Repeated Dose	Skin Sensitization	Respiratory Sensitization	Eye Irritation	Dermal Irritation	Acute	Chronic	Persistence	Bioaccumulation
Fyrol™ HF-5*	Proprietary	L	*M*[§]	*M*	L	M	M[§]	M[d]	*L*		M	L	VH	VH	*VH*	*H*[‡]
Confidential A	Confidential	L	*L*	*M*	*L*	*L*	*M*	*L*[d]	*L*		M	L	*L*	*L*	*VH*	*L*
Confidential B	Confidential	L	*M*[§]	L	L	M	M[§]	M	*L*		L	VL	VH	VH[∞]	M	*H*[‡]

	CASRN: Confidential
	MW: Confidential
	MF: Confidential
	Physical Forms: Liquid **Neat:**
	Use: Flame retardant
SMILES: Confidential	
Synonyms: Confidential	
Chemical Considerations: This alternative is a mixture that contains polymeric components. Residual monomers, unreacted starting material and low MW oligomers are expected to be present at a level requiring their assessment. The oligomers that have a MW >1,000 are assessed using the available polymer assessment literature. The lower MW components and oligomers with a MW <1,000 are assessed with EPI v4.11 and ECOSAR v1.11 estimates due to an absence of publicly available experimental data (Boethling and Nabholz, 1997).	
Polymeric: Yes **Oligomeric:** Confidential oligomers	
Metabolites, Degradates and Transformation Products: None identified; although biodegradation or hydrolysis pathways may yield confidential substances (Professional judgment)	
Analog: Aryl phosphates and other confidential analogs **Endpoint(s) using analog values:** Carcinogenicity and Neurotoxicity	**Analog Structure:** Not applicable
Structural Alerts: Organophosphates, neurotoxicity (EPA, 2012).	
Risk Phrases: Not classified by Annex VI Regulation (EC) No 1272/2008 (ESIS, 2012).	
Hazard and Risk Assessments: None identified.	

Fyrol™ HF-5			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
PHYSICAL/CHEMICAL PROPERTIES			
Melting Point (°C)	**Confidential B:** -12 (Measured)	Confidential study	The reported values are for the pour point of the commercial polymeric mixture, which is a liquid at room temperatures.
	Confidential B: -13 (Measured)	Confidential study	The reported values are for the pour point of the commercial polymeric mixture, which is a liquid at room temperatures.
	Confidential B: -16.7 (Measured)	Confidential study	The reported values are for the pour point of the commercial polymeric mixture, which is a liquid at room temperatures.
Boiling Point (°C)	**Confidential A:** >300 (Estimated)	EPI v4.11; Professional judgment; EPA, 1999	Estimate based on representative oligomers where with MW < 1,000. Also estimated for oligomers with MWs >1,000. Cutoff value according to HPV assessment guidance and cutoff value used for large, high MW solids.
	Confidential B: 300 (Measured)	Confidential study	Decomposition may occur before the boiling point is reached.
	Confidential B: >300 (Measured)	Confidential study	Decomposition may occur before the boiling point is reached.
	Confidential B: 370 Decomposes (Measured)	Confidential study	Decomposition may occur before the boiling point is reached.
	Confidential B: > 400 Decomposes (Measured)	Confidential study	Decomposition may occur before the boiling point is reached.
	Confidential B: 38 at 138 Pa (Measured)	Confidential study	Decomposition may occur before the boiling point is reached.
Vapor Pressure (mm Hg)	**Confidential A:** 3.6×10^{-6} for n=1 2.1×10^{-8} for n=2-5 (Estimated)	EPI v4.11	Estimates based on representative oligomers.
	Confidential A: $<10^{-8}$ (Estimated)	Professional judgment; Boethling and Nabholz, 1997	Cutoff value for large, high MW polymers.

Fyrol™ HF-5			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	Confidential B: $1.9x10^{-5}$ at 20°C (Measured)	EPA, 2010	The reported experimental data is for the commercial polymeric mixture.
	Confidential B: 0.007 at 38°C (Measured)	Confidential study	The reported experimental data is for the commercial polymeric mixture.
	Confidential B: 0.28 (Measured)	Confidential study	The reported experimental data is for the commercial polymeric mixture.
	Confidential B: <0.075 at 38°C (Measured)	IUCLID, 2001	The reported experimental data is for the commercial polymeric mixture.
Water Solubility (mg/L)	**Confidential A:** 3,375 mg/L for n=1 933 mg/L for n=2 233 mg/L for n=3 1 mg/L for n=6 (Estimated)	EPI v4.11	Estimates based on representative oligomers.
	Confidential A: Soluble (Measured)	Confidential study	Non-quantitative value from a MSDS for a confidential commercial product containing 95-100% pure material.
	Confidential A: Miscible (Measured)	Submitted confidential study	Non-quantitative value with limited details reported.
	Confidential B: 1.05 (Measured) at 20°C	EPA, 2010	The reported experimental data is for the commercial polymeric mixture.
Log K_{ow}	**Confidential A:** -0.58 (Measured)	Submitted confidential study	Limited study details provided in a confidential source.
	Confidential A: 0.42 for n=1 -0.03 for n=2 -0.48 for n=3 -1.33 for n=6 (Estimated)	EPI v4.11	Estimates based on representative oligomers
	Confidential A: <-1 (Measured)	Confidential study	From a MSDS for a confidential commercial product containing 95-100% pure material.

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PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	Confidential B: 4.93 (Measured)	EPA, 2010; Confidential study	The reported experimental data is for the commercial polymeric mixture.
	Confidential B: 4.9 (Measured)	Confidential study	The reported experimental data is for the commercial polymeric mixture
Flammability (Flash Point)	**Confidential A:** Not flammable (Measured)	Confidential study	From a MSDS for a confidential commercial product containing 95-100% pure material.
	Confidential B: 302°C (Measured)	Confidential study	Adequate.
	Confidential B: >240°C (Measured)	Confidential study	Adequate.
	Confidential B: >230°C (Measured)	Confidential study	Adequate.
Explosivity	**Confidential A:** Not explosive (Measured)	Confidential study	From a MSDS for a confidential commercial product containing 95-100% pure material.
	Confidential B: Not explosive (Measured)	IUCLID, 2001; Confidential study	Insufficient study details to assess the quality of this value.
Pyrolysis			No data located.
pH	**Confidential A & B:** Not applicable (Estimated)	Professional judgment	Does not contain functional groups that are expected to ionize.
pK_a	**Confidential A & B:** Not applicable (Estimated)	Professional judgment	Does not contain functional groups that are expected to ionize.

Fyrol™ HF-5				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
HUMAN HEALTH EFFECTS				
Toxicokinetics		**Confidential B is readily absorbed via the oral route and was absorbed to a lesser extent following dermal exposure. Metabolism was extensive with metabolites excreted in feces, urine, and in expired air as CO_2. Absorption is expected to be low for all routes for Confidential A.**		
Dermal Absorption *in vitro*				No data located.
Absorption, Distribution, Metabolism & Excretion	**Oral, Dermal or Inhaled**	**Confidential B:** Studies were conducted on rats, mice and monkeys following exposure to Confidential B (purity: 99%) via intravenous injection, oral, inhalation, and dermal routes of exposure. Blood, urine and feces were collected for approximately 7 days and metabolites were isolated and characterized; the brain, mesenteric fat, kidneys, liver, lungs, tests/ovaries and spleen were collected from rats at time of necropsy Confidential B was absorbed and was extensively metabolized; Metabolism was consistent between species, sexes, and individual animals; Excretion occurred primarily in the feces and then urine	Confidential study	Non-guideline study.

Fyrol™ HF-5				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		Confidential B: Rats were exposed to radiolabeled Confidential B (purity: 99%) via a single oral gavage dose of 100 mg/kg 83% of the administered dose of Confidential B was absorbed; 80% of the absorbed radiolabelled dose was excreted in the feces as metabolites, 7% was excreted in the urine and 5% was excreted as CO_2 in expired air. Un-metabolized Confidential B was found in the feces following oral exposure, indicating that some of the administered oral dose was not absorbed through the gastrointestinal route.	Confidential study	Non-guideline study.

Fyrol™ HF-5				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		Confidential B: Rats and monkeys were administered a dermal dose of 100 mg/kg radiolabelled ^{14}C-Confidential B (purity: 99%) for 6 hours 20% of Confidential B was absorbed in the systemic circulation in rats following the six-hour exposure and < 10% was absorbed in monkeys. 7 days post-exposure, rats eliminated 7, 32, and 1% of administered dose in the urine, feces, and expired air, respectively. 1% of the administered dose was eliminated in expired air in monkeys after 7 days; the remaining absorbed dose was excreted by day 28.	Confidential study	Non-guideline study.
		Confidential B: Rats were exposed to Confidential B via nose-only inhalation for 6 hours at a target delivered dose of 100 mg/kg 60% of Confidential B was excreted in the feces in males and 52% in females following exposure. 10% in males and 7% in females was excreted in the urine.	Confidential study	Non-guideline study; doses are not reported in standard mg/L units; the authors state that actual retained dose in the lung cannot be measured accurately for the inhalation study.

Fyrol™ HF-5				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Other	**Confidential A:** For low MW components (n < 6), absorption is expected to be low for all routes based on confidential analogs. For high MW components, no absorption is expected through the skin and gastrointestinal tract. Poor absorption is expected in the lungs because the polymer is dispersible due to its physical chemical properties. (Estimated)	Professional judgment	Estimated based on analogy to a confidential analog, physical chemical properties, and professional judgment.
		Confidential B: Rats and mice were administered a single intravenous dose of 100 mg/kg Confidential B (purity: 99%) In rats, 13%, 45 %, and 7% of the administered intravenous dose was excreted in urine, feces, and expired air (as CO_2), respectively, 7 days after exposure In monkeys, 24% and 26% was excreted in urine and feces, respectively; expired air was not measured There were no data reported for mice following intravenous exposure.	Confidential study	Non-guideline study.

Fyrol™ HF-5				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Acute Mammalian Toxicity		**LOW: Based on oral and dermal LD_{50} values >2,000 mg/kg.**		
Acute Lethality	**Oral**	**Confidential A:** Rat oral LD_{50} = 5,000 mg/kg	Submitted confidential study	Data reported in a confidential study submitted to EPA for the polymeric mixture that included LMW components.
		Confidential B: Rat Oral LD_{50} >5,000 mg/kg-bw	EPA, 2010	Guideline study reported in a secondary source. Data are for the commercial polymeric mixture.
	Dermal	**Confidential A:** Rabbit dermal LD_{50} >2,000 mg/kg	Submitted confidential study	Data reported in a confidential study submitted to EPA for the polymeric mixture that included LMW components.
		Confidential B: Rat Dermal LD_{50} >2,000 mg/kg-bw	EPA, 2010	Guideline study reported in a secondary source. Data are for the commercial polymeric mixture.
	Inhalation	**Confidential B:** Rat Inhalation (aerosol, nose-only) LC_{50} >4.14 mg/L	EPA, 2010	The study is a quality guideline study reported in a secondary source; It cannot be used to determine a hazard designation because there were no effects at the highest concentrations tested (4.14 mg/L); From this data, it cannot be determined if effects happened at 4.15 mg/L (MODERATE) or at a concentration that can be considered LOW; therefore, this study cannot be used to determine a hazard designation.
Carcinogenicity		**MODERATE: Confidential B is estimated to have uncertain potential for carcinogenicity based on analogy to related chemicals and professional judgment. Confidential A is estimated to have low potential for carcinogenicity.**		

Fyrol™ HF-5				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	OncoLogic Results	**Confidential A:** Based on estimates considering that the residual monomers do not contain substituted terminal double bonds; the low MW species do not contain reactive-functional-group-bearing side chains; the polymer is cross-linked, is not linear, and has a MW of less than 100,000	OncoLogic, 2008	Estimated for the polymer containing lower MW components.
		Confidential B:	OncoLogic, 2008	Structure could not be evaluated by OncoLogic.
	Carcinogenicity (Rat and Mouse)	**Confidential B:** Uncertain potential for oncogenicity (Estimated by analogy)	Professional judgment	Estimated by analogy.
	Combined Chronic Toxicity/Carcinogenicity			No data located.
	Other			No data located.
Genotoxicity		**MODERATE: There is uncertain concern for mutagenicity of Confidential A. This substance did not cause gene mutations in bacteria; however, there is uncertainty due to the lack of experimental data for this endpoint. Complete data requirements for this endpoint are both gene mutation and chromosomal aberration assays. For instances of incomplete or inadequate mutagenicity/genotoxicity data, a Low hazard designation cannot be given. The genotoxicity hazard of Confidential B is LOW based on negative results in *in vitro* and *in vivo* studies.**		
	Gene Mutation *in vitro*	**Confidential A:** Uncertain concern for mutagenicity (Estimated)	Professional judgment	Estimated for the low MW component due to ethyl substituted phosphate.
		Confidential A: Negative for gene mutation in an Ames test in *S. typhimurium* and *E. coli*.	Submitted confidential study	Data reported in a submitted confidential study.

Fyrol™ HF-5				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		Confidential B: Negative in *Salmonella typhimurium* (strains not indicated) with and without metabolic activation at concentrations up to 5,000 µg/plate. No cytotoxicity was evident.	EPA, 2010; Confidential study	Guideline study. Data are for the commercial polymeric mixture.
		Confidential B: Negative in *Escherichia coli* (strains not indicated) with and without metabolic activation at concentrations up to 5,000 µg/plate. No cytotoxicity was evident.	EPA, 2010; Confidential study	Guideline study. Data are for the commercial polymeric mixture.
	Gene Mutation *in vivo*			No data located.
	Chromosomal Aberrations *in vitro*	**Confidential B:** Negative in chromosomal aberration test (cultured human lymphocytes) with and without metabolic activation at concentrations up to 625 µg/mL. Cytotoxicity data not indicated.	EPA, 2010; Confidential study	Guideline study. Data are for the commercial polymeric mixture.
	Chromosomal Aberrations *in vivo*	**Confidential B:** Negative in mammalian erythrocyte micronucleus test (Swiss mice) following a single oral dose of 5,000 mg/kg-bw	EPA, 2010; Confidential study	Guideline study. Data are for the commercial polymeric mixture.
		Confidential B: Negative in mammalian erythrocyte micronucleus test (mice) following single oral dose of 500 mg/kg-bw		Reported in a submitted confidential study; Study was conducted in accordance with GLP and OECD Guideline 474.
	DNA Damage and Repair			No data located.
	Other			No data located.

Fyrol™ HF-5				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Reproductive Effects		**LOW: Experimental data for Confidential B indicate no adverse effects on reproductive performance or fertility parameters at doses up to 1,000 mg/kg-day (highest dose tested) in a two generation dietary study in rats. There may be potential for reproductive toxicity based on analogy to a confidential analog. Confidential A is also estimated to have a LOW potential for reproductive effects based on expert judgment and a lack of structural alert for this endpoint.**		
	Reproduction/Developmental Toxicity Screen			No data located.
	Combined Repeated Dose with Reproduction/ Developmental Toxicity Screen			No data located.
	Reproduction and Fertility Effects	**Confidential B:** Two generation dietary reproduction study in rats. Sprague-Dawley rats (30/sex/dose) were fed 0, 50, 500, or 1,000 mg/kg-day Confidential B in the diet for 10 weeks. No clinical signs of toxicity. No effects on litter survival. No adverse effects on any reproductive or fertility parameter measured. No treatment-related lesions in any reproductive organ. NOAEL (parental systemic and reproductive toxicity) ≈ 1,000 mg/kg-day LOAEL: not established	EPA, 2010; Confidential study	Study details reported in a secondary source. Data are for the commercial polymeric mixture.

Fyrol™ HF-5				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		Confidential B: Potential for reproductive toxicity; no pregnancies (1,000 mg/kg-day); reduced litter size and weight (250 mg/kg-day) NOEL: 50 mg/kg-day LOEL: 205 mg/kg-day (Estimated by analogy)	Professional judgment; Submitted confidential study	Estimated by analogy to confidential analog.
	Other	**Confidential A:** There is low potential for reproductive effects (Estimated)	Expert judgment	Estimated based on expert judgment and the lack of structural alerts.
Developmental Effects		**MODERATE: Based on a NOAEL of 50 mg/kg bw-day in a two generation dietary reproduction study in rats fed Confidential B. Adverse effects included delayed vaginal opening and preputial separation at a dose of 500 mg/kg bw-day. No adverse developmental effects were observed in rabbits following oral administration of Confidential B at doses up to 1,000 mg/kg bw-day. Confidential A is estimated to have a low potential for developmental effects based on expert judgment and a lack of structural alert for this endpoint.** **There were no data located for the developmental neurotoxicity endpoint.**		
	Reproduction/ Developmental Toxicity Screen			No data located.

Fyrol™ HF-5				
PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
	Combined Repeated Dose with Reproduction/ Developmental Toxicity Screen	**Confidential B:** Two generation dietary reproduction study in rats. Sprague-Dawley rats (30/sex/dose) were fed 0, 50, 500, or 1,000 mg/kg-day Confidential B in the diet for 10 weeks. Vaginal opening and preputial separation were delayed at 500 and 1,000 mg/kg-day. This effect was considered by study authors to be secondary to reduction of body weight in F_1 generation during week 1 (treated animals had decreased body weights compared to controls during week 1, reportedly due to an initial aversion to taste of diet). NOAEL: 50 mg/kg bw-day (for vaginal opening and preputial separation) LOAEL: 500 mg/kg bw-day	EPA, 2010; Confidential study	Guideline study. Data are for the commercial polymeric mixture.

Fyrol™ HF-5				
PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
		Confidential B: Developmental oral gavage study in rabbits. Pregnant New Zealand white rabbits (27/group) were dosed with 0, 50, 200 or 1,000 mg/kg-day Confidential B by oral gavage on GD 6-28. No clinical signs of toxicity. No adverse effects on maternal food consumption, body weight gain or organ weights. No adverse effects on fetal body weights, viability, or any developmental endpoint measured. NOAEL (maternal and developmental toxicity): 1,000 mg/kg-day LOAEL: not established as highest concentration tested did not produce adverse effects	EPA, 2010	Guideline study reported in a secondary source. Data are for the commercial polymeric mixture.

Fyrol™ HF-5				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Prenatal Development	**Confidential B:** Pregnant rabbits; oral gavage; GD 6-23; 0, 50, 200 or 1,000 mg/kg-day test material No deaths or clinical signs of toxicity. No significant effect on body weight, body weight gain, food consumption or organ weight. No significant effect on litter weight or pup viability. No gross external, skeletal or soft tissues malformations or anomalies. NOAEL: 1,000 mg/kg-day (highest dose tested) LOAEL = Not established	Confidential study	Study details reported in a secondary source; Study conducted according to GLP.
	Postnatal Development			No data located.
	Prenatal and Postnatal Development			No data located.
	Developmental Neurotoxicity			No data located.
	Other	**Confidential A:** There is low potential for developmental effects (Estimated)	Expert judgment	Estimated based on expert judgment and the lack of structural alerts.
Neurotoxicity		**MODERATE: Based on a 28-day inhalation LOAEL of 0.5 mg/L for inhibition of plasma ChE in rats (NOAEL = 0.1 mg/L) following exposure to Confidential B; criteria values are tripled for chemicals evaluated in 28-day studies; the LOAEL of 0.5 mg/kg-day falls within the Moderate hazard criteria (0.06 - 0.6 mg/L). Confidential A is estimated to have uncertain potential for neurotoxic effects based on a structural alert and professional judgment.**		
	Neurotoxicity Screening Battery (Adult)	**Confidential B:** 28-day oral (gavage) study NOAEL: 1,000 mg/kg (Estimated by analogy)	Professional judgment; Submitted confidential study	Estimated based on analogy to a confidential analog.

Fyrol™ HF-5				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		Confidential B: 28-day inhalation study in rats; 0, 0.1, 0.5 and 2.0 mg/L (aerosol) Significant inhibition of plasma ChE (0.5 and 2.0 mg/L). No clinical signs suggestive of neurotoxic effect and ChE was not affected after study termination NOAEL: 0.1 mg/L LOAEL: 0.5 mg/L (plasma ChE inhibition)	Confidential study; EPA, 2010	Study details reported in a secondary source; study was not designed to assess all neurological parameters; criteria values are tripled for chemicals evaluated in 28-day studies; the LOAEL of 0.5 mg/kg-day falls within the Moderate hazard criteria (0.06 - 0.6 mg/L).
		Confidential B: 28-day oral (gavage) study in mice; 0, 500, 1,500, 5,000 mg/kg Dose-related decrease in plasma ChE compared to controls, which was no longer apparent after the 60 day recovery period. No NOAEL/LOAEL determined	Confidential study	Study details reported in a secondary source; study was not designed to assess all neurological parameters; cannot rule out all neurotoxicity.
	Other	**Confidential A:** There is potential for neurotoxic effects based on a structural alert for organophosphates. (Estimated)	Professional judgment	Estimated based on a structural alert and professional judgment.
		Confidential A: Uncertain concern for neurotoxicity (Estimated)	Professional judgment	Estimated for the low MW component due to ethyl substituted phosphate.

Fyrol™ HF-5				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Repeated Dose Effects		**MODERATE: Experimental data reported alveolar histiocytosis in rats following a 4-week inhalation exposure to 0.5 mg/L Confidential B aerosol (NOAEL = 0.1 mg/L). The criteria threshold for a low hazard designation is 0.2 mg/L for mists based on 90-day repeated dose studies; guidance values are tripled for 28-day study evaluations making the MODERATE hazard range from 0.06 – 0.6 mg/L No other exposure-related gross or microscopic pathology was identified in any organ. There is also potential for liver toxicity based on a confidential analog, though no effects occurred at 300 mg/kg-day for that analog (higher than the criteria threshold for a low hazard designation). Confidential A is estimated to have low potential for repeated dose effects based on expert judgment.**		
		Confidential A: Estimated to have low potential for repeated dose effects for the low MW components of this substance. This substance may contain polymer components with a MW >1,000. In this case, it is expected to have limited bioavailability; however, there is the possibility of lung overloading. (Estimated)	Professional judgment	Estimated based on professional judgment.
		Confidential B: 28-day oral study, rats Potential for liver toxicity. NOEL: 300 mg/kg-day (Estimated based on analogy)	Submitted confidential study; Professional judgment	Estimated based on analogy to confidential analog.

Fyrol™ HF-5				
PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
		Confidential B: In a 28 day inhalation study Sprague-Dawley rats (10/sex/group) were exposed (aerosol, nose only) to 0, 100, 500 or 2,000 mg/m^3 (0, 0.1, 0.5, or 2 mg/L) Confidential B. No deaths or clinical signs of toxicity. Decreased body weight and food consumption in males and significant inhibition of plasma cholinesterase in females at 2,000 mg/m^3. White foci in the lungs at 2,000 mg/m^3 and alveolar histiocytosis at 500 and 2,000 mg/m^3. Although lung changes are relevant, they were not considered to be a reflection of a specific toxic response to Confidential B; these changes are characteristic of exposure to non-cytotoxic water-insoluble materials. No other gross or microscopic pathology in any organ. NOAEC: 100 mg/m^3 (0.1 mg/L) LOAEC: 500 mg/m^3 (0.5 mg/L) based on alveolar histiocytosis)	EPA, 2010; Confidential study	Guideline study reported in a secondary source. Data are for the commercial polymeric mixture.

Fyrol™ HF-5				
PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
	Immune System Effects	**Confidential B:** Oral gavage study in mice. Female B6C3F1 mice (50/group) were exposed via oral gavage to 0, 500, 1,500, or 5,000 mg/kg-day Confidential B for 28 days. No deaths, clinical signs of toxicity, or effects on body or organ weights. No adverse histopathological changes or necropsy findings. No treatment-related changes in peritoneal cell numbers or cell types, peritoneal macrophage phagocytic activity or host susceptibility to infection. No adverse effect on splenic natural killer cell activity, lymphocyte blastogenesis, or antibody-forming cell function. There were significant decreases in erythrocyte cholinesterase activity and plasma pseudocholinesterase activity in all dose groups, but both enzyme activities returned to control levels at the end of the 60 day recovery period. NOAEL: 5,000 mg/kg-day (highest dose tested) LOAEL: Not established	EPA, 2010	Guideline study reported in a secondary source. Data are for the commercial polymeric mixture.

Fyrol™ HF-5				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Skin Sensitization		**LOW: Confidential A and B are estimated to have low potential for skin sensitization based on expert judgment. There was no experimental data located.**		
	Skin Sensitization	**Confidential A:** There is low potential for skin sensitization (Estimated)	Expert judgment	Estimated based on expert judgment.
		Confidential B: No potential for skin sensitization (Estimated)	Expert judgment	Estimated by expert judgment.
Respiratory Sensitization		**No data located.**		
	Respiratory Sensitization			No data located.
Eye Irritation		**MODERATE: Confidential A was moderately to slightly irritating to rabbit eyes. Confidential B produced mild irritation in rabbit eyes; however, clearing occurred within 24 hours.**		
	Eye Irritation	**Confidential A:** Moderate to slight eye irritation in rabbits; conjunctival irritation with redness and discharge; cleared within 96 hours.	Submitted confidential study	Data reported in a confidential study submitted to EPA.
		Confidential B: Rabbit, minimally irritating. 0.1 ml instilled into the left eyes of 3 rabbits produced slight conjunctival redness and chemosis that was reversible by 24 hours.	EPA, 2010	Guideline study reported in a secondary source. Data are for the commercial polymeric mixture.
Dermal Irritation		**LOW: Confidential A is slightly irritating to rabbit skin with irritation clearing within 3 days. Confidential B is not a dermal irritant in rabbits.**		
	Dermal Irritation	**Confidential A:** Slightly irritating to rabbit skin	Submitted confidential study	Data reported in a confidential study submitted to EPA
		Confidential A: Mild and transient dermal irritation in rabbits; cleared within 3 days.	Submitted confidential study	Data reported in a confidential study submitted to EPA.
		Confidential B: Rabbit, not irritating	EPA, 2010	Guideline study reported in a secondary source. Data are for the commercial polymeric mixture.

Fyrol™ HF-5			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
Endocrine Activity	**Confidential B caused delayed vaginal opening and preputial separation at a dose of 500 mg/kg bw-day (NOAEL: 50 mg/kg bw-day) in a two generation dietary reproduction study in rats. A metabolite of the test substance is listed as a suspected endocrine disruptor by the EU. The potential for endocrine activity for Confidential A is uncertain.**		
	Confidential B: Listed as a potential endocrine disruptor on the EU Priority List of Suspected Endocrine Disruptors.	European Commission, 2012	Potential for endocrine disruption. *In vitro* data indicating potential for endocrine disruption in intact organisms. Also included effects *in vivo* that may, or may not, be endocrine disruption-mediated. May include structural analyses and metabolic considerations".
	Confidential B: Two generation dietary reproduction study in rats. Sprague-Dawley rats (30/sex/dose) were fed 0, 50, 500, or 1,000 mg/kg-day Confidential B in the diet for 10 weeks. Vaginal opening and preputial separation were delayed at 500 and 1,000 mg/kg-day. This effect was considered by study authors to be secondary to reduction of body weight in F_1 generation during week 1 (treated animals had decreased body weights compared to controls during week 1, reportedly due to an initial aversion to taste of diet). NOAEL: 50 mg/kg bw-day (for vaginal opening and preputial separation) LOAEL: 500 mg/kg bw-day	EPA, 2010; Confidential study	Guideline study. Data are for the commercial polymeric mixture.

Fyrol™ HF-5				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Immunotoxicity		**Confidential B had no effect on immunological parameters at doses up to 5,000 mg/kg-day (highest dose tested) in an oral gavage study in mice. Confidential A is estimated to have a low potential for immunotoxic effects based on expert judgment.**		
	Immune System Effects	**Confidential A:** There is low potential for immunotoxic effects (Estimated)	Expert judgment	Estimated based on expert judgment.

Fyrol™ HF-5				
PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
		Confidential B: Negative, oral gavage study in mice. Female B6C3F1 mice (50/group) were exposed via oral gavage to 0, 500, 1,500, or 5,000 mg/kg-day Confidential B for 28 days. No deaths, clinical signs of toxicity, or effects on body or organ weights. No adverse histopathological changes or necropsy findings. No treatment-related changes in peritoneal cell numbers or cell types, peritoneal macrophage phagocytic activity or host susceptibility to infection. No adverse effect on splenic natural killer cell activity, lymphocyte blastogenesis, or antibody-forming cell function. There were significant decreases in erythrocyte cholinesterase activity and plasma pseudocholinesterase activity in all dose groups, but both enzyme activities returned to control levels at the end of the 60 day recovery period. NOAEL: 5,000 mg/kg-day LOAEL: not established, as highest dose tested did not produced adverse effects.	EPA, 2010	Guideline study reported in a secondary source. Data are for the commercial polymeric mixture.

Fyrol™ HF-5			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
ECOTOXICITY			
ECOSAR Class			
Acute Aquatic Toxicity	**VERY HIGH: Based on measured EC_{50} values for daphnia following exposure to Confidential B. Measured values for fish and algae are higher than the water solubility limit, suggesting no effects at saturation (NES). Acute aquatic toxicity is expected to be LOW for Confidential A.**		
Fish LC_{50}	**Confidential A:** *Danio rerio* (Zebrafish) 96-hour LC_{50} >1,000 mg/L according to OECD 203 (Experimental)	Clariant, 2011	Data reported in a confidential study submitted to EPA; the toxicity value is well above the water solubility for this substance; therefore NES is predicted.
	Confidential A: Freshwater fish 96-hour LC_{50} > 100 mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	Estimates based on representative oligomers where n=1-6. Estimates for the Esters class were provided for comparative purposes. See Section 5.5.1.
	Confidential B: *Brachydanio rerio* 96-hour LC_{50} = 12.3 mg/L (Experimental)	EPA, 2010	Guideline study reported in a secondary source (OECD Guide-line 203). Data are for the commercial polymeric mixture. Given that the reported value is greater than the water solubility, NES were observed for this endpoint.

Fyrol™ HF-5			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	Confidential B: Fish 96-hour LC_{50} = NES (Estimated) ECOSAR: Esters	ECOSAR v1.11	Estimates were performed on oligomers of the polymeric mixture that have a MW <1,000; NES are estimated for the n=1 and higher oligomers. Estimate for the Esters class was provided for comparative purposes. See Section 5.5.1.
Daphnid LC_{50}	**Confidential A:** *Daphnia magna* 48-hour LC_{50} > 100 mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	Estimates based on representative oligomers where n=1-6. Estimates for the Esters class were provided for comparative purposes. See Section 5.5.1.
	Confidential B: *Daphnia magna* 48-hour EC_{50} = 0.7 mg/L (Experimental)	EPA, 2010	Guideline study reported in a secondary source (U.S. EPA OPPTS 850.1010). Data are for the commercial polymeric mixture.
	Confidential B: *Daphnia magna* 48-hour LC_{50} = NES (Experimental) ECOSAR: Esters	ECOSAR v1.11	Estimates were performed on oligomers of the polymeric mixture that have a MW <1,000; NES are estimated for the n=1 and higher oligomers. Estimate for the Esters class was provided for comparative purposes. See Section 5.5.1.

Fyrol™ HF-5			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
Green Algae EC_{50}	**Confidential A:** Green algae 96-hour EC_{50} > 100 mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	Estimates based on representative oligomers where n=1-6. Estimates for the Esters class were provided for comparative purposes. See Section 5.5.1.
	Confidential B: *Pseudokirchneriella subcapitata* 72-hour EC_{50} = 48.6 mg/L (Experimental)	EPA, 2010	Guideline study reported in a secondary source (OECD 201). Data are for the commercial polymeric mixture. Given that the reported value is greater than the water solubility, NES was observed for this endpoint.
	Confidential B: Green algae 96-hour EC_{50} = NES (Estimated) ECOSAR: Esters	ECOSAR v1.11	Estimates were performed on oligomers of the polymeric mixture that have a MW <1,000; NES are estimated for the n=1 and higher oligomers Estimate for the Esters class was provided for comparative purposes. See Section 5.5.1.

Fyrol™ HF-5			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
Chronic Aquatic Toxicity	**VERY HIGH: Based on an experimental 21-day NOEC = 0.021 mg/L in *Daphnia magna* following exposure to Confidential B that may contain a residual impurity (up to 5%) with a Very High chronic aquatic toxicity. There were no effects observed at the highest dose tested (0.021 mg/L); however, this value is within the "Very High" hazard criteria range. It is not certain if effects may occur within this range (up to 0.1 mg/L). For Confidential A, an estimated chronic aquatic toxicity value was derived using an acute-to-chronic ratio (ACR) for the phosphate ester class and was applied to the available experimental acute data for this chemical and indicated a Low hazard.**		
Fish ChV	**Confidential A:** Freshwater fish ChV ≥ 41.7 mg/L (Estimated)	Professional judgment	An ACR of 24 was derived for the phosphate ester class based on experimental data for Tris (p-t-butylphenyl) phosphate (TBPP). The acute-to-chronic ratio was applied to available experimental acute fish data for this chemical (ChV = >1000 mg/L /24 = 41.7 mg/L)
	Confidential A: Freshwater fish ChV > 10 mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	Estimates based on representative oligomers where n=1 -6. Estimates for the Esters class were provided for comparative purposes. See Section 5.5.1.
	Confidential B: ChV = NES (Estimated) ECOSAR: Esters	ECOSAR v1.11	Estimates were performed on oligomers of the polymeric mixture that have a MW <1,000; NES are estimated for the n=1 and higher oligomers. Estimate for the Esters class was provided for comparative purposes. See Section 5.5.1.

Fyrol™ HF-5			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
Daphnid ChV	**Confidential A:** *Daphnia magna* ChV > 10 mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	Estimates based on representative oligomers where n=1 -6. Estimates for the Esters class were provided for comparative purposes. See Section 5.5.1.
	Confidential B: *Daphnia magna* Mean measured concentrations of 0.99, 3.1, 5.0, 9.3, and 21 µg/L were administered in flow-through test conditions. 21-day NOEC = 0.021 mg/L (Highest concentration tested) 21-day EC_{50} > 0.021 mg/L (immobility and reproduction) (Experimental)	Submitted confidential study	Reported in a submitted confidential study. The test substance is identified as the n=1 oligomer. There were no effects observed at the highest dose tested (0.021 mg/L); however, this value is within the "Very High" hazard criteria range. It is not certain if effects may occur within this range (up to 0.1 mg/L). This substance also contains a residual impurity (up to 5%) that is known to be toxic to aquatic organisms.
	Confidential B: *Daphnia magna* 21-day NOEC = 0.021 mg/L 21-day EC_{50} = 0.037 mg/L Semi-static (Experimental)	Submitted confidential study	Reported in a submitted confidential study; Study conducted according to GLP and OECD guideline 211 The test substance is identified as the n=1 oligomer. This substance also contains a residual impurity (up to 5%) that is known to be toxic to aquatic organisms.

Fyrol™ HF-5			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	Confidential B: 21-day ChV = NES (Estimated) ECOSAR: Esters	ECOSAR v1.11	Estimates were performed on oligomers of the polymeric mixture that have a MW <1,000; NES are estimated for the n=1 and higher oligomers. Estimate for the Esters class was provided for comparative purposes. See Section 5.5.1.
Green Algae ChV	**Confidential A:** Green algae ChV > 10 mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	Estimates based on representative oligomers where n=1-6. Estimates for the Esters class were provided for comparative purposes. See Section 5.5.1.
	Confidential B: *Pseudokirchneriella subcapitata* 72-hour NOEC = 10 mg/L (WAF) 72-hour LOEC = 100 mg/L (WAF) (Experimental)	Confidential study	Study details reported in a secondary source. Study conducted according to GLP and OECD guideline 201.
	Confidential B: ChV = NES (Estimated) ECOSAR: Esters	ECOSAR v1.11	Estimates were performed on oligomers of the polymeric mixture that have a MW <1,000; NES are estimated for the n=1 and higher oligomers. Estimate for the Esters class was provided for comparative purposes. See Section 5.5.1.

Fyrol™ HF-5				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
ENVIRONMENTAL FATE				
Transport		**The environmental fate for the lower MW oligomers; with MW<1,000 is based on the estimated moderate water solubility and low vapor pressure indicating that the lower MW oligomers are anticipated to partition predominantly to soil. The higher MW oligomers where with MW>1,000 are expected to have negligible water solubility and negligible vapor pressure indicating that the higher MW oligomers are anticipated to partition predominantly to soil and sediment. The components of the mixture are expected to be immobile in soil based on the estimated K_{oc} values. Leaching through soil to groundwater is not expected to be an important transport mechanism. Estimated volatilization half-lives indicate that the components will be non-volatile from surface water. Volatilization from dry surface is also not expected based on its vapor pressure. In the atmosphere, the mixture components are expected to exist solely in the particulate phase, based on its estimated vapor pressure. Particulates may be removed from air by wet or dry deposition.**		
	Henry's Law Constant (atm-m^3/mole)	**Confidential A:** $<10^{-8}$ for n≥1 (Estimated)	EPI v4.11 ; Professional judgment; Boethling and Nabholz, 1997	Estimates based on representative oligomers; cutoff values for nonvolatile compounds. Estimated by the HENRYWIN Group SAR Method with no measured chemical property inputs. High MW polymers are expected to have low vapor pressure and are not expected to undergo volatilization.
		Confidential B: $<10^{-8}$ for n≥1 (Estimated)	EPI v4.11	Cutoff value for nonvolatile compounds. Higher MW components are also expected to have Henry's Law Constant values below this cutoff.
	Sediment/Soil Adsorption/Desorption - K_{oc}	**Confidential A:** 11,000 for n=1; >30,000 for n≥2 (Estimated)	EPI v4.11; Professional judgment	Using MCI Method KOCWIN v2.00, estimate based on representative oligomers. Also estimated for oligomers with MWs >1,000 based on professional judgment.
		Confidential B: >30,000 for n≥1 (Estimated)	EPI v4.11; EPA, 2005	Cutoff value for nonmobile compounds according to HPV assessment guidance. Higher MW components are also expected to have K_{oc} values above this cutoff.

Fyrol™ HF-5				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Level III Fugacity Model	**Confidential A:** Air = 0% Water = 15% Soil = 80% Sediment = 4.8% (Estimated)	EPI v4.11	Estimate based on representative oligomer where n=1.
		Confidential B: Air = 1% Water = 1% Soil = 40% Sediment = 59% (Estimated for n = 1)	EPI v4.11	Estimates were performed on representative components of the polymer.

Fyrol™ HF-5				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Persistence		**VERY HIGH: The persistence designation is based on the higher MW components (MW >1,000). The lower MW oligomers (MW <1,000) are expected to have lower persistence because of their higher water solubility and increased bioavailability to microorganisms. The higher MW components are expected to have higher persistence because of their low water solubility and poor bioavailability, indicating that neither biodegradation nor hydrolysis are expected to be important environmental fate processes. A ready test using the OECD guideline 301D demonstrated 0% biodegradation occurred after 28 days and 2% biodegradation was achieved after 140 days. In a nonguideline study with limited details, slow hydrolysis was reported for a confidential commercial product at normal temperatures in acidic and alkaline aqueous solutions. Additionally, this mixture does not contain components with functional groups that would be expected to absorb light at environmentally significant wavelengths. Experimental values for commercial products and evaluation of the higher MW components of this polymer suggest an environmental half-life of >180 days. Moderate persistence is expected for Confidential B based on experimental biodegradation studies.**		
Water	**Aerobic Biodegradation**	**Confidential A:** Passes Ready Test: No Test method: OECD TG 301D: Closed Bottle Test This commercial product biodegraded 0% at day 28 and 2% at day 140 (Measured)	Confidential study	From a MSDS for a confidential commercial product containing 95-100% pure material.
		Confidential A: Hours-days (Primary Survey Model) **Confidential A:** Weeks (Ultimate Survey Model) (Estimated)	EPI v4.11	Estimate based on representative oligomers where n=1-2.

Fyrol™ HF-5				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		Confidential B: Study results: 37%/28 days Test method: Other 37% degradation after 28 days; 66% degradation after 56 days Using Directive 84/449/EEC, C.6 (Measured) inherent biodegradation, 2.7 mg/L of compound in activated sludge (Measured)	IUCLID, 2001	The data is for the commercial product.
	Volatilization Half-life for Model River	**Confidential A:** >1 year for n≥1 (Estimated)	EPI v4.11	Estimate based on representative oligomers.
		Confidential B: >1 year for n=1 and n=2 (Estimated)	EPI v4.11	Based on the magnitude of the estimated Henry's Law Constant.
	Volatilization Half-life for Model Lake	**Confidential A:** >1 year for n≥1 (Estimated)	EPI v4.11	Estimate based on representative oligomers.
		Confidential B: >1 year for n=1 and n=2 (Estimated)	EPI v4.11	Based on the magnitude of the estimated Henry's Law Constant.
Soil	**Aerobic Biodegradation**			No data located.
	Anaerobic Biodegradation	**Confidential A:** Probable (Anaerobic-methanogenic biodegradation probability model)	EPI v4.11	Estimate based on representative oligomers where n=1.
		Confidential B: Not probable; according to the anaerobic-methanogenic biodegradation probability model	EPI v4.11	Estimated for the n≥1 components.
	Soil Biodegradation with Product Identification			No data located.
	Sediment/Water Biodegradation			No data located.

Fyrol™ HF-5				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Air	**Atmospheric Half-life**	**Confidential A:** 0.086 days for n=1 0.056 days for n=2 0.042 days for n=3 0.025 days for n=6 (Estimated)	EPI v4.11	Estimate based on representative oligomers.
		Confidential B: 0.5 days or 6 hours (Estimated for n=1) 0.3 days or 4 hours (Estimated for n=2)	EPI v4.11	
Reactivity	**Photolysis**	**Confidential A & B:** Not a significant fate process (Estimated)	Professional judgment; Mill, 2000	The substance does not contain functional groups that would be expected to absorb light at wavelengths >290 nm.
	Hydrolysis	**Confidential A:** Hydrolyzes slowly at normal temperatures in acidic or alkaline aqueous solutions (Measured)	Confidential study	Non-quantitative value from a MSDS for a confidential commercial product containing 95-100% pure material.
		Confidential A: 50%/3.3 years at pH 5-8 50%/3 years at pH 9 for n=1 (Estimated)	EPI v4.11	Estimate based on representative oligomer.

Fyrol™ HF-5				
PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
		Confidential A: Linear phosphoric acids are strongly hygroscopic. These substances undergo viscosity changes and hydrolysis to less complex forms when exposed to moist air. Hydrolytic degradation to phosphoric acid occurs upon dissolution in water. The rate of hydrolysis temperature dependent; at 25°C, the half-life is several days and at 100°C, the half-life is minutes.	Confidential study	Supporting information about this related class of compounds.
		Confidential B: Half-life = 320 days at pH 7 Half-life = 32 days at pH 8 Half-life = 3 days pH 9 (for n=1) Half-life = 240-320 days at pH 7 Half-life = 24-32 days at pH 8 Half-life = 2-3 days pH 9 (for n=2) (Estimated)	EPI v4.11	Hydrolysis rates are expected to be pH-dependent and may be limited by the low water solubility of this compound. Under basic conditions, sequential dephosphorylation reactions may occur.
		Confidential B: Half-life = 11 days (20°C; pH 4) Half-life = 17 days (20°C; pH 7) Half-life = 21 days (20°C; pH 9) OECD 111 (Measured)	IUCLID, 2001	Inadequate. Although reported as a guideline study, phosphate esters as a chemical class have been observed to hydrolyze more rapidly under basic pHs then under neutral or acidic conditions. The reported half-lives do not follow this trend, and are therefore suspect. Under basic conditions, sequential dephosphorylation reactions may occur.

Fyrol™ HF-5				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Environmental Half-life		**Confidential A:** >180 days (Estimated)	Professional judgment	The oligomers with a MW >1,000 are not anticipated to be assimilated by microorganisms. Therefore, biodegradation is not expected to be an important removal process. The higher MW oligomers are also not expected to be removed by other degradation processes under environmental conditions because of limited water solubility and limited partitioning to air.
		Confidential A: 30 (Estimated)	PBT Profiler	Half-life estimated for the predominant compartment, soil, for the oligomer where n=1, as determined by EPI and the PBT Profiler methodology.
		Confidential B: >180 days	PBT Profiler	Half-life estimated for the predominant compartment, soil, as determined by EPI and the PBT Profiler methodology.
Bioaccumulation		**HIGH: Based on the estimated BCF value for the lower MW components (MW<1,000); it is above the High hazard designation criteria indicating a high potential for bioaccumulation. The oligomers with a MW >1,000 are expected to have limited water solubility, poor bioavailability and are not expected to be bioaccumulative.**		
	Fish BCF	**Confidential A:** 3.2 (Estimated)	EPI v4.11	Estimate based on representative oligomers with a MW <1,000.
		Confidential A: <100 oligomers (Estimated)	Professional judgment	The substance has a MW >1,000 and is not anticipated to be taken up by aquatic organisms; therefore, bioconcentration is not expected.
		Confidential B: 1,300 for n=1 59 for n=2 (Estimated)	EPI v4.11	
	Other BCF			No data located.

Fyrol™ HF-5				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	BAF	**Confidential A:** 0.94 for n=1 0.91 for n=2 0.90 for n=3-5 (Estimated)	EPI v4.11	Estimate based on representative oligomers with a MW <1,000.
		Confidential A: n≥6 oligomers (Estimated)	Professional judgment	No data located for MW >1,000 oligomers.
		Confidential B: 81 for n=1 7 for n=2 (Estimated)	EPI v4.11	
	Metabolism in Fish			No data located.
ENVIRONMENTAL MONITORING AND BIOMONITORING				
Environmental Monitoring		No data located.		
Ecological Biomonitoring		No data located.		
Human Biomonitoring		This chemical was not included in the NHANES biomonitoring report (CDC, 2013).		

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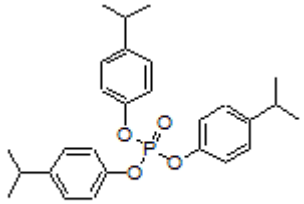
Isopropylated triphenyl phosphate (IPTPP)

Screening Level Toxicology Hazard Summary

This table contains hazard information for each chemical; evaluation of risk considers both hazard and exposure. Variations in end-of-life processes or degradation and combustion by-products are discussed in the report but not addressed directly in the hazard profiles. The caveats listed below must be taken into account when interpreting the information in the table.

VL = Very Low hazard L = Low hazard M = Moderate hazard H = High hazard VH = Very High hazard – Endpoints in colored text (VL, L, M, H, and VH) were assigned based on empirical data. Endpoints in black italics *(VL, L, M, H,* and *VH*) were assigned using values from estimation software and professional judgment [(Quantitative) Structure Activity Relationships "(Q)SAR"].

Chemical	CASRN	Human Health Effects										Aquatic Toxicity		Environmental Fate	
		Acute Toxicity	Carcinogenicity	Genotoxicity	Reproductive	Developmental	Neurological	Repeated Dose	Skin Sensitization	Respiratory Sensitization	Eye Irritation	Dermal Irritation	Acute	Chronic	Persistence	Bioaccumulation
Isopropylated triphenyl phosphate (IPTPP)	68937-41-7	L	*M*	L	H	*H*	*H*	H	L		L	L	VH	VH	M	*H*



Representative Structure

CASRN: 68937-41-7

MW: 452

MF: $C_{27}H_{33}O_4P$

Physical Forms: Liquid
Neat:

Use: Flame retardant

SMILES: O=P(Oc2ccc(cc2)C(C)C)(Oc3ccc(cc3)C(C)C)Oc1ccc(cc1)C(C)C (Representative structure for tris(isopropylphenyl) phosphate)
c1(C(C)C)ccc(OP(=O)(Oc3ccc(C(C)C)cc3)Oc2ccccc2)cc1 (Representative structure for di(isopropylphenyl) phenyl phosphate)
c1(C(C)C)ccc(OP(=O)(Oc3ccccc3)Oc2ccccc2)cc1 (Representative structure for isopropylphenyl diphenyl phosphate)

Synonyms: Phenol, isopropylated, phosphate (3:1); IPPP; ITP; IPTPP; TIPPP; Isopropylated triphenyl phosphate; Isopropylated phenol phosphate

Chemical Considerations: The alternative, isopropylated triphenyl phosphate, may contain a mixture consisting of isopropylated triphenyl phosphates, with an unspecified amount of isopropylation. Mono- to nona- isopropylphenyl phosphate have been found, for example tris[2,4,6-tri(propan-2-yl)phenyl] phosphate. The majority of isomers contain isopropyl substitution at the ortho- and para- position although meta isomers may be present to a lesser extent. The isopropyl groups are typically distributed between the three phenyl rings however di- and tri- alkylation may be present on a single phenyl ring (for example, diisopropylphenyl diphenyl phosphate (CASRN 58570-87-9)). Isomers expected to be present will be discussed in this report as appropriate when determining hazard designations. A description of the test sample and isomer content is included in the data entries when available. However test substance composition was not consistently reported in the literature. Chemical, fate, and toxicity data for components of the mixture represented by other CASRN were collected in the preparation of this AA and are listed below:

- Phenol, isopropylated, phosphate (3:1) (CASRN 68937-41-7)
- Triphenyl phosphate, TPP (CASRN 115-86-6)
- 4-isopropylphenyl diphenyl phosphate (CASRN 55864-04-5)
- 2-isopropylphenyl diphenyl phosphate (CASRN 64532-94-1)
- Isopropyl phenyl diphenyl phosphate (CASRN 28108-99-8); (CASRN 101299-37-0)
- 2-(1-Methylethyl)phenyldiphenyl ester phosphoric acid mixture w/triphenyl phosphate (CASRN 96300-97-9); (CASRN 66797-44-2)
- Di(isopropylphenyl)phenylphosphate (CASRN 28109-00-4)
- Di(2-isopropylphenyl)phenylphosphate (CASRN 69500-29-4)
- Tri(3-isopropylphenyl)phosphate (CASRN 72668-27-0)
- Tri(isopropylphenyl)phosphate (CASRN 26967-76-0)
- Tri(4-isopropylphenyl)phosphate (CASRN 2502-15-0)
- 3,4-bis(1-methylethyl)phenyl diphenyl ester (CASRN 68155-51-1)

Estimated values using representative structures as indicated in the SMILES section of this assessment will be used to fill assessment data gaps. EPI v4.11 was used to estimate physical/chemical and environmental fate values due to an absence of experimental data (Weil, 2001; ECHA, 2013b).

Polymeric: No **Oligomeric:** Not applicable	
Metabolites, Degradates and Transformation Products: Phenol (CASRN 108-95-2), isopropylphenol (CASRN 25168-06-3); diphenyl phosphate (CASRN 838-85-7); 2-isopropyl phenol (CASRN 88-69-7), 4-isopropyl phenol (CASRN 99-89-8), 3-isopropylphenol (CASRN 618-45-1) and diisopropyl phenols (CASRN 27923-56-4) along with the corresponding mono and diphenyl phosphates by hydrolysis. Cyclic metabolites of isopropylated phenyl phosphates by metabolism in rabbit bile; diphenyl phosphate in fish (Nobile et al., 1980; Huckins and Petty, 1983; Muir et al., 1989; Yang et al., 1990).	
Analog: Tris(isopropylphenyl) phosphate isomers and other isopropyl substituted phenyl phosphate esters anticipated to be present in the commercial product were considered in the evaluation, as indicated in the chemical considerations section; orthocresyl phosphate **Endpoint(s) using analog values:** Neurotoxicity	**Analog Structure:** Not applicable
Structural Alerts: Organophosphates; Neurotoxicity (EPA, 2012).	
Risk Phrases: R48/22 - harmful: danger of serious damage to health by prolonged exposure if swallowed; R62 - possible risk of impaired fertility; R63 - possible risk of harm to the unborn child; R50/R53 - Very toxic to aquatic organisms. May cause long-term adverse effects in the aquatic environment. There is currently no classification of "dangerous to the environment" for isopropylated triphenyl phosphate, itself. The commercial products containing isopropylated triphenyl phosphate are generally classified based on the triphenyl phosphate content of the product (Environment Agency, 2009; ECHA, 2013b).	
Hazard and Risk Assessments: An Environmental Risk Evaluation report for isopropylated triphenyl phosphate was published in August 2009. This substance is part of EPA's HPV Challenge and is a registered substance with the European Chemicals Agency (Great Lakes Chemical Corporation, 2001; Environment Agency, 2009; ECHA, 2013a, 2013b).	

Isopropylated triphenyl phosphate CASRN 68937-41-7			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
PHYSICAL/CHEMICAL PROPERTIES			
Melting Point (°C)	<-20 Pour point; OECD Guideline 102 (Measured)	ECHA, 2013b	Test material identified as phenol, isopropylated, phosphate (3:1).
	-26 Reported as a range -12 to -26°C (Measured)	IUCLID, 2001	Reported in a secondary source for isopropylated triphenyl phosphates. The broad melting point range is consistent with a mixture.
	-26 Reported as a melting/pour point (Measured)	Muir, 1984	Reported in a secondary source for isopropylphenyl diphenyl phosphate.
Boiling Point (°C)	>300 Decomposes (Measured)	Environment Agency, 2009	Reported in a secondary source for a commercial isopropylphenyl diphenyl phosphate product, Reofos 50.
	>300 Decomposes (Measured)	Environment Agency, 2009	Data are for a commercial triisopropylphenyl phosphate product, Durad 310M; reported in a secondary source.
	>400 at 735 mmHg No boiling point observed up to 400°C; OECD Guideline 103 (Measured)	ECHA, 2013b	Data for a commercial product, Reofos 65; reported in a secondary source.
	>175°C at 0.05 mm Hg for o-isopropylphenyl diphenyl phosphate; 180°C at 0.2 mm Hg m-isopropylphenyl diphenyl phosphate; 185°C at 0.05 mm Hg p-isopropylphenyl diphenyl phosphate (Measured)	Wightman and Malaiyandi, 1983 (as cited in Environment Agency, 2009)	Data are for pure isomers at reduced pressures; reported in a secondary source. The diisopropylated phenyl phosphate and higher alkylated isomers are expected to boil at higher temperatures.
	>220 at 1 mmHg	Muir, 1984; Boethling and Cooper,	Reported in a secondary source for

Isopropylated triphenyl phosphate CASRN 68937-41-7			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	Reported as 220-230°C at 1 mm Hg for commercial isopropylphenyl diphenyl phosphate (Measured)	1985	a commercial isopropylphenyl diphenyl phosphate product, at reduced pressure.
	>220 at 4 mmHg Reported as 220-270° at 5.32 hPa (Measured)	IUCLID, 2001	Data are for commercial products Reofos and Durad; reported in a secondary source.
Vapor Pressure (mm Hg)	$2.8x10^{-7}$ at 30°C (Measured)	Environment Agency, 2009	Reported in a secondary source for a commercial isopropylphenyl diphenyl phosphate.
	$5.8x10^{-6}$ at 70°C Reported for triphenyl phosphates with a relatively high degree of alkylation (such as tris(isopropylphenyl) phosphate) (Measured)	Environment Agency, 2009	Reported in a secondary source.
	$2.3x10^{-5}$ at 70°C Reported for triphenyl phosphates with a relatively low degree of alkylation (such as isopropylphenyl diphenyl phosphate) (Measured)	Environment Agency, 2009	Reported in a secondary source.
	<0.026 at 150°C Reported as 0.0346 hPa at 150°C (Measured)	IUCLID, 2001	Reported in a secondary source for commercial products, Reofos and Durad.
	3.4 at 20°C OECD Guideline 104; additional study 4.4 mm Hg at 25°C (Measured)	ECHA, 2013b	Reported in a secondary source for commercial product, Reofos 65.
	$4x10^{-8}$ at 25°C (Estimated)	EPI v4.11	Based on a representative structure for a component of the mixture, with one isopropyl substituent

Isopropylated triphenyl phosphate CASRN 68937-41-7			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
			group.
	<$2x10^{-8}$ at 25°C (Estimated)	EPI v4.11	Based on representative structures for components of the mixture, with two or more isopropyl substituent groups.
Water Solubility (mg/L)	0.026 (Estimated)	EPI v4.11	Based on a representative structure for a component of the mixture, with one isopropyl substituent group.
	0.00083 (diisopropylated triphenyl phosphate isomer); $2.6x10^{-5}$ (triisopropylated triphenyl phosphate isomer) (Estimated)	EPI v4.11; EPA, 1999	Estimated value is less than the cutoff value, <0.001 mg/L, for non-soluble compounds according to HPV assessment guidance. Based on representative structures for components of the mixture, with two or more isopropyl substituent groups.
	<2.2 (Measured) Shake flask method	Saeger et al., 1979 (as cited in Environment Agency, 2009)	Reported in a secondary source for Kronitex 1000, consisting of isopropylphenyl diphenyl phosphate along with triphenyl phosphate and bis(isopropylphenyl) phenyl phosphate.
	<2 (Measured) Reported as 0.7 to 2 mg/L in water considered insoluble in water	IUCLID, 2001	Reported in a secondary source for commercial products Reofos and Durad.
	0.33 (Measured) OECD 105; analyzed using GC/MS	ECHA, 2013b	Reported in a secondary source for a commercial product Reofos 65.

Isopropylated triphenyl phosphate CASRN 68937-41-7			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	0.367 mg/L (Measured) OECD 105; performed at 20°C	ECHA, 2013b	Data for commercial products, REOFOS 35 using a guideline study. Reported in a secondary source.
Log K_{ow}	6.2 (monoisopropylated triphenyl phosphate); 7.6 (diisopropylated triphenyl phosphate); 9.1 (triisopropylated triphenyl phosphate); (Estimated)	EPI v4.11	Estimated using representative structures indicated in the SMILES section for isopropylated phenyl phosphate with one, two and three isopropyl substituent groups respectively.
	<5.44 (Measured)	IUCLID, 2001	Inadequate. Reported in a secondary source for commercial product Reofos and Durad. The components of this mixture are expected to have a range of K_{ow} values not represented in the study result.
	5.3 Modified shake flask method (Measured)	Saeger et al., 1979 (as cited in Environment Agency, 2009)	Inadequate since the study was performed on a commercial product, Kronitex 1000, consisting of isopropylphenyl diphenyl phosphate along with triphenyl phosphate and bis(isopropylphenyl) phenyl phosphate. The components of this mixture are expected to have a range of K_{ow} values not represented in the study result.
	4.92 to 5.17 (Measured)	ECHA, 2013b	Data for commercial products, Kronitex 50, Kronitex 100 and Kronitex 200. Reported in a

Isopropylated triphenyl phosphate CASRN 68937-41-7			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
			secondary source.
	<6.57 3.23 (for triphenyl phosphate) and 4.30, 5.40 and 6.57 (for three other components of the isopropylphenyl diphenyl phosphate mixture); the mean value obtained for all components was 5.99 High performance thin layer chromatography (HPTLC) method for a commercial product (Measured)	Renberg et al., 1980 (as cited in Environment Agency, 2009)	Inadequate, reported in a secondary source for a commercial product, Kronitex 1000. The components of this mixture are expected to have a range of K_{ow} values.
Flammability (Flash Point)	Flash points: >220°C, 200°C, 199°C Reported for commercial products, Reofos 50, Durad 310M, and for isopropylated triphenyl phosphates, respectively (Measured)	IUCLID, 2001 (as cited in Environment Agency, 2009)	Reported in a secondary source for commercial products.
	Auto ignition temperatures: 585°C, 565°C and 551°C at 101.3 Pa reported for commercial products Reofos 50; Durad 310M and isopropylated triphenyl phosphates, respectively (Measured)	IUCLID, 2001 (as cited in Environment Agency, 2009)	Reported in a secondary source for commercial products.
Explosivity	Not expected to form explosive mixtures with air (Estimated)	Professional judgment	No experimental data located; based on its use as a flame retardant.
Pyrolysis			No data located.
pH	Not applicable (Estimated)	Professional judgment	Does not contain functional groups that are expected to ionize under environmental conditions.

Isopropylated triphenyl phosphate CASRN 68937-41-7			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
pK_a	Not applicable (Estimated)	Professional judgment	Does not contain functional groups that are expected to ionize under environmental conditions.

Isopropylated triphenyl phosphate CASRN 68937-41-7				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
HUMAN HEALTH EFFECTS				
Toxicokinetics		**No data were available on the absorption, distribution or metabolism of isopropylated triphenyl phosphates in experimental animals or humans. Isopropylated phenyl phosphates, R3 (tri-(o-iso-propylphenyl phosphate)) and Reolube HYD 46, were metabolized within 24 hours and detected in the bile of rabbits following oral administration. Dermal absorption rates in human epidermis studies for IPTPP component TPP were 0.67 and 0.9 µg/cm^2/h for Reolube HYD 46 and Reofos 50, respectively. Absorption rates for IPTPP component 2-IDPP were 0.54 and 3.32 µg/cm^2/h, for Reolube HYD 46 and Reofos 50, respectively. Steady state was achieved within one hour. Experimental data for the FM550 (a mixture made up of a sum total of TBB and TBPH of 50% with other components identified as IPTPP and TPP) indicate that absorption of TBB can occur in rats following oral exposure from gestation through lactation. At least one component of the mixture was detected in tissues of exposed dams and the pups following exposure to FM550.**		
Dermal Absorption *in vitro*		Two *in vitro* studies using the human epidermis to investigate absorption rates of IPTPP commercial formulations Reolube HYD 46 and Reofos 50. Absorption rates for IPTPP component TPP were 0.67 and 0.9 µg/cm^2/h for Reolube HYD 46 and Reofos 50, respectively. Absorption rates for IPTPP component 2-IDPP were 0.54 and 3.32 µg/cm^2/h, for Reolube HYD 46 and Reofos 50, respectively. Steady state was achieved within one hour.	IUCLID, 2000; Environment Agency, 2009	Limited study details reported in a secondary source. Study was conducted on commercial products Reolube HYD 46 and Reofos 50 (concentrations not specified)
Absorption, Distribution, Metabolism & Excretion	**Oral, Dermal or Inhaled**	Rabbits were administered single oral doses of isopropylated phenyl phosphates via gavage. Cyclic metabolites of isopropylated phenyl phosphates were detected in the bile collected from the rabbits for up to 24 hours post-administration.	Yang et al., 1990	Reliable primary source. Study was conducted using Isopropylated phenyl phosphates, including R3 (tri-(o-iso-propylphenyl phosphate)) and Reolube Hyd 46
		Pregnant rats were administered 0, 0.1 or 1 mg/kg-day of FM550 in the diet	Patisaul et al., 2013	Non guideline study indicates that absorption of this compound can

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		across gestation and through lactation (GD8 - PND 21). FM550 components including TBPH was detected in adipose, liver, and muscle tissues in Dams at PND 21 with the highest concentration in the adipose tissue (768 ng/g w.w. in high dose, 29.6 ng/g w.w. in low dose, < 7.0 ng/g w.w. in controls). The primary metabolite of TBB (TBBA) was also detected in liver tissue of dams on PND 21. TBB was detected in pooled PND21 pup adipose tissue. TBB was not detected in pooled pup adipose tissue by PND220.		occur in rats through oral exposure; the test substance identified as FM550 is a mixture made up of TBB, TBPH (sum total of TBB and TBPH is approximately 50%), TPP and IPTPP; it is unclear if absorption in pups occurred due to gestational exposure or through lactation.
	Other			No data located.
Acute Mammalian Toxicity		**LOW: Based on the weight of evidence for multiple studies. The test substance was not acutely toxic to rats, rabbits, and Chinese hamsters via the oral route and rats and rabbits via the dermal route of exposure. Acute inhalation data were inadequate to assess hazard. Oral and dermal LD_{50} values ranged from >2,000 to >20,000 mg/kg. Adequate data for the inhalation route were not located.**		
Acute Lethality	**Oral**	Rabbit oral lethal dose low (LD_{Lo}) = 3.2 mL/kg (~3,520 mg/kg)	FMC Corporation, 1990	Sufficient study details reported in a primary source. Study was conducted using Durad 110 (100% phenol, isopropylated phosphate (3:1)); limit test using 3 rats/sex. The LD_{Lo} value was converted to mg/kg using a density of 1.108 g/cm^3.
		Rat oral LD_{50} >5,000 mg/kg	EPA, 2010	Limited study details reported in a secondary source. Study was conducted using Durad 300 or Reofos 50.
		Rat Oral LD_{50} <20,000 mg/kg (females); >20,000 mg/kg (males)	IUCLID, 2000, 2001	Limited study details reported in a secondary source. Study was

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		Reofos 50 and Reofos 65: 0/5 deaths in males and 4/5 deaths in females Reofos 95 and Durad 300: no deaths		conducted using Reofos 50, Reofos 65, Reofos 95 or Durad 300.
		Chinese hamster oral LD_0 >5,000 mg/kg	IUCLID, 2000	Limited study details reported in a secondary source. Study was conducted using Reofos 50.
	Dermal	Rabbit Dermal LD_{Lo} = 2.5 mL/kg (~ 2,750 mg/kg)	ChemID, 2013	Limited study details reported in a secondary source. The LD_{Lo} value was converted to mg/kg using a density of 1.108 g/cm^3.
		Rat Dermal LD_{50} >2,000 mg/kg	IUCLID, 2000	Limited study details reported in a secondary source.
		Rabbit Dermal LD_{50} >10,000 mg/kg	IUCLID, 2000	Limited study details reported in a secondary source.
	Inhalation	Rat Inhalation 1-hour LC_{50} >200 mg/L	IUCLID, 2001	Limited study details reported in a secondary source. This study was classified as "invalid" in the IUCLID document.
Carcinogenicity		**MODERATE: No adequate carcinogenicity studies were located. The OncoLogic program estimates marginal risk for carcinogenicity; In addition, there is uncertainty regarding the carcinogenicity of Isopropylated triphenyl phosphate due to the lack of data for this substance. Carcinogenic effects cannot be completely ruled out.**		
	OncoLogic Results	Marginal	OncoLogic, 2008	
	Carcinogenicity (Rat and Mouse)			No data located.
	Combined Chronic Toxicity/Carcinogenicity			No data located.

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	Other	3 days of exposure to [Formulation 7], tested at concentrations between 0.04 and 5.0 g/mL, did not induce cell transformation in cultured Balb/c-3T3 cells (with or without metabolic activation)	Submitted confidential study	Data are inadequate as described in an robust summary not yet validated; test substance undefined and identified only as formulation 7; data are intended to support any adequate carcinogenicity data.
Genotoxicity		**LOW: Based on weight of evidence that includes negative results in gene mutation tests (*in vitro* and *in vivo*) and no evidence of chromosomal aberrations (*in vivo*) in mice. One chromosomal aberration test in hamsters resulted in positive results; however, based on weight of evidence, it seems the potential for genotoxicity is Low. All studies were conducted using commercial mixtures of Reofos 50 and/or Reolube HYD 46 (composition not specified).**		
	Gene Mutation *in vitro*	Negative, gene mutations in cultured L5178Y mouse lymphoma cells with and without metabolic activation.	IUCLID, 2000	Limited study details reported in a secondary source. Study was conducted using commercial mixture Reofos 50 (30% TPP, 70% IPTPP). GLP-compliant.
		Negative, gene mutations in Balb/3T3 mouse embryo fibroblasts with and without metabolic activation	IUCLID, 2000	Limited study details reported in a secondary source. Studies were conducted using commercial mixtures Reofos 50 (30% TPP, 70% IPTPP) and Reolube HYD 46 (composition not specified).
		Negative, multiple studies using several strains of *Salmonella typhimurium* with and without metabolic activation.	IUCLID, 2000, 2001	Limited study details in secondary sources; commercial mixtures tested included: Reofos 50 (30% TPP, 70% IPTPP), Reofos 65 (20% TPP, 80% IPTPP), Reofos 95 (9% TPP, 91% IPTPP), Durad 300 (5% TPP, 95% IPTPP) and Reolube HYD 46 (composition not specified).
		Negative, *Salmonella typhimurium* (5 strains, unspecified) with and without	IUCLID, 2001	Limited study details reported in a secondary source. This study is

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		metabolic activation		classified as "not assignable" in the IUCLID document.
	Gene Mutation *in vivo*	Negative, dominant lethal mutations in mature germ cells of male *Drosophila melanogaster*	IUCLID, 2000	Limited study details reported in a secondary source. Studies were conducted using commercial mixture Reofos 50 (30% TPP, 70% IPTPP). GLP-compliant.
	Chromosomal Aberrations *in vitro*			No data located.
	Chromosomal Aberrations *in vivo*	Negative, sister chromatid exchanges (SCEs) in male and female Chinese hamsters (single oral gavage)	IUCLID, 2000	Limited study details reported in a secondary source. Studies were conducted using commercial mixtures Reofos 50 (30% TPP, 70% IPTPP) and Reolube HYD 46 (composition not specified). Non-GLP.
		Negative, micronuclei induction in NMRI female mice (single oral gavage)	IUCLID, 2000	Limited study details reported in a secondary source. Study was conducted using commercial mixture Reolube HYD 46 (composition not specified). Non-GLP, non-guideline.
		Negative, chromosomal aberrations in bone marrow from male and female Chinese hamsters administered Reofos 50 or Reolube HYD 46 by gavage at 5000 mg/kg.	IUCLID, 2000	Limited study details reported in a secondary source. Studies were conducted using commercial mixtures Reofos 50 (30% TPP, 70% IPTPP and Reolube HYD 46 (composition not specified). GLP-compliant, according to OECD guideline 475.
		Positive, significantly increased incidence of anomalies of nuclei in bone	IUCLID, 2000	Limited study details reported in a secondary source. Studies were

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		marrow cells from male and female Chinese hamsters administered Reofos 50 or Reolube HYD 46 by single gavage at doses up to 5,000-6,000 mg/kg		conducted using commercial mixtures Reofos 50 (30% TPP, 70% IPTPP) and Reolube HYD 46 (composition not specified). GLP-compliant, non-guideline.
	DNA Damage and Repair	Negative, DNA damage and repair in cultured rat hepatocytes with and without metabolic activation	Environment Agency, 2009	Limited study details reported in a secondary source. Studies were conducted using commercial mixtures Reofos 50 (30% TPP, 70% IPTPP) and Reolube HYD 46 (composition not specified). Non-GLP.
	Other			No data located.
Reproductive Effects		**HIGH: Based on a LOAEL of 25 mg/kg-day in a combined subchronic reproductive/developmental toxicity screening test in rats. Effects included changes in ovarian and epididymal weights (25 and 100 mg/kg-day, respectively) and reduced fertility (100 and 400 mg/kg-day); the final study results were not available and the formulation of the test substance was not specified. In addition, this substance has been assigned the risk phrase R62 - possible risk of impaired fertility. In a dermal study with Reolube HYD (components not specified) in rats, reduced absolute and relative testicular weights and slight testicular tubular atrophy were observed at 1,000 mg/kg-day.**		
	Reproduction/Developmental Toxicity Screen			No data located.

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PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
	Combined Repeated Dose with Reproduction/ Developmental Toxicity Screen	In a combined repeated dose reproductive/developmental toxicity screening study, male and female rats were orally gavaged with 0, 25, 100 or 400 mg/kg-day test substance (isopropylated triphenyl phosphate; specific formulation confidential) for 14 days premating, during mating for a total of at least 28 days of treatment of males, and during gestation and up to 4 days postpartum for a total of up to 53 days of treatment of females. Results: Limited to summary statements that indicated decreased fertility at mid- and high-dose levels, decreased litter size and pup survival at least at high dose, and treatment-related changes in selected organ weights at all dose levels. NOAEL: Not established LOAEL: 25 mg/kg-day (treatment-related organ weight changes)	Submitted confidential study; Great Lakes Chemical Corporation, 2004a, 2004b	Results from 2 combined repeated dose reproduction/developmental toxicity screening tests of isopropylated triphenyl phosphate (formulation confidential).
	Reproduction and Fertility Effects			No data located.

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Other	In a dermal study in rats, test substance was applied to shaved skin at 0, 40, 200 or 1,000 mg/kg for 6 hours/day, 5 days/week for 4 weeks. Reduced absolute and relative testicular weights (1,000 mg/kg-day); slight testicular tubular atrophy (control and high-dose males). No associated microscopic findings). NOAEL: 200 mg/kg-day LOAEL: 1,000 mg/kg-day	IUCLID, 2000	Limited study details reported in a secondary source. Study conducted using commercial mixture Reolube HYD (components not specified).
Developmental Effects		**HIGH: Estimated based on analogy to Kronitex TCP (1330-78-5). Reduced fetal body weight was reported at 20 mg/kg-day (NOAEL not established; lowest dose tested) in a developmental study in rats orally exposed to the analog. In addition, increased skeletal variations were reported at 750 mg/kg-day for the analog. A LOAEL of 400 mg/kg-day (NOAEL = 100 mg/kg-day) was reported following exposure to Isopropylated triphenyl phosphate in a combined subchronic reproductive/developmental toxicity screening test in rats. Effects included reduced pre- and post-natal survival; the final study results were not available and the formulation of the test substance was not specified. Development effects were reported in a study in pregnant Wistar rats administered a FM550 mixture (sum total of TBB and TBPH approximately 50% with additional components identified as IPTPP and TPP) during gestation though lactation (GD8 - PND21); developmental effects included early female puberty, weight gain, altered exploratory behavior, and increased male left ventricle thickness (LOAEL = 1 mg/kg-day, NOAEL = 0.1 mg/kg-day). It is uncertain which component or components of the FM 550 mixture is driving the reported developmental effects. This substance has been assigned the risk phrase R63 - possible risk of harm to the unborn child. There were no experimental data for the neurodevelopmental toxicity endpoint located; There is uncertain concern for developmental neurotoxicity based on the potential for Cholinesterase (ChE) inhibition in dams that may result in alterations of fetal neurodevelopment.**		
	Reproduction/ Developmental Toxicity Screen			No data located.

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PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
	Combined Repeated Dose with Reproduction/ Developmental Toxicity Screen	In a combined repeat dose/reproductive/developmental toxicity screening study, male and female rats were orally gavaged with 0, 25, 100 or 400 mg/kg-day test substance (isopropylated triphenyl phosphate; specific formulation confidential) for 14 days premating, during mating for a total of at least 28 days of treatment for males, and during gestation and up to 4 days postpartum for a total of up to 53 days of treatment for females. Results: Limited to summary statements that indicated decreased fertility at mid- and high-dose levels, decreased litter size and pup survival at least at high dose, and treatment-related changes in selected organ weights at all dose levels. NOAEL (maternal): Not established LOAEL (maternal): 25 mg/kg-day (treatment-related organ weight changes) NOAEL (developmental): 100 mg/kg-day LOAEL (developmental): 400 mg/kg-day (decreased litter size and pup survival)	Submitted confidential study; Great Lakes Chemical Corporation, 2004b	Results from 2 combined repeated dose reproduction/developmental toxicity screening tests of isopropylated triphenyl phosphate (formulation confidential).

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Prenatal Development	In a developmental study, female rats were orally gavaged with 0, 20, 100, 400, and 750 mg/kg-day of the analog tricresyl phosphate (TCP) on GD 0-19. Maternal toxicity was evident at ≥ 100 mg/kg-day and included increased frequency of salivation, hair loss, and unkempt appearance. Reduced body weight and body weight gain was observed at 400 and 750 mg/kg-day. There were no maternal macroscopic findings. Fetal body weight was reduced at all dose levels and there was an increase in skeletal variations (indicating delayed fetal ossification) at 750 mg/kg-day. Maternal toxicity: NOAEL: 20 mg/kg-day LOAEL: 100 mg/kg-day Developmental toxicity: NOAEL: Not established LOAEL: 20 mg/kg-day (lowest dose tested) (Estimated by analogy)	ECHA, 2013a	Estimated based on analogy; study was conducted using Kronitex TCP (tris (methylphenyl) phosphate; CASRN 1330-78-5).
	Postnatal Development			No data located.
	Prenatal and Postnatal Development	Pregnant Wistar rats were administered 0, 0.1 or 1 mg/kg-day of the analog FM550 in the diet during gestation and through lactation (GD8 - PND 21); Maternal toxicity: Increased serum thyroxine (T4) levels in the high dose	Patisaul et al., 2013	Estimated based on data for FM550 mixture; non guideline study; the test substance identified as FM550 is a mixture made up of TBB, TBPH (sum total of TBB and TBPH is approximately

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		dams compared to controls was reported. There was no significant change in triiodothyronine (T3) levels in dam serum. Decreased hepatic carboxylesterease activity was also reported in dams in the high dose group. Developmental toxicity: female offspring in the high dose group displayed a significantly earlier vaginal opening when compared to controls. A statistically significant increase in weight was reported in both males and females in the high dose group at PND 120. This effect persisted through PND 180 to PND 220 with high dose males and females having significantly higher weights than same sex controls. A dose-dependent decrease in the number of rats to enter with open arms, (indicating anxiety), was reported in both male and female offspring. Increased blood glucose levels were reported in male offspring in the high-dose group compared to controls. There was no statistically significant difference in heart weight of male or female offspring. Left ventricular (LV) free wall thickness was significantly increased in male offspring in the high dose group; there were no changes in LV thickness in females at any dose. Maternal Toxicity: NOAEL: 0.1 mg/kg-day		50%), TPP and IPTPP; it is not clear which component or components of the mixture are driving the reported developmental effects.

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PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
		LOAEL: 1 mg/kg-day Developmental toxicity: NOAEL: 0.1 mg/kg-day LOAEL: 1 mg/kg-day (based on early vaginal opening in females, increased weight in males and females, decreased open arm behavior, increased blood glucose levels in males and increased LV thickness in males)		
	Developmental Neurotoxicity	Uncertain concern for developmental neurotoxicity based on the potential for Cholinesterase (ChE) inhibition in dams that may result in alterations of fetal neurodevelopment	Professional judgment	Estimated based on a structural alert for organophosphates for the neurotoxicity endpoint.
	Other			No data located.

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Neurotoxicity		**HIGH: Based on analogy to ortho-cresyl phosphate; IPTPP has the potential to undergo a similar mechanism of action as ortho-cresyl phosphate with the formation of an intermolecular intermediate that effects the nervous system. Significant inhibition of brain ChE and NTE activity was observed in rats following single oral gavage with 2,000 mg/kg of commercial mixture Reofos 54. Inhibition of ChE was also seen in rats following dermal exposure with 500 and 1,000 mg/kg of commercial mixtures Kronitex 50 and Reolube HYD, respectively. There is potential for neurotoxicity based on a structural alert for organophosphates.**		
	Neurotoxicity Screening Battery (Adult)	Male rats (5/group) were administered 2,000 mg/kg Reofos 65 via single oral gavage. No clinical signs of toxicity in treated animals; positive control animals gavaged with tri-o-cresyl phosphate (TOCP) displayed lacrimation, tremors, staining and had lowered body temperatures. Significant inhibition of brain cholinesterase and neuropathy target esterase activity (35 and 50% less than controls, respectively) in treated animals. Serum cholinesterase activity in treated animals was 87% less than that of controls, compared to 94% less in positive control (TOCP-treated) animals.	IUCLID, 2000	Limited study details reported in a secondary source. Study conducted using commercial mixture Reofos 65 (20% TPP, 80% IPTPP).
		Rats were exposed (head only) for 20 minutes to an unspecified concentration of smoke and decomposition gases from foam containing equal proportions of the test substance; There were no convulsive seizures or characteristic of exposure to toxic bicyclic phosphites or phosphates observed.	Submitted confidential study	Study was not conducted according to standard guidelines; study evaluated neurotoxicity of test substance. Test substance identified as combustion products of an isopropylated triaryl phosphates/ triphenyl phosphate mixture in the presence of cyclic phosphonate compounds; exposure concentration not specified.
	Other	In a dermal study in rats, test substance	IUCLID, 2000	Limited study details reported in a

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		was applied to shaved skin at 0, 40, 200 or 1,000 mg/kg for 6 hours/day, 5 days/week for 4 weeks. Slightly depressed plasma ChE activity (females at 1,000 mg/kg-day) NOAEL: 200 mg/kg-day LOAEL: 1,000 mg/kg-day		secondary source. Study conducted using commercial mixture Reolube HYD (components not specified)
		In a dermal study in rats (5/sex/group), Kronitex 50 was applied to shaved skin at 0, 100, 500 or 2,000 mg/kg 6 hours/day, 5 days/week for 4 weeks. Decreased plasma cholinesterase (ChE) activity (females at 500 and 2,000 mg/kg-day); decreased erythrocyte ChE activity (males, 2,000 mg/kg-day) NOAEL: 100 mg/kg-day LOAEL: 500 mg/kg-day	IUCLID, 2000	Limited study details reported in a secondary source. Study conducted using commercial mixture Kronitex 50 (components not specified). Limited number of endpoints assessed.
		There is potential for neurotoxicity based on the presence of the organophosphates structural alert. (Estimated)	Professional judgment	Estimated based on structural alert for organophosphates.
		Numerous studies assessed the potential for commercial isopropylated phenyl phosphate test substances (e.g., Reofos 50, Reofos 65, Reofos 95, Reofos 120, Reolube HYD 46) to cause delayed neuropathy in hens. Ataxia and axonal degeneration could be elicited by single dosing at 2,000 mg/kg or higher and by repeated dosing at 90 mg/kg-day or higher. One study employed the	IUCLID, 2000	Sufficient evidence that commercial isopropylated phenyl phosphate formulations cause delayed neuropathy in hens. IUCLID (2000) summarized results from a number of unpublished studies.

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		inhalation exposure route and reported ataxia and degenerative neurological effects following single 8-hour exposure to aerosols of Reofos 50 at 2.4 mg/L (no effects at 0.62 mg/L).		
		Potential for neurological effects; this substance has the potential to undergo a similar mechanism of action as ortho-cresyl phosphate with the formation of an intermolecular intermediate that effects the nervous system. (Estimated by analogy)	Professional judgment	Estimated based on analogy to ortho-cresyl phosphate and professional judgment.

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Repeated Dose Effects		**HIGH: Based on a combined repeated dose with reproductive/developmental toxicity screen test in rats; a LOAEL of 25 mg/kg-day (lowest dose tested) was determined for changes in organ weights (NOAEL was not established); final study results were not available and the test substance formulation was not specified. A LOAEL of 460 mg/kg-day in rats following 28 days of dietary exposure to commercial mixture Kronitex-100 (composition not specified). Dermal NOAELs were 100 and 200 mg/kg-day in rats following 4 weeks of exposure to commercial mixtures Kronitex 50 and Reolube HYD, respectively. In addition, there may be some potential for repeated dose effects based on analogy to TPP, a component of the commercial mixture.**		
		In a combined repeated dose reproductive/developmental toxicity screening study, male and female rats were orally gavaged with 0, 25, 100 or 400 mg/kg-day test substance (isopropylated triphenyl phosphate; specific formulation confidential) for 14 days premating, during mating for a total of at least 28 days of treatment of males, and during gestation and up to 4 days postpartum for a total of up to 53 days of treatment of females. Treatment-related changes in selected organ weights at all dose levels NOAEL: Not established LOAEL: 25 mg/kg-day (based on changes in organ weights)	Submitted confidential study; Great Lakes Chemical Corporation, 2004a, 2004b	Limited study results reported in study summary statements; screening tests of isopropylated triphenyl phosphate (formulation confidential).
		Sprague-Dawley rats (10/sex) were exposed to Kronitex 100 in the diet at concentrations of 0, 0.1, 0.5, or 1.0% (~0, 91, 460, or 910 mg/kg-day) for 28 days; Mortalities included 12 rats (1 control, 4 low-dose, 4 mid-dose, and 3 high-dose) that were determined not to be treatment related; there were no	Submitted confidential study; IUCLID, 2000, 2001	Limited study details provided in a secondary source. Study was conducted using commercial mixture Kronitex K-100 (purity, composition not specified). Doses were reported as % in the diet but were converted by SRC, Inc. to mg/kg bw-day using EPA 1988

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		effects on urinalysis results or incidence of gross lesions at necropsy. Reduced feed consumption was observed in the mid-dose group in both sexes and reduced body weight gain was noted in high-dose females. Abnormalities (not specified) were observed in clinical chemistry measurements in mid- and high-dose groups and in hematology parameters at the high dose. Relative liver weights were elevated in all treated groups. There were no indications of treatment-related histopathologic lesions in livers or kidneys of high-dose groups. NOAEL: 0.1% (~91 mg/kg-day) LOAEL: 0.5% (~460 mg/kg-day) based on unspecified abnormalities in clinical chemistry		reference values for body weight and food consumption.
		In a dermal study in rats (5/sex/group), Kronitex 50 was applied to shaved skin at 0, 100, 500 or 2,000 mg/kg 6 hours/day, 5 days/week for 4 weeks. Decreased plasma cholinesterase (ChE) activity (females at 500 and 2,000 mg/kg-day); decreased erythrocyte ChE activity (males, 2,000 mg/kg-day); increased adrenal weights and slight fatty change of the adrenal cortex (males at 500 and 2,000 mg/kg-day NOAEL: 100 mg/kg-day LOAEL: 500 mg/kg-day	IUCLID, 2000	Limited study details reported in a secondary source. Study conducted using commercial mixture Kronitex 50 (components not specified). Limited number of endpoints assessed.

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		In a dermal study in rats, test substance was applied to shaved skin at 0, 40, 200 or 1,000 mg/kg for 6 hours/day, 5 days/week for 4 weeks. Slightly depressed plasma ChE activity (females at 1,000 mg/kg-day); reduced absolute and relative testicular weights (1,000 mg/kg-day); slight testicular tubular atrophy (control and high-dose males); slightly increased absolute and relative adrenal weights (no associated microscopic findings). NOAEL: 200 mg/kg-day LOAEL: 1,000 mg/kg-day	IUCLID, 2000	Limited study details reported in a secondary source. Study conducted using commercial mixture Reolube HYD (components not specified)
Skin Sensitization		**LOW: The commercial mixtures Reofos 50 and Reolube HYD 46 were not sensitizing to guinea pigs**		
	Skin Sensitization	Not sensitizing to guinea pig skin following intracutaneous injection and challenge treatment using Reofos 50 and Reolube HYD 46.	IUCLID, 2000	Limited study details reported in a secondary source. Study was conducted using commercial mixtures Reofos 50 (30% TPP, 70% IPTPP) and Reolube HYD 46 (components not specified in secondary source)

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		Inconclusive; shown to be ambiguous for sensitization potential in the Local Lymph Node Assay in mice. Stimulation Indices (SI) of 7.4, 12.9 and 10.4 were calculated for applied concentrations of 25%, 50% and 100% IPTPP, respectively. No dose-response relationship was observed within the study.	ECHA, 2013b	Limited study details reported in a secondary source. Test substance: Reofos 65 (Phenol, isopropylated, phosphate); conducted according to OECD guideline 429. The SI threshold value of at least 3, would normally be classified as a sensitizer' however, a dose-response relationship was not observed, which is required of the LLNA test design.
Respiratory Sensitization		**No data located**		
	Respiratory Sensitization			No data located.
Eye Irritation		**LOW: Based on no irritation to slight ocular irritation that cleared within 10 days postinstillation.**		
	Eye Irritation	In a number of acute eye irritation tests using a variety of commercial isopropylated phenyl phosphate formulations, Reofos 50 was determined to be nonirritating (1 study) to slightly irritating (2 studies); Reolube HYD 46 was slightly irritating (slight-to-moderate redness that cleared in 10 days); Reofos 65, Refos 95, and Durad 300 were nonirritating.	IUCLID, 2000, 2001	Weight of evidence indicates that commercial isopropylated phenyl phosphate is not a primary eye irritant
		Slight conjunctival erythema in rabbits; cleared within 48 hours; characterized as "practically non-irritating" based on a maximum irritation score of 1.3/110 at 24 hours; no conjunctival discharge or effects on the cornea or iris were	Submitted confidential study	Study is inadequate to determine if this substance is an eye irritant because data are on an undefined chemical composition; rabbit eyes were instilled with 0.01 mL of a test substance identified as a

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		reported.		mixture of isopropylated triaryl phosphates and triphenyl phosphate [formulation 1].
		non-irritating in rabbits; there were no signs of eye irritation observed at 1,24,48, or 72 hours	Submitted confidential study	Study is inadequate to determine if this substance is an eye irritant because data are on an undefined chemical composition; rabbit eyes were instilled with 0.01 mL of a test substance identified as a mixture of isopropylated triaryl phosphates and triphenyl phosphate [formulation 2].
Dermal Irritation		**LOW: Based on no evidence of irritation in rabbit skin. Two of the studies were conducted using mixtures of isopropylated triaryl phosphates and triphenyl phosphate with undefined chemical compositions. The data may not be suitable to determine the potential for skin irritancy.**		
	Dermal Irritation	In a number of acute dermal irritation tests using a variety of commercial isopropylated phenyl phosphate formulations, Reofos 50 was nonirritating; Reolube HYD 46 was slightly irritating (slight erythema for up to 72 hours); Refos 95 and Durad 300 were nonirritating.	IUCLID, 2000; IUCLID, 2001	Weight of evidence indicates that commercial isopropylated phenyl phosphate is not a primary dermal irritant.
		Not irritating to rabbit skin following dermal exposure for 4 hours on two occluded test sites (0.5 mL per site); there was no sign of irritation at 4.5, 24, 48, or 72 hours following exposure; irritation scores were 0/8.0 at all time points.	Submitted confidential study	Study is inadequate to determine if this substance is skin irritant because data are on an undefined chemical composition; test substance identified as a mixture of isopropylated triaryl phosphates and triphenyl phosphate [formulation 2].
		Not irritating to rabbit skin following	Submitted confidential study	Study is inadequate to determine if

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		dermal exposure for 4 hours on two occluded test sites (0.5 mL per site); there was no sign of irritation at 4.5, 24, 48, or 72 hours following exposure; irritation scores were 0/8.0 at all time points.		this substance is skin irritant because data are on an undefined chemical composition; test substance identified as a mixture of isopropylated triaryl phosphates and triphenyl phosphate [formulation 1].
Endocrine Activity		**No data were available for this test substance. Effects to the adrenal glands were reported following dermal application of the commercial mixture Kronitex 50 to shaved rat skin. Changes to adrenal weights and testicular weights were also reported following exposure to a commercial mixture of Kronitex 50 (Components not specified); these changes may be indicative of endocrine activity. Increased serum thyroxine (T4) levels were reported in the serum of dams following oral administration to the analog FM550 (mixture of 50% sum total of TBB and TBPH and additional components identified as IPTPP and TPP). It is unclear which component or components of the mixture are driving the endocrine activity effects.**		
		Male and female rats (5/sex/group), the analog Kronitex 50 was applied to shaved skin at 0, 100, 500 or 2,000 mg/kg bw 6 hours/day, 5 days/week for 4 weeks. Increased adrenal weights and slight fatty change of the adrenal cortex (males at 500 and 2,000 mg/kg-bw NOAEL = 100 mg/kg bw LOAEL = 500 mg/kg bw (adrenal weights) (Estimated by analogy)	IUCLID, 2000	Limited study details reported in a secondary source. Study conducted using commercial mixture Kronitex 50 (components not specified). Limited number of endpoints assessed.
		In a dermal study in rats, test substance was applied to shaved skin at 0, 40, 200 or 1,000 mg/kg for 6 hours/day, 5 days/week for 4 weeks. Reduced absolute and relative testicular weights (1,000 mg/kg-day); slight	IUCLID, 2000	Limited study details reported in a secondary source. Study conducted using commercial mixture Reolube HYD (components not specified); these effects may be indicative of endocrine activity.

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		testicular tubular atrophy (control and high-dose males); slightly increased absolute and relative adrenal weights (no associated microscopic findings).		
		Pregnant Wistar rats were administered 0, 0.1 or 1 mg/kg-day of the analog FM550 in the diet during gestation and through lactation (GD8 - PND 21); Increased serum thyroxine (T4) levels (increase of 65%) in the high dose dams compared to controls was reported. There was no significant change in triiodothyronine (T3) levels in dam serum. There was no reported statistically significant change in T4 or T3 levels in pup serum on PND 21 when compared to controls.	Patisaul et al., 2013	Estimated based on experimental data for the FM550 mixture; non guideline study; the test substance identified as FM550 is a mixture made up of TBB and TBPH (sum total of TBB and TBPH is approximately 50%) and other compounds including TPP and IPTPP; it is not clear which component or components of the mixture are driving the reported endocrine activity effects.
Immunotoxicity		**No data located.**		
	Immune System Effects			No data located.
ECOTOXICITY				
ECOSAR Class				

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PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
Acute Aquatic Toxicity	**VERY HIGH: Based on experimental LC_{50} values of <0.3 mg/L in fish (conducted using commercial mixture Phosflex [28-30% triphenyl phosphate, along with isomers of isopropylphenyl diphenyl phosphate, isomers of diisopropylphenyl diphenyl phosphate and tri-substituted phenol phosphates]) and 0.25 mg/L in daphnia (conducted using isopropyl phenyl diphenyl phosphate [composition not specified]). The reported water solubility values from studies on commercial mixtures may not adequately represent all components of the mixture. The tris(isopropylphenyl) phosphate isomers and other isopropyl substituted phenyl phosphate ester components anticipated to be present in the commercial product are expected to have a range of water solubility values. Therefore NES may be predicted for some components but not others. Estimated data using the ECOSAR program predicted no effects at saturation (NES) for these organisms. Two experimental studies were available for green algae which determined a 14-day NOEC and LOEC of 0.1 mg/L for Kronitex 200 and Phosflex 31P (major components triphenyl phosphate and 2-isopropylphenyl diphenyl phosphate), respectively. Estimated data based on the monoisopropyl diphenyl phosphate predict Very High hazard for algae; however, estimated data using other isomers predicted no effects at saturation (NES). In addition, this substance has been assigned the risk phrase R50/R53 - Very toxic to aquatic organisms. May cause long-term adverse effects in the aquatic environment.**		
Fish LC_{50}	Fish (*Ictalurus punctatus*) 96-hour LC_{50} <0.3 mg/L The test was performed under static test conditions using acetone as solvent; test substance concentrations were nominal (Experimental)	Cleveland et al., 1986	Adequate, primary source. Study was conducted using the commercial mixture Phosflex 31P (28-30% triphenyl phosphate, along with isomers of isopropylphenyl diphenyl phosphate, isomers of diisopropylphenyl diphenyl phosphate and tri-substituted phenol phosphates); water solubility of the commercial mixture tested was not reported.
	Fish (*Ictalurus punctatus*) 96-hour LC_{50} = 43 mg/L The test was performed under static test conditions using acetone as solvent; test substance concentrations were nominal. (Experimental)	Nevins and Johnson 1978 (as cited in Environment Agency, 2009)	Adequate study reported in a secondary source. Study was conducted using commercial product Houghto-Safe 1120 (isopropylphenyl diphenyl phosphate as the principal

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			component); the LC_{50}> value of 43 is sufficiently above the water solubility for the principal component; NES is predicted.
	Fish (*Ictalurus punctatus*) 96-hour LC_{50} = 15 mg/L 30-day LC_{50} = 4.5 mg/L The test was performed under flow-through test conditions using acetone as solvent; test substance concentrations were nominal. (Experimental)	Nevins and Johnson 1978 (as cited in Environment Agency, 2009)	Adequate study reported in a secondary source. Study was conducted using commercial product, Houghto-Safe 1120 (with isopropylphenyl diphenyl phosphate as the principal component).
	Fish (*Oncorhynchus mykiss*) 96-hour LC_{50} = 0.65 mg/L 8-day LC_{50} = 0.59 mg/L The test was performed under flow-through test conditions using acetone as solvent; test substance concentrations were nominal. (Experimental)	Nevins and Johnson 1978 (as cited in Environment Agency, 2009)	Adequate study reported in a secondary source. Study was conducted using commercial product, Houghto-Safe 1120 (with isopropylphenyl diphenyl phosphate as the principal component).
	Fish (*Oncorhynchus mykiss*) 96-hour LC_{50} = 0.9 mg/L The test was performed under static test conditions using acetone as solvent; test substance concentrations were nominal (Experimental)	Cleveland et al., 1986	Adequate primary source. Study was conducted using the commercial mixture Phosflex 31P (28-30% triphenyl phosphate, along with isomers of isopropylphenyl diphenyl phosphate, isomers of diisopropylphenyl diphenyl phosphate and tri-substituted phenol phosphates).
	Fish (*Oncorhynchus mykiss*) 96-hour LC_{50} = 1.15 mg/L NOEC: 0.4 mg/L	IUCLID, 2000	Limited study details reported in a secondary source. Study was conducted using commercial

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	LOEC: 0.74 mg/L Test was performed under semi-static test conditions; not stated whether the effect level values were nominal or measured concentrations. (Experimental)		product Reofos 50 (30% TPP, 70% IPTPP). Reliability of this study was not specified in the IUCLID.
	Fish (*Oncorhynchus mykiss*) 96-hour LC_{50} = 1.7 mg/L The test was performed under static test conditions; test substance concentrations were nominal; at least 8 concentrations tested. (Experimental)	Nevins and Johnson 1978 (as cited in IUCLID, 2001; Environment Agency, 2009)	Adequate study reported in a secondary source. Study was conducted using commercial product Houghto-Safe 1120 (isopropylphenyl diphenyl phosphate as the principal component).
	Fish (*Oncorhynchus mykiss*) 96-hour LC_{50} = 4.5 mg/L (Experimental)	Nevins and Johnson 1978 (as cited in Environment Agency, 2009)	Adequate study reported in a secondary source. Study was conducted using the commercial mixture Kronitex 200 (4-6% triphenyl phosphate, 7-10% 2-isopropylphenyl diphenyl phosphate, 20-25% 4-isopropylphenyl diphenyl phosphate, along with bis-(2-isopropylphenyl) phenyl phosphate and minor amounts of di-, tri- and tetraisopropyl-substituted triphenyl phosphates).
	Fish (*Lepomis macrochirus*) 96-hour LC_{50} = 2.6 mg/L The test was performed under static test conditions using acetone as solvent; test substance concentrations were nominal. (Experimental)	Cleveland et al., 1986	Adequate study reported in a secondary source. Study was conducted using the commercial mixture Phosflex 31P (28-30% triphenyl phosphate, along with isomers of isopropylphenyl diphenyl phosphate, isomers of

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			diisopropylphenyl diphenyl phosphate and tri-substituted phenol phosphates).
	Fish (*Lepomis macrochirus*) 96-hour LC_{50} = 11 mg/L 17-day LC_{50} = 5.0 mg/L The test was performed under flow-through test conditions using acetone as solvent; test substance concentrations were nominal. (Experimental)	Nevins and Johnson 1978 (as cited in Environment Agency, 2009)	Adequate study reported in a secondary source. Study was conducted using commercial product, Houghto-Safe 1120 (with isopropylphenyl diphenyl phosphate as the principal component).
	Fish (*Lepomis macrochirus*) 96-hour LC_{50} = 12 mg/L The test was performed under static test conditions using acetone as solvent; test substance concentrations were nominal and at least 8 concentrations were tested. (Experimental)	Nevins and Johnson 1978 (as cited in Environment Agency, 2009)	Adequate study reported in a secondary source. Study was conducted using commercial product Houghto-Safe 1120 (isopropylphenyl diphenyl phosphate as the principal component).
	Fish (*Lepomis macrochirus*) 96-hour LC_{50} = 29 mg/L The test was performed under static test conditions using acetone as solvent; test substance concentrations were nominal (Experimental)	Cleveland et al., 1986	Adequate study reported in a secondary source. Study was conducted using the commercial mixture Kronitex 200 (4-6% triphenyl phosphate, 7-10% 2-isopropylphenyl diphenyl phosphate, 20-25% 4-isopropylphenyl diphenyl phosphate, along with bis-(2-isopropylphenyl) phenyl phosphate and minor amounts of di-, tri- and tetraisopropyl-substituted triphenyl phosphates); The value is well above the water solubility of the test substance.

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	Fish (*Pimephales promelas*) 96-hour LC_{50} = 1.7 mg/L The test was performed under static test conditions using acetone as solvent; test substance concentrations were nominal. (Experimental)	Cleveland et al., 1986	Adequate study reported in a secondary source. Study was conducted using the commercial mixture Phosflex 31P (28-30% triphenyl phosphate, along with isomers of isopropylphenyl diphenyl phosphate, isomers of diisopropylphenyl diphenyl phosphate and tri-substituted phenol phosphates).
	Fish (*Pimephales promelas*) 96-hour LC_{50} = 10.8 mg/L NOEC = 3.2 mg/L The test was performed under static test conditions using acetone as solvent; test substance concentrations were nominal (Experimental)	IUCLID, 2000, 2001	Limited study details reported in a secondary source. Study was conducted using commercial product Reofos 50 (30% TPP, 70% IPTPP).
	Fish (*Pimephales promelas*) 96-hour LC_{50} = 17 mg/L 20-day LC_{50} = 8.5 mg/L The test was performed under static test conditions using acetone as solvent; test substance concentrations were nominal (Experimental)	Nevins and Johnson 1978 (as cited in Environment Agency, 2009)	Limited study reported in a secondary source. Study was conducted using commercial product, Houghto-Safe 1120 (with isopropylphenyl diphenyl phosphate as the principal component).
	Fish (*Pimephales promelas*) 96-hour LC_{50} = 35 mg/L The test was performed under static test conditions using acetone as solvent; test substance concentrations were nominal. (Experimental)	Nevins and Johnson 1978 (as cited in Environment Agency, 2009)	Adequate study reported in a secondary source. Study was conducted using commercial product Houghto-Safe 1120 (isopropylphenyl diphenyl phosphate as the principal component); the value is well above the water solubility of the test substance.

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PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	Fish (*Pimephales promelas*) 96-hour LC_{50} = 14.9 mg/L The test was performed under static test conditions using acetone as solvent; test substance concentrations were nominal. (Experimental)	IUCLID, 2000	Limited study details reported in a secondary source. Study was conducted using commercial product Reofos 65 (components not specified). The value is well above the water solubility of the test substance.
	Fish (*Pimephales promelas*) 96-hour LC_{50} = 50.1 mg/L The test was performed under static test conditions using acetone as solvent; test substance concentrations were nominal. (Experimental)	IUCLID, 2001	Limited study details reported in a secondary source. Study was conducted using commercial product Reofos 65 (20% TPP, 80% IPTPP). The value is well above the water solubility of the test substance.
	Fish (*Oncorhynchus mykiss*) 96-hour LC_{50} = 1.6 mg/L NOEC <1 mg/L The test was performed under static test conditions using acetone as solvent; test substance concentrations were nominal. (Experimental)	IUCLID, 2000, 2001	Limited study details reported in a secondary source. Two studies conducted using commercial product Reofos 50 (30% TPP, 70% IPTPP) and Kronitex 50.
	Fish (*Oncorhynchus mykiss*) 96-hour LC_{50} = 2.4 mg/L NOEC <1 mg/L The test was performed under static test conditions with nominal test concentrations (1.0, 1.8, 3.2, 5.6, 10.0 mg/L) (Experimental)	IUCLID, 2001	Limited study details reported in a secondary source. Study was conducted using commercial mixture K-100 (composition not specified).
	Fish (*Oncorhynchus mykiss*) 96-hour LC_{50} = 4.46 mg/L NOEC <0.56 mg/L The test was performed under static test	IUCLID, 2001	Limited study details reported in a secondary source. Study was conducted using commercial mixture K-200 (composition not

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	conditions with nominal test concentrations (Experimental)		specified).
	Fish (*Brachydanio rerio*) 96-hour LC_{50} >1,000 mg/L The study was conducted using nominal test conditions; test chamber conditions (static, flow-through, etc.) not specified (Experimental)	IUCLID, 2000	Limited study details reported in a secondary source. Study was conducted using commercial product Reolube HYD 46 (components not specified). This was a water accommodated fraction (WAF) test. The test substance was reported as being mixed with lecithin using ultrasonication to form an emulsion, which resulted in turbid test solutions. The results cannot be considered valid.
	Fish 96-hour LC_{50} = 0.005 mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	Estimations for triisopropyl phenyl phosphate; Estimate for the Esters class was provided for comparative purposes. See Section 5.5.1. the log K_{ow} of 9.1 for this chemical exceeds the SAR limitation for log K_{ow} of 5.0; NES are predicted for these endpoints.
	Fish 96-hour LC_{50} = 0.03 mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	Estimations for diisopropyl phenyl phosphate; Estimate for the Esters class was

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			provided for comparative purposes. See Section 5.5.1. The log K_{ow} of 7.6 for this chemical exceeds the SAR limitation for log K_{ow} of 5.0; NES are predicted for these endpoints.
	Fish 96-hour LC_{50} = 0.18 mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	Estimations for monoisopropyl phenyl phosphate; Estimate for the Esters class was provided for comparative purposes. See Section 5.5.1. The log K_{ow} of 6.2 for this chemical exceeds the SAR limitation for log K_{ow} of 5.0; NES are predicted for these endpoints.
Daphnid LC_{50}	*Daphnia magna* 48-hour LC_{50} = 0.25 mg/L The test was performed under static test conditions (Experimental)	Ziegenfuss et al., 1986 (as cited in Environment Agency, 2009)	Adequate study reported in a secondary source. Study was conducted using isopropyl phenyl diphenyl phosphate (purity not given).
	Daphnia magna 48-hour EC_{50} = 0.83 mg/L NOEC = 0.32 mg/L The test was performed under static test conditions; test substance concentrations were nominal. (Experimental)	IUCLID, 2001	Limited study details reported in a secondary source. Study was conducted using Kronitex-100 (components not specified).

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PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	Daphnia magna 48-hour EC_{50} = 1.5 mg/L NOEC = 1 mg/L The test was performed under static test conditions using a cosolvent; test substance concentrations were nominal. (Experimental)	IUCLID, 2001	Limited study details reported in a secondary source. Study was conducted using Kronitex-200 (components not specified).
	Daphnia magna 48-hour EC_{50} = 2.44 mg/L NOEC = 0.56 mg/L The test was performed under static test conditions; test substance concentrations were nominal. (Experimental)	IUCLID, 2001	Limited study details reported in a secondary source. Study was conducted using Kronitex-5 (components not specified).
	Daphnia magna 48-hour EC_{50} = 3.2 mg/L The test was performed under static test conditions using an acetone solvent; test substance concentrations were nominal. (Experimental)	Sanders et al., 1985	Adequate guideline study. Study was conducted using the commercial mixture Kronitex 200 (major components: triphenyl phosphate and 2-isopropylphenyl diphenyl phosphate).
	Daphnia magna 48-hour EC_{50} = 6.8 mg/L The test was performed under static test conditions; test substance concentrations were nominal. (Experimental)	Sanders et al., 1985	Adequate study reported in a secondary source. Study was conducted using the commercial mixture Phosflex 31P (major components being triphenyl phosphate and 2-isopropylphenyl diphenyl phosphate).
	Daphnia magna 48-hour EC_{50} = 14 mg/L 48-hour NOEC = 0.3 mg/L Test substance concentrations were nominal; 13 concentrations tested between 0.14 and 167 mg/L. (Experimental)	IUCLID, 2000	Adequate study reported in a secondary source. Study was conducted using commercial product Reolube HYD 46 (components not specified). The substance was reported to have been tested as an emulsion using lecithin and ultrasonic dispersion.

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			The results of the study are questionable.
	Daphnia magna 48-hour EC_{50} = 31.3 mg/L (Experimental)	IUCLID, 2000	Adequate study reported in a secondary source. Study was conducted using commercial product Reofos 50 (components not specified); the value is well above the water solubility of the test substance.
	Daphnia magna 48-hour EC_{50} >1,000 mg/L (as WAF) semi-static test conditions (renewal every 24 hours); (Experimental)	Knight and Allan, 2002 (as cited in Environment Agency, 2009)	Limited study details reported in a secondary source. Study was conducted using a commercial tris(isopropyl phenyl) phosphate product; Durad 310M (5% dodecyl phosphate, 4% triphenyl phosphate, with the remainder made up of isopropylated triaryl phosphates). There were uncertainties in the results that included possible presence of some test substance in the control water and adherence of test substance to daphnia. The test substance was not acutely toxic to daphnid at concentrations up to the solubility limit (0.77 mg/L).
	Daphnid 48-hour LC_{50}= 0.004 mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	Estimations for triisopropyl phenyl phosphate; Estimate for the Esters class was provided for comparative purposes.

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PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
			See Section 5.5.1. The log K_{ow} of 9.1 for this chemical exceeds the SAR limitation for log K_{ow} of 5.0; NES are predicted for these endpoints.
	Daphnid 48-hour LC_{50} = 0.03 mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	Estimations for diisopropyl phenyl phosphate; Estimate for the Esters class was provided for comparative purposes. See Section 5.5.1. The log K_{ow} of 7.6 for this chemical exceeds the SAR limitation for log K_{ow} of 5.0; NES are predicted for these endpoints.
	Daphnid 48-hour LC_{50} = 0.25 mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	Estimations for monoisopropyl phenyl phosphate; Estimate for the Esters class was provided for comparative purposes. See Section 5.5.1. The log K_{ow} of 6.2 for this chemical exceeds the SAR limitation for log K_{ow} of 5.0; NES are predicted for these endpoints.

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Green Algae EC_{50}	Green algae (*Selenastrum capricornutum*) 14-day LOEC = 0.1 mg/L (lowest concentration tested) 50% growth inhibition between 1.0 and 10.0 mg/L (Experimental)	Sanders et al., 1985	Adequate primary source. Study was conducted using commercial mixture Phosflex 31P (major components triphenyl phosphate and 2-isopropylphenyl diphenyl phosphate).
	Green algae (*Selenastrum capricornutum*) 14-day NOEC = 0.1 mg/L The test substance concentrations were nominal using an acetone solvent. Nominal exposure level of 100 mg/L resulted in 53% growth inhibition (Experimental)	Sanders et al., 1985	Adequate primary source. Study was conducted using commercial mixture Kronitex 200 (major components: triphenyl phosphate and 2-isopropylphenyl diphenyl phosphate).
	Green algae 96-hour EC_{50} < 0.001 mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	Estimations for triisopropyl phenyl phosphate; Estimate for the Esters class was provided for comparative purposes. See Section 5.5.1. The log K_{ow} of 9.1 for this chemical exceeds the SAR limitation for log K_{ow} of 6.4; NES are predicted for these endpoints.
	Green algae 96-hour EC_{50} = 0.006 mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	Estimations for diisopropyl phenyl phosphate; Estimate for the Esters class was provided for comparative purposes.

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			See Section 5.5.1. The log K_{ow} of 7.6 for this chemical exceeds the SAR limitation for log K_{ow} of 6.4; NES are predicted for these endpoints.
	Green algae 96-hour EC_{50} = 0.05 mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	Estimations for monoisopropyl phenyl phosphate; Estimate for the Esters class was provided for comparative purposes. See Section 5.5.1. The log K_{ow} of 9.1 for this chemical exceeds the SAR limitation for log K_{ow} of 6.4; NES are predicted for these endpoints.

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PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
Chronic Aquatic Toxicity	**VERY HIGH: Based on experimental LOECs < 0.1 mg/L in daphnia using commercial mixtures Kronitex 200 and Phosflex 31. The reported water solubility values from studies on commercial mixtures may not adequately represent all components of the mixture. The tris(isopropylphenyl) phosphate isomers and other isopropyl substituted phenyl phosphate ester components anticipated to be present in the commercial product are expected to have a range of water solubility values. Therefore NES may be predicted for some components but not others. Experimental data for fish and algae indicate a High hazard designation.Estimated data using the ECOSAR program and monoisopropyl class predict very high hazard for fish, daphnia and algae; however, estimated data using other isomers predict no effects at saturation (NES) for all organisms. In addition, this substance has been assigned the risk phrase R50/R53 - Very toxic to aquatic organisms. May cause long-term adverse effects in the aquatic environment.**		
Fish ChV	Fish (*Pimephales promelas*) 30-, 60- and 90-day NOEC (growth) = 0.5 mg/L (nominal) 30-day LOEC (growth) = 1.0 mg/L NOEC (mortality) =1.0 mg/L (nominal) The study was conducted using flow-through test conditions. Measurements of test substance at 2-week intervals only evaluated levels of triphenyl phosphate (28-30% of the composition of Phosflex 31P) and isodecyl diphenyl phosphate (percentage composition of Phosflex 31P not stated). Triphenyl phosphate and isodecyl diphenyl phosphate accounted for 5.8-20.5% of the nominal test substance concentration. (Experimental)	Cleveland et al., 1986	Study was conducted using the commercial mixture Phosflex 31P (28-30% triphenyl phosphate, along with isomers of isopropylphenyl diphenyl phosphate, isomers of diisopropylphenyl diphenyl phosphate and tri-substituted phenol phosphates).
	Fish (*Pimephales promelas*) 30-day NOEC (growth) = 0.5 mg/L (nominal)	Cleveland et al., 1986	Study was conducted using commercial mixture Kronitex 200

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	60 and 90 day NOEC (growth) = 1.0 mg/L (nominal) The study was conducted using flow-through test conditions. Measurements of test substance at 2-week intervals only evaluated levels of triphenyl phosphate and isodecyl diphenyl phosphate which comprised 31-41% of the test substance and the sum of these components only accounted for 4.8-8.8% of the nominal test substance concentration. (Experimental)		(4-6% triphenyl phosphate, 7-10% 2-isopropylphenyl diphenyl phosphate, 20-25% 4-isopropylphenyl diphenyl phosphate, along with bis-(2-isopropylphenyl) phenyl phosphate and minor amounts of di-, tri- and tetraisopropyl-substituted triphenyl phosphates). The 60- and 90-day NOEC is greater than the 30-day NOEC which indicates that the decreased growth at 30 days may be a spurious result.
	Fish ChV = 0.006 mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	Estimations for monoisopropyl phenyl phosphate. Estimate for the Esters class was provided for comparative purposes. See Section 5.5.1.
	Fish ChV < 0.001 mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	Estimations for triisopropyl phenyl phosphate; Estimate for the Esters class was provided for comparative purposes. See Section 5.5.1. The log K_{ow} of 9.1 for this chemical exceeds the SAR limitation for log K_{ow} of 8.0; NES

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			are predicted for these endpoints.
	Fish ChV < 0.001 mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	Estimations for diisopropyl phenyl phosphate. Estimate for the Esters class was provided for comparative purposes. See Section 5.5.1.
Daphnid ChV	*Daphnia magna* 21-day LOEC (reproduction) = 0.027 mg/L 21-day NOEC (reproduction) = 0.006 mg/L 21-day NOEC (survival) = 0.027 mg/L The study was conducted under flow-through test conditions; test concentrations: 0, 0.006, 0.027, 0.072, 0.154 mg/L (100% mortality at 0.072 and 0.154 mg/L) (Experimental)	Sanders et al., 1985	Study was conducted using the commercial mixture Kronitex 200 (major components: triphenyl phosphate and 2-isopropylphenyl diphenyl phosphate).
	Daphnia magna 21-day LOEC (reproduction) = 0.056 mg/L 21-day NOEC (reproduction) = 0.028 mg/L 21-day NOEC (survival) = 0.028 mg/L The study was conducted under flow-through test conditions; test concentrations were nominal (0.00085-0.056 mg/L) (Experimental)	Sanders et al., 1985	Study was conducted using the commercial mixture Phosflex 31P (major components: triphenyl phosphate and 2-isopropylphenyl diphenyl phosphate).
	Daphnid ChV < 0.001 mg/L	ECOSAR v1.11	Estimations for triisopropyl phenyl

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	(Estimated) ECOSAR: Esters		phosphate; Estimate for the Esters class was provided for comparative purposes. See Section 5.5.1. The log K_{ow} of 9.1 for this chemical exceeds the SAR limitation for log K_{ow} of 8.0; NES are predicted for these endpoints.
	Daphnid ChV = 0.004 mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	Estimations for diisopropyl phenyl phosphate; Estimate for the Esters class was provided for comparative purposes. See Section 5.5.1.
	Daphnid ChV = 0.05mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	Estimations for monoisopropyl phenyl phosphate. Estimate for the Esters class was provided for comparative purposes. See Section 5.5.1.
Green Algae ChV	Green algae (*Selenastrum capricornutum*) 14-day LOEC = 0.1 mg/L (lowest concentration tested) 50% growth inhibition between 1.0 and 10.0 mg/L (Experimental)	Sanders et al., 1985	Adequate primary source. Study was conducted using commercial mixture Phosflex 31P (major components triphenyl phosphate and 2-isopropylphenyl diphenyl phosphate).

Isopropylated triphenyl phosphate CASRN 68937-41-7			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	Green algae (*Selenastrum capricornutum*) 14-day NOEC = 0.1 mg/L The test substance concentrations were nominal using an acetone solvent. Nominal exposure level of 100 mg/L resulted in 53% growth inhibition (Experimental)	Sanders et al., 1985	Adequate primary source. Study was conducted using commercial mixture Kronitex 200 (major components: triphenyl phosphate and 2-isopropylphenyl diphenyl phosphate).
	Green algae ChV = 0.002 mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	Estimations for triisopropyl phenyl phosphate; Estimate for the Esters class was provided for comparative purposes. See Section 5.5.1. The log K_{ow} of 9.1 for this chemical exceeds the SAR limitation for log K_{ow} of 8.0; NES are predicted for these endpoints.
	Green algae ChV = 0.009 mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	Estimations for diisopropyl phenyl phosphate. Estimate for the Esters class was provided for comparative purposes. See Section 5.5.1. The estimated effect exceeds the water solubility by 10x. NES are predicted for these endpoints.
	Green algae ChV = 0.05 mg/L	ECOSAR v1.11	Estimations for monoisopropyl

Isopropylated triphenyl phosphate CASRN 68937-41-7				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		(Estimated) ECOSAR: Esters		phenyl phosphate. Estimate for the Esters class was provided for comparative purposes. See Section 5.5.1. The effect level exceeds the water solubility of 0.027 mg/L, but not by 10x as required to be considered NES by ECOSAR.
ENVIRONMENTAL FATE				
Transport		**Level III fugacity models incorporating available physical and chemical property data indicate that at steady state, isopropylated triphenyl phosphate is expected to be found primarily in soil and to a lesser extent, sediment and water. Isopropylated triphenyl phosphate is expected to have low mobility in soil, based on estimated K_{oc} values of the components. Leaching through soil to groundwater may occur, though it is not expected to be an important transport mechanism. Estimated volatilization half-lives indicate that the components of this mixture will be non-volatile from surface water. Volatilization from dry surface is also not expected based on its vapor pressure. In the atmosphere, isopropylated triphenyl phosphate is expected to exist in both the vapor phase and particulate phase, based on its vapor pressure. Vapor phase isopropylated triphenyl phosphate will be degraded in the atmosphere by reaction with photochemically-produced hydroxyl radicals; the half-life for this reaction in air is estimated to be 0.7 days. Particulates may be removed from air by wet or dry deposition.**		
	Henry's Law Constant (atm-m^3/mole)	$7.7x10^{-8}$ for the monoisopropylated triphenyl phosphate; $1.5x10^{-7}$ for the diisopropylated triphenyl phosphate; $2.9x10^{-7}$ for the diisopropylated triphenyl phosphate isomer Bond estimate (Estimated)	EPI v4.11	Based on representative structures for components of the mixture using the HENRYWIN (v3.20) Program.
		0.000012 for TPP (CASRN 115-86-6) a possible mixture component (Estimated	Mayer et al., 1981; Huckins et al., 1991	Reported for triphenyl phosphate (CASRN 115-86-6).

Isopropylated triphenyl phosphate CASRN 68937-41-7				
PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
		by analogy)		
	Sediment/Soil Adsorption/Desorption - K_{oc}	>30,000 for the mono, di and tri-isopropylated phenyl phosphates (Estimated)	EPI v4.11; EPA, 2005	Estimated using the representative structures indicated in the SMILES section. Cutoff value for nonmobile compounds.
		2,514-3,561 in silty clay, loamy sand and silt loam; for TPP (CASRN 115-86-6) a possible component of the mixture (Estimated by analogy)	Anderson et al., 1993	Reported for triphenyl phosphate (CASRN 115-86-6) a component of the mixture.
	Level III Fugacity Model	Air = 0.2% Water = 9.3% Soil = 76% Sediment = 14% (Estimated)	EPI v4.11	Based on a representative structure for a component of the mixture, tri-IPTPP.

Isopropylated triphenyl phosphate CASRN 68937-41-7				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Persistence		**MODERATE: The environmental half-life of the isopropylated triphenyl phosphate is expected to be >16 days based on experiments using commercial mixtures of this alternative. Commercial isopropylated triphenyl phosphate mixtures passed some ready biodegradable tests, but not all (17.9% degradation in 28 days using a closed bottle test, OECD 301D). Substantial degradation seen over extended time periods indicates that the substance can be considered to be inherently biodegradable. Ultimate degradation is expected based on studies with mixed microbial populations from sludge acclimated to the test substance in a semi-continuous activated sludge system (SCAS), a modified Sturm method experiment and a die-away test. Some degradation under anaerobic conditions of the triaryl phosphate isomers mixture is also expected based on an anaerobic sediment study. The isopropylated triphenyl phosphate mixture components will undergo hydrolysis under alkaline conditions, with estimated hydrolysis half-lives of <13 days at pH 9. The mixture is expected to be relatively stable to hydrolysis under neutral and acidic conditions, with estimated half-lives of >2 years at pH 7. Isopropylated triphenyl phosphate mixture components are not expected to be susceptible to direct photolysis by sunlight, since they do not absorb light at wavelengths >290 nm. The atmospheric half-live of vapor-phase isopropylated triphenyl phosphate mixture components is estimated to be <12 hours.**		
Water	**Aerobic Biodegradation**	Passes Ready Test: No Test method: OECD TG 301D: Closed Bottle Test 17.9 % after 28 days in activated sludge from a domestic waste water treatment plant (Measured)	ECHA, 2013b	Reported in a secondary source for a commercial product Reofos 65.
		Passes Ready Test: No Test method: OECD TG 301B: CO_2 Evolution Test 21% and 13% biodegradation after 28 days using activated sludge from a sewage treatment plant (with 10.6 mg/L and 21.5 mg/L, respectively) (Measured)	IUCLID, 2001 (as cited in Environment Agency, 2009)	Reported in a secondary source for a commercial product, Reofos 120.
		Passes Ready Test: No Test method: OECD TG 301B: CO_2 Evolution Test	IUCLID, 2001 (as cited in Environment Agency, 2009)	Reported in a secondary source for a commercial product Reolube HYD 46.

Isopropylated triphenyl phosphate CASRN 68937-41-7				
PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
		29% and 40% degradation based on CO_2 evolution (with 10 mg/L and 20 mg/L, respectively) (Measured)		
		Passes Ready Test: Yes Test method: OECD TG 301B: CO_2 Evolution Test 74% at 10 mg/L and 80% at 20 mg/L using an activated sludge inoculum after 28 days (Measured)	IUCLID, 2001 (as cited in Environment Agency, 2009)	Reported in a secondary source for a commercial product, Reofos 50.
		Passes Ready Test: No Test method: OECD TG 301F: Manometric Respirometry Test 47% degradation after 28 days and 60% degradation after 68 days (Measured)	Sherren, 2003 (as cited in Environment Agency, 2009)	Reported in a secondary source for a commercial product, Reofos 120.
		Passes Ready Test: Yes Test method: OECD TG 301A: DOC Die-Away Test 94% degradation after 26 days; the test protocol was not followed (Measured)	IUCLID, 2001 (as cited in Environment Agency, 2009)	Reported in a secondary source for a commercial product, Reofos 50.
		Passes Ready Test: No Test method: OECD TG 301F: Manometric Respirometry Test 46% ThOD after 28 days (Measured)	Environment Agency, 2009	This study is not sufficient to fully characterize the aerobic biodegradation under environmental conditions.
		Passes Ready Test: Yes Test method: OECD TG 301A: DOC Die-Away Test 86% degradation was seen after 31 days	IUCLID, 2001 (as cited in Environment Agency, 2009)	Reported in a secondary source for a commercial product Reolube HYD 46. Results should be considered with caution as the Die-Away test is not currently

Isopropylated triphenyl phosphate CASRN 68937-41-7				
PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
		using an activated sludge inoculum and a test concentration of 32.6 mg/L. (Measured)		recommended for substances of low water solubility (below 100 mg/L).
		Study results: 80%/28 days Test method: Die-Away Using settled Mississippi River water; 1 mg/L commercial product Kronitex 1000 (Measured)	Saeger et al., 1979 (as cited in Environment Agency, 2009)	Reported in a secondary source using a commercial product, Kronitex 1000.
		Study results: Inherently Test method: Other Inherently biodegradable based on study based on the modified Sturm method using acclimated bacteria; CO_2 evolved from the test substance (expressed as a percentage of the maximum theoretical amount): 9% after seven days, 49% after 28 days and 62% after 48 days (Measured)	Saeger et al., 1979 (as cited in Environment Agency, 2009)	Reported in a secondary source using a commercial product, Kronitex 1000.
		Study results: 49% Test method: Other An equilibrium removal rate of 49 ± 8% at 3 mg/L and 35 ± 11% at 13 mg/L using a semi-continuous activated sludge (SCAS) unit (Measured)	Saeger et al., 1979 (as cited in Environment Agency, 2009)	Reported in a secondary source using a commercial product, Kronitex 1000.
	Volatilization Half-life for Model River	177 days (Estimated)	EPI v4.11	Based on a representative structure for a component of the mixture, with three isopropyl substituent groups.
		>1 year (Estimated)	EPI v4.11	Based on a representative structure for a component of the mixture,

Isopropylated triphenyl phosphate CASRN 68937-41-7				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
				with one isopropyl substituent group.
	Volatilization Half-life for Model Lake	>1 year (Estimated)	EPI v4.11	Based on a representative structure for a component of the mixture, with three isopropyl substituent groups.
		>1 year (Estimated)	EPI v4.11	Based on a representative structure for a component of the mixture, with one isopropyl substituent group.
Soil	**Aerobic Biodegradation**	Study results: 50%/50-60 days Test method: Other under aerobic conditions in hydrosoil from a small pond; TPP (CASRN 115-86-6) initial concentration of 0.05 ppm; major product is diphenyl phosphate (Estimated by analogy)	Muir et al., 1989	Nonguideline study for a component, TPP (CASRN 115-86-6) of the mixture.
	Anaerobic Biodegradation	Not probable (Anaerobic-methanogenic biodegradation probability model)	EPI v4.11	
	Soil Biodegradation with Product Identification			No data located.
	Sediment/Water Biodegradation	7.3% mineralization after 28 days; ^{14}C-labeled isopropylphenyl diphenyl phosphate at 22°C, pH 7.1-7.7 in 10 g (wet weight) of sediment and 90 ml of water taken from the littoral zone of a slightly eutrophic reservoir. (Measured)	Heitkamp et al., 1984 (as cited in Environment Agency, 2009)	Reported in a secondary source for a component of the mixture, isopropylphenyl diphenyl phosphate.
		8.4%/28 days 7.1%-8.4% mineralization after 28 days by ^{14}C-labeled isopropyl phenyl diphenyl phosphate at 22°C, pH 7.1-7.7 in 10 g (wet weight) of sediment	Heitkamp et al., 1984 (as cited in Environment Agency, 2009)	Reported in a secondary source.

Isopropylated triphenyl phosphate CASRN 68937-41-7				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		and 90 ml of water taken from the littoral zone of a slightly eutrophic reservoir (Measured)		
Air	**Atmospheric Half-life**	0.8 days (Estimated)	EPI v4.11	Based on a representative structure, monoisopropylated triphenyl phosphate isomer.
		0.5 days (Estimated)	EPI v4.11	Based on a representative structure, triisopropylated triphenyl phosphate isomer.
Reactivity	**Photolysis**	Not a significant fate process (Estimated)	Professional judgment; Mill, 2000	The components of this mixture do not contain functional groups that would be expected to absorb light of wavelengths >290 nm.
	Hydrolysis	50%/3.5 years at pH 7; 50%/13 days at pH 9 (Estimated)	EPI v4.11	Based on a representative structure, with three isopropyl substituent groups.
		50%/1.7 years at pH 7; 50%/6.2 days at pH 9 (Estimated)	EPI v4.11	Based on a representative structure, with one isopropyl substituent groups.
		50%/18.5 days at pH 7, 25°C 50%/43 days at pH 7, 15°C; 50%/16.5 days at pH 9, 15°C; 50%/6.1 days at pH 9, 25°C; stable at pH 4 In accordance with the OECD 111 using GC/MS analysis (Measured)	ECHA, 2013b	Guideline study reported in a secondary source based on a commercial product, Reofos 65.
		Samples of Kronitex 100 and Kronitex 50 were refluxed under basic conditions for several hours The solutions were acidified and	Nobile et al., 1980	Nonguideline study reported for commercial products.

Isopropylated triphenyl phosphate CASRN 68937-41-7				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		extracted; hydrolysis products (phenol, 2-isopropyl phenol, 4-isopropyl phenol, 3-isopropylphenol and diisopropyl phenols) were identified by infrared spectrometry (IR), gas liquid chromatograph-mass spectrometry (GLC-MS) and nuclear magnetic resonance (NMR) (Measured)		
Environmental Half-life		120 days in Soil (Estimated)	EPI v4.11; PBT Profiler	Half-life estimated for the predominant compartment, as determined by EPI and the PBT Profiler methodology; using a representative structure for a component of the mixture, with three isopropyl substituent groups.
Bioaccumulation		**HIGH: The bioaccumulation designation is based on the estimated BAF values for the isopropylated triphenyl phosphate compounds; these values are >1,000. Measured BCF of <9,250, are available for a commercial mixture containing isopropylated triphenyl phosphate. However, there is lower confidence in the experimental BCF values because they are not consistent with the limited water solubility of this chemical, and because the studies were performed on a mixture of unquantified components. Toxicokinetic and fish metabolism studies determined that in some species, isopropylated phenyl phosphate is likely to be bioavailable and undergo metabolism and elimination. Additional, lower BCF values were reported from studies with the isomer isopropylphenyl diphenyl phosphate that would result in a Moderate designation. The BAF was used preferentially as the removal rate of isopropylated triphenyl phosphates in some species of fish may not compete with the rate of uptake.**		
	Fish BCF	<9,250 *Pimephales promelas* flow-through system; fish were exposed to five concentrations of the test substance, samples taken at 30, 60 and 90 days of exposure and analyzed for both isopropylphenyl diphenyl phosphates and triphenyl phosphate (Measured)	Cleveland et al., 1986 (as cited in Environment Agency, 2009)	Reported in a secondary source for commercial products, Kronitex 200 and Phosflex 31P.
		495 *Pimephales promelas* flow-through	Environment Agency, 2009	Adequate, nonguideline study

Isopropylated triphenyl phosphate CASRN 68937-41-7				
PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
		system; using ^{14}C-labelled isopropylphenyl diphenyl phosphate, at a concentration of 2.5 µg/l for 28 days (Measured)		using labeled components of the mixture.
		440-550; in fathead minnows using deuterium and ^{14}C labeled 2-isopropyldiphenyl phosphate (Measured)	Huckins and Petty, 1983	Adequate, nonguideline study using labeled components of the mixture.
		998 (Estimated)	EPI v4.11	Based on a representative structure for a component of the mixture, with two isopropyl substituent groups.
		570 (Estimated)	EPI v4.11	Based on a representative structure for a component of the mixture, with one isopropyl substituent group.
		193 (Estimated)	EPI v4.11	Based on a representative structure for a component of the mixture, with three isopropyl substituent groups.
	Other BCF			No data located.
	BAF	TBB was detected in adipose, liver, and muscle tissues in rat dams and rat pup adipose tissue. The primary metabolite of TBB (TBBA) was also detected in liver tissue of rat dams. The pregnant rats were administered 0, 0.1 or 1 mg/kg-day of FM550 by oral gavage across gestation and through lactation (GD8 - PND 21). This study did not analyze the samples for the presence of IPTPP. (Estimated by analogy)	Patisaul et al., 2013	BAFs were not calculated. Non guideline study indicates that absorption of TBB can occur in rats through oral exposure; the test substance identified as FM550 is a mixture made up of TBB, TBPH (CASRN 26040-51-7), IPTPP (CASRN 68937-41-7) and TPP (CASRN 115-86-6).

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PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
		320,000 (Estimated)	EPI v4.11	Based on a representative structure for a component of the mixture, with three isopropyl substituent groups.
		69,000 (Estimated)	EPI v4.11	Based on a representative structure for a component of the mixture, with two isopropyl substituent groups.
		700 (Estimated)	EPI v4.11	Based on a representative structure for a component of the mixture, with one isopropyl substituent group.
		1,300-1,900 for Trixylenyl phosphate; 400 for Tricresyl phosphate Based on whole fish wet-weight, equilibrium in the fish was not reached for these compounds (Estimated by analogy)	Bengtsson et al., 1986	Non-guideline study using commercial mixtures.
	Metabolism in Fish	Fathead minnows were exposed to ^{14}C-2-isopropylphenyl diphenyl phosphate for 28 days followed by a 14 day elimination phase Labeled diphenyl phosphate was identified as a major metabolite in whole body fish samples; additional ^{14}C-residues were associated with lipid and protein materials (Measured)	Huckins and Petty, 1983 (as cited in Environment Agency, 2009)	Adequate, nonguideline study.
		The major route of metabolism of isopropylphenyl diphenyl phosphate in rainbow trout (*Oncorhynchus mykiss*) is O-dearylation to yield diphenyl phosphate; the diphenyl phosphate is then eliminated either as the compound	Muir, 1984 (as cited in Environment Agency, 2009); Boethling and Cooper, 1985	Adequate, nonguideline study.

Isopropylated triphenyl phosphate CASRN 68937-41-7			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	itself or as a conjugate (Measured)		
ENVIRONMENTAL MONITORING AND BIOMONITORING			
Environmental Monitoring	Isopropylated triphenyl phosphate was detected in Beale AFB soils; air, water, sediment and soil in the US (Boethling and Cooper, 1985; David and Seiber, 1999; Environment Agency, 2009; Salamova et al., 2014).		
Ecological Biomonitoring	Isopropylphenyl diphenyl phosphate was found in vegetation in the US (Boethling and Cooper, 1985 (as cited in Environment Agency, 2009)).		
Human Biomonitoring	Isopropylated triphenyl phosphate was not included in the NHANES biomonitoring report (CDC, 2013).		

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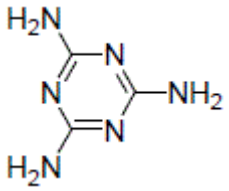
Melamine

Screening Level Toxicology Hazard Summary

This table contains hazard information for each chemical; evaluation of risk considers both hazard and exposure. Variations in end-of-life processes or degradation and combustion by-products are discussed in the report but not addressed directly in the hazard profiles. The caveats listed below must be taken into account when interpreting the information in the table.

VL = Very Low hazard L = Low hazard M = Moderate hazard H = High hazard VH = Very High hazard – Endpoints in colored text (VL, L, M, H, and VH) were assigned based on empirical data. Endpoints in black italics *(VL, L, M, H,* and *VH*) were assigned using values from estimation software and professional judgment [(Quantitative) Structure Activity Relationships "(Q)SAR"].

		Human Health Effects										Aquatic Toxicity		Environmental Fate	
Chemical	CASRN	Acute Toxicity	Carcinogenicity	Genotoxicity	Reproductive	Developmental	Neurological	Repeated Dose	Skin Sensitization	Respiratory Sensitization	Eye Irritation	Dermal Irritation	Acute	Chronic	Persistence	Bioaccumulation
Melamine	108-78-1	M	M	M	H	*M*	*L*	M	L		L	VL	L	L	H	L

	**CASRN:** 108-78-1
	MW: 126.13
	MF: $C_3H_6N_6$
	Physical Forms: Solid **Neat:** Solid
	Use: Flame retardant
SMILES: n1c(N)nc(N)nc1(N)	
Synonyms: 1,3,5-triazine-2,4,6-triamine; Cyanuramide; Cyanurotriamide; Cymel, Isomelamine; Melamine; 2,4,6-triamino-S-triazine; S-Triazinetriamine; 1,3,5-triazine-2,4,6(1H,3H,5H)-triimine	
Chemical Considerations: This is a discrete organic chemical with a MW below 1,000. EPI v4.11 was used to estimate physical/chemical and environmental fate values in the absence of experimental data. Measured values from experimental studies were incorporated into the estimations.	
Polymeric: No **Oligomeric:** Not applicable	
Metabolites, Degradates and Transformation Products: Hydrolysis products: ammeline, ammelide and cyanuric acid; Metabolites: cyanuric acid; Pyrolysis: ammonia, melem, melone (OECD-SIDS, 1998; Crews et al., 2006; Liu et al., 2010; Zheng et al., 2013).	
Analog: None **Endpoint(s) using analog values:** Not applicable	**Analog Structure:** Not applicable
Structural Alerts: Substituted triazines, aquatic toxicity; toxicity to the respiratory system, basic amines; systemic effects, amine groups; potential nephrotoxins, amines; genetic toxicity, aromatic amines; developmental toxicity, aromatic amines (EPA, 2010, 2012).	
Risk Phrases: None identified (ESIS, 2012).	
Hazard and Risk Assessments: Melamine was assessed under the Screening information data set (SIDS) for HPV chemicals (OECD-SIDS, 1998).	

Melamine CASRN 108-78-1			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
PHYSICAL/CHEMICAL PROPERTIES			
Melting Point (°C)	350 Decomposes and sublimes; ammonia will be split off at >300°C and possibly cyanuric acid at >600°C which burns in the open flame (Measured)	OECD-SIDS, 1998; ECHA, 2013	This substance sublimes according to results reported in secondary source.
	361 using the DSC method; using 99.9% pure melamine (Measured)	ECHA, 2013	Guideline study reported in secondary source.
	345 (Measured)	PhysProp, 2012	Reported in a secondary source.
	354 Decomposes at >280°C forming ammonia (Measured)	OECD-SIDS, 1998	Reported in a secondary source.
Boiling Point (°C)	>280 Decomposes Sublimes; Heat of sublimation: -121 kJ/mol at 25°C (Measured)	OECD-SIDS, 1998; ECHA, 2013	This substance sublimes according to results reported in secondary source. Also indicated in the melting point entry above.
Vapor Pressure (mm Hg)	$3.59x10^{-10}$ at 20°C (Extrapolated)	PhysProp, 2012	Consistent with other reported extrapolated values.
	$3.52x10^{-10}$ at 20°C Reported as $4.7x10^{-8}$ Pa at 20°C; Dynamic method with N_2 or NH_3 (Extrapolated)	OECD-SIDS, 1998; ECHA, 2013	Nonguideline study reported in secondary source.
Water Solubility (mg/L)	3,480 (Measured) using OECD 105	ECHA, 2013	Guideline study reported in a secondary source.

Melamine CASRN 108-78-1			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	3,200 (Measured) at 20°C; pH 7-8	OECD-SIDS, 1998	Reported in a secondary source.
	3,000 (Measured) at 20°C; pH 8.4-8.9	OECD-SIDS, 1998	Reported in a secondary source.
Log K_{ow}	-1.14 at 25°C; OECD 107 Shake flask method (Measured)	OECD-SIDS, 1998	Guideline study reported in a secondary source.
	-1.22 OECD 107 Shake flask method (Measured)	ECHA, 2013	Guideline study reported in a secondary source.
	-1.37 (Measured)	PhysProp, 2012	Reported in secondary source.
Flammability (Flash Point)	Not flammable (Measured)	OECD-SIDS, 1998	Reported in a secondary source.
	Flash point: >280°C (Measured)	ECHA, 2013	Reported in a secondary source; study details not provided.
Explosivity	Not explosive according to Directive 84/449/EEC, A.10 (Measured)	OECD-SIDS, 1998	Guideline study reported in a secondary source.
	Weakly explosive according to Method VDI 3673 (Measured)	OECD-SIDS, 1998	Reported in a secondary source.

Melamine CASRN 108-78-1			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
Pyrolysis	Deammoniation and condensation lead to compounds with higher molecular mass when melamine is heated above 300°C (in the absence of ammonia or at low ammonia partial pressure). Thermal degradation starts with the release of ammonia and the formation of melem (CASRN 1502-47-2). Heating to 600°C yields more ammonia and melone (CASRN 32518-77-7) (Measured)	Crews et al., 2006	Supporting information provided.
pH	7.5 and 9.5; Test substance: 100 g/L of melamine (99.8%) in 10% aqueous suspension; Borealis internal test method No. 210 (Measured)	ECHA, 2013	Reported in a secondary source.
	8 (Measured)	OECD-SIDS, 1998	Approximate value reported in a secondary source. No study details provided.
pK_a	pK_{b1} = 7.3; pK_{b2} = 11.4 according to OECD 112 (Measured)	ECHA, 2013	Guideline study reported in a secondary source.
	pK_{b1} = 9 There are several amino groups that result in basic properties. (Measured)	Baynes et al., 2008	Reported from a nonguideline study.
	pK_{b1} = 9 pK_{b2} = 14 $Kb_1 = 1.1x10^{-9}$ $Kb_2 = 1.0x10^{-14}$ at 25°C (Measured)	Crews et al., 2006	Study details were not available.
	Considered a weak base	OECD-SIDS, 1998	Supporting information provided in a secondary source.

Melamine CASRN 108-78-1			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	Neutral at pH values of 6 to 13; Cation formation at the triazine ring nitrogen at pH values of 1 to 4 (Measured)		
	5 (Measured)	Weber, 1970; HSDB, 2008	Reported in a secondary source.

Melamine CASRN 108-78-1				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
HUMAN HEALTH EFFECTS				
Toxicokinetics		**Melamine was rapidly absorbed, distributed to body fluids, cleared from plasma and excreted mainly via urine in monkeys. In rats, melamine was distributed to the stomach, small intestine, cecum, and large intestine, and found in blood and urine. Following a single oral exposure to pregnant rats, melamine was detected in the maternal serum, breast milk, whole foetus, amniotic fluid, neonatal serum and neonatal kidney. There is evidence that Melamine passed through the placenta, reached the fetus and accumulated in the lactating mammary gland. Excretion occurred through the placenta of the fetus and the kidneys of neonates and was later excreted into amniotic fluid. Melamine was transferred quickly to fetal circulation in studies where placentas from mothers following caesarean section or normal delivery were perfused with melamine. Melamine was readily cleared by the kidney in pigs administered melamine intravenously; distribution may be limited to the extracellular fluid compartment. There was no concern for binding in tissues. The half-life was reported as 4.04 hours. In monkeys, the half-life in plasma was ~4.41 hours. Other data for the melamine indicate an elimination phase half-life of 2.7 hours from plasma and 3 hours for urine.**		
Dermal Absorption *in vitro*				No data located.
Absorption, Distribution, Metabolism & Excretion	**Oral, Dermal or Inhaled**	Rhesus monkeys were orally administered melamine at a single dose of 1.4 mg/kg bw. Melamine was rapidly absorbed, distributed to body fluids, rapidly cleared from plasma and excreted mainly via urine. The half-life in plasma was ~4.41 hours. There was no correlation (concentration-time curve in plasma and urine) between melamine and cyanuric acid, suggesting that melamine may not be metabolized to cyanuric acid *in vivo*.	Liu et al., 2010	Adequate, primary source
		Pregnant Sprague-Dawley rats were administered a single oral dose of melamine (~6-7 mg in <2 ml water) on GD 17. Melamine was also administered to neonates at postnatal day 14 ((~0.3-0.6mg in <0.2 mL in	Chu et al., 2010	Adequate primary source

Melamine CASRN 108-78-1				
PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
		water). Melamine was detected in the maternal serum, breast milk, whole foetus, amniotic fluid, neonatal serum and neonatal kidney. This is evidence that Melamine passed through the placenta, reached the fetus and accumulated in the lactating mammary gland. Excretion occurred through the placenta of the fetus and the kidneys of neonates and was later excreted into amniotic fluid.		
		Distributed to stomach, small intestine, cecum, and large intestine, and found in blood and urine of rats.	ECHA, 2013	Study details reported in a secondary source.
		The elimination phase half-life calculated from plasma data was 2.7 hours, and the urinary half-life was 3.0 hours. The renal clearance was determined to be 2.5 mL/min.	Mast et al., 1983	Adequate, non-guideline study.
	Other	Pigs (5 weanling) were administered Melamine intravenously at a dose of 6.13 mg/kg. Melamine is readily cleared by the kidney; distribution may be limited to the extracellular fluid compartment. No concern for binding in tissues. Half-life: 4.04 hours; clearance: 0.11 L/h/kg; volume distribution: 0.61 L/kg.	Baynes et al., 2008	Adequate primary source
		Placentas from mothers following caesarean section or normal delivery were perfused with 0 mM or 1 mM melamine, or 10 mM melamine with	Partanen et al., 2012	Adequate, primary study

Melamine CASRN 108-78-1				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		10 nM cyanuric acid (CYA). Melamine (34-45%) was transferred quickly to fetal circulation (0.12-1.34% within 5 minutes, 34% within 4 hours); addition of CYA had no effect. Functionality of the placental tissue was not affected. Viability of BeWo cells was decreased. It is concluded that melamine may be fetotoxic.		
Acute Mammalian Toxicity		**MODERATE: Based on an inhalation LC_{50} of 3.25 mg/L, a dermal LD_{50} of > 1,000 mg/kg, and a structural alert for basic amines. Oral LD_{50} values were > 2,000 mg/kg.**		
Acute Lethality	**Oral**	Rat LD_{50} = 3,160 mg/kg (male), 3,850 mg/kg (female)	Trochimowicz et al., 2001	Sufficient study details were not reported.
		Rat LD_{50} = 3,161 mg/kg (male), 3,828 mg/kg (female)	NTP, 1983; Melnick et al., 1984	Sufficient study details reported.
		Rat LD_{50} >6,400 mg/kg	BASF, 1969	Sufficient study details were not available.
		Mouse LD_{50} = 3,296 mg/kg (male), 7,014 mg/kg (female)	NTP, 1983; Melnick et al., 1984	Sufficient study details reported.
		Mouse LD_{50} = 4,550 mg/kg	American Cyanamid Company, 1955; May, 1979; Trochimowicz et al., 2001	Sufficient study details were not available. Reported in secondary sources.
		LD_{50} ~ 4,800 mg/kg	Hoechst, 1963	Sufficient study details were not available.
	Dermal	Rabbit LD_{50} >1,000 mg/kg	Unknown, 1990; ECHA, 2013	Sufficient study details were not available. Study was not conducted according to any specific guideline; insufficient description of the method.
	Inhalation	Rat LC_{50} = 3.248 mg/L	Ubaidullajev, 1993	The study details, if present, were not translated into English.

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		Rat inhalation 4-hour LC_{50} >5.19 mg/L (nose only)	ECHA, 2013	Adequate study reported in a secondary source. Study was conducted according to OECD Guideline 403 and GLP.
		Potential for toxicity to the respiratory system based on a structural alert for basic amines.	Professional judgment	Estimated based on a structural alert for basic amines and professional judgment.
Carcinogenicity		**MODERATE: The carcinogenicity hazard potential for melamine is based on evidence that oral exposure to melamine causes cancer in experimental animals. However, there is no evidence for carcinogenicity to humans. In addition, OncoLogic estimated a marginal concern that is consistent with DfE Moderate hazard criteria. Tumor formation in animals appeared to be due to mechanical irritation by bladder calculi/stones. IARC classifies melamine as Group 3: *not classifiable as to its carcinogenicity to humans*.**		
	OncoLogic Results	Marginal	OncoLogic, 2005	
	Carcinogenicity (Rat and Mouse)	Group 3: melamine is not classifiable as to its carcinogenicity to humans; there is inadequate evidence in humans for the carcinogenicity of melamine, and there is sufficient evidence in experimental animals for the carcinogenicity of melamine under conditions in which it produces bladder calculi.	IARC, 1999	IARC classification statement.
		Significant formation of transitional cell carcinomas in the urinary bladder of dosed male rats and significant chronic inflammation in the kidney of dosed female rats were observed following exposure in the feed for up to 103 weeks. Carcinoma formation was significantly correlated with the incidence of bladder stones. A transitional-cell papilloma was	NTP, 1983; Huff, 1984; Melnick et al., 1984	Sufficient study details reported.

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PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
		observed in the urinary bladder of a single high dose male rat, and compound related lesions were observed in the urinary tract of dosed animals. Based on the mechanical nature of tumor formation, FDA and EPA considered melamine noncarcinogenic.		
		Increased incidence of acute and chronic inflammation and epithelial hyperplasia of the urinary bladder was observed in male mice following oral (feed) exposure for up to 103 weeks. Bladder stones and compound related lesions were observed in the urinary tract of test animals. There was no evidence of bladder tumor development. Melamine was not considered carcinogenic.	NTP, 1983; Melnick et al., 1984	Sufficient study details reported.
		Melamine-induced proliferative lesions of the rat urinary tract were directly due to the irritant stimulation of calculi, and not to molecular interactions between melamine or its metabolites with the bladder epithelium.	Okumura et al., 1999	Sufficient study details reported.
		Water intake, used as an index of urinary output, was increased by NaCl treatment. Calculus formation resulting from melamine administration was suppressed dose-dependently by the simultaneous NaCl treatment. The main constituents of calculi were	Ogasawara et al., 1995	Sufficient study details reported.

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PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
		melamine and uric acid (total contents 61.1-81.2%). The results indicate that melamine-induced proliferative lesions of the urinary tract of rats were directly due to the irritation induced-stimulation of calculi, and not molecular interactions between melamine itself or its metabolites with the bladder epithelium.		
		Melamine: As an initiator, melamine caused no significant increase in papillomas per mouse when compared to controls.	Perrella and Boutwell, 1983	Sufficient study details reported; non-guideline study.
		Diffuse papillary hyperplasia of the bladder epithelium and bladder calculi were observed in all melamine treated rats. Elevated spermidine/spermine N1-acetyltransferase (SAT) activity following melamine treatment was considered to be an indicator of cell proliferation.	Matsui-Yuasi et al., 1992	Sufficient study details reported; non-guideline study.
		Decreased antitumor activity was correlated with increasing demethylation; melamine was considered inactive as an antitumor drug.	Rutty and Connors, 1977	Sufficient study details were not available.
		In an *in vitro* cytotoxicity study in cultured ADJ/PC6 plasmacytoma ascites tumor cells the ID_{50} (median ineffective dose) was 470 µg/mL after 72 hours of treatment.	Rutty and Abel, 1980	Sufficient study details were not available.

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Combined Chronic Toxicity/Carcinogenicity	No effects were observed in rats fed 1,000 ppm of melamine. Four of the 10 rats fed 10,000 ppm of melamine had bladder stones associated with the development of benign papillomas.	American Cyanamid Company, 1958	Sufficient study details were not available.
		Increased incidence of urinary bladder stones (6/20 rats) was noted in the 10,000 ppm dose group, and was associated with an increase in benign papillomata. The NOAEL was determined to be 1,000 ppm (67 mg/kg).	American Cyanamid Company, 1955	Sufficient study details were not available.
	Other			No data located.
Genotoxicity		**MODERATE: Based a weight of evidence from multiple studies. Results were positive for chromosomal aberrations and sister chromatid exchange *in vivo* in mice exposed to melamine. There were also positive results *in vitro* for DNA synthesis-inhibition in Hela S3 cell and genetic toxicity in *Escherichia coli* WP2s in a microscreen assay following exposure to melamine. In addition, there is estimated potential for genotoxicity based on a structural alert for aromatic amines.**		
	Gene Mutation *in vitro*	Bacterial forward mutation assay: Negative with and without liver activation	Haworth et al., 1983; NCI/NTP, 2007	Sufficient study details reported
		Bacterial forward mutation assay: Negative	Seiler, 1973	Sufficient study details were not available.
		Bacterial reverse mutation assay: Negative with and without liver activation	Lusby et al., 1979	Sufficient study details were not available.
		Bacterial reverse mutation assay: Negative with and without unspecified metabolic activation	Mast et al., 1982b	Sufficient study details were not available.
		In vitro mouse lymphoma test: Negative with and without liver activation	McGregor et al., 1988	Sufficient study details reported.

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		CHO/HGPRT forward mutation assay: Negative with and without liver activation	Mast et al., 1982b	Sufficient study details were not available.
	Gene Mutation *in vivo*			No data located.
	Chromosomal Aberrations *in vitro*	*In vitro* chromosomal aberrations test: Negative in CHO with and without liver activation	Galloway et al., 1987; NCI/NTP, 2007	Sufficient study details reported.
		In vitro sister chromatid exchange assay: Negative in CHO with and without liver activation	Mast et al., 1982b	Sufficient study details were not available.
		In vitro sister chromatid exchange assay: Negative in CHO with and without liver activation	Galloway et al., 1987; NCI/NTP, 2007	Sufficient study details reported.
	Chromosomal Aberrations *in vivo*	*In vivo* mouse micronucleus test: The initial test gave a positive trend (P = 0.003) for chromosomal damage; however, both peripheral blood smears and the repeat bone marrow test were negative. The overall conclusion was that melamine does not induce chromosomal damage.	NTP, 1983; Shelby et al., 1993	Sufficient study details reported.
		In vivo mouse micronucleus test: Negative without activation	Mast et al., 1982b	Sufficient study details were not available.
		In vivo chromosome aberrations test in mice: Positive	NCI/NTP, 2007	Sufficient study details reported.
		In vivo sister chromatid exchange assay in mice: Positive	NCI/NTP, 2007	Sufficient study details reported.

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	DNA Damage and Repair	*In vivo* and *in vitro* unscheduled DNA synthesis (UDS) test: None of the tested chemicals, including melamine, were genotoxic hepatocarcinogens in the *in vivo* assay, and melamine was negative for UDS in the *in vitro* assay	Mirsalis et al., 1983	In vivo and in vitro unscheduled DNA synthesis (UDS) test: None of the tested chemicals, including melamine, were genotoxic hepatocarcinogens in the in vivo assay, and melamine was negative for UDS in the in vitro assay
		SOS/*umu* test: Negative for its ability to result in DNA damage and induce the expression of the *umu* operon	Heil and Reifferscheid, 1992	Non-guideline study.
		DNA synthesis-inhibition test in Hela S3 cells: Inhibits DNA synthesis by 50% (DI_{50}) at >300 µM	Heil and Reifferscheid, 1992	Sufficient study details were not available.
	Other	Potential for genotoxicity based on a structural alert for aromatic amines	Professional judgment	Estimated based on a structural alert for aromatic amines and professional judgment.
		Sex-linked recessive lethal mutations were not induced in *Drosophila melanogaster*.	IARC, 1986; OECD-SIDS, 1998	Secondary source; sufficient study details were not available.
		Drosophila Muller-5 test: Negative for mutagenicity	Rohrborn, 1959	Sufficient study details were not available.
		Drosophila melanogaster Sex-linked recessive lethal: No mutagenic effects were observed.	Luers and Rohrborn, 1963	Sufficient study details were not available.
		In vitro flow cytometric DNA repair assay: Negative for genotoxic effects	Selden et al., 1994	Non-guideline study.
		Microscreen assay: Positive for genetic toxicity in *E. coli* WP2s	Rossman et al., 1991	Non-guideline study.
		Growth and genotoxic effects to bacteria (*Salmonella typhimurium*) and yeast (*Saccharomyces cerevisiae*): Non-mutagenic in *S.typhimurium* with	Sugita et al., 1991	Sufficient study details were not available.

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		or without S-9 mix. The growth of eight out of nine strains tested was delayed by 10 mM melamine during 24-hour cultivation. *S. cerevisiae* strain was tested, and did not recover its growth following 48-hour cultivation.		
Reproductive Effects		**HIGH: Based on a NOAEL = 10 mg/kg-day (LOAEL of 50 mg/kg-day) for increased apoptotic index of spermatogenic cells in male mice orally administered melamine for 5 days. In addition, altered epididymal sperm morphology and damage of testicular DNA were reported at a dietary dose of 412 mg/kg-day (lowest dose tested).**		
	Reproduction/Developmental Toxicity Screen			No data located.
	Combined Repeated Dose with Reproduction/ Developmental Toxicity Screen			No data located.
	Reproduction and Fertility Effects	In a 5-day study, male mice (8/group) were orally administered melamine only at doses of 0, 2, 10 and 50 mg/kg-day or melamine in combination with cyanuric acid at doses of 0, 1, 5 and 25 mg/kg-day. Sperm abnormalities were evaluated in a separate select group of mice (8/group), which were fed melamine only at doses of 0, 412, 824, and 1648 mg/kg-day, or melamine in combination with cyanuric acid at doses of 0, 206, 412, or 824 mg/kg-day. No deaths in mice fed 2, 10 and 50 mg/kg-day melamine or 1 and 5 mg/kg-day melamine and cyanuric acid; 3 deaths in co-administration	Yin et al., 2013	Adequate, primary study

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PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
		group fed 25 mg/kg/day. Grossly enlarged, pale yellow kidneys in all mice that survived. Increase in apoptotic index of spermatogenic cells in mice fed 50 mg/kg-day melamine-only; more severe apoptosis in co-administered mice at 5 and 25 mg/kg-day. NOAEL: 10 mg/kg-day LOAEL: 50 mg/kg-day (increased apoptotic index of spermatogenic cells) Sperm abnormality group: no deaths in mice administered melamine-only; all co-administered mice died before day 6 and exhibited anorexia, decreased activity and hunched posture. Altered epididymal sperm morphology (particularly the head abnormality) and damage of testicular DNA in all melamine-only treatment groups. NOAEL: not established LOAEL: 412 mg/kg-day (altered epididymal sperm morphology; damage of testicular DNA)		
		There were no treatment-related macroscopic or microscopic effects on mammary glands, ovaries, prostate, seminal vesicles, testes and uterus in rats and mice in a 13-week study.	OECD-SIDS, 1999	Study details, including administered dose information, were not provided.

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Other			No data located.
Developmental Effects		**MODERATE: Estimated based on a structural alert for aromatic amines. Limited experimental data indicated no developmental effects in rats exposed during gestation to doses up to 1,060 mg/kg-day. This experimental data is insufficient to determine a hazard designation for this endpoint.**		
	Reproduction/ Developmental Toxicity Screen			No data located.
	Combined Repeated Dose with Reproduction/ Developmental Toxicity Screen			No data located.
	Prenatal Development	Melamine was administered to pregnant female Wistar rats in the diet at concentrations of 1,500 ; 4,500 and 15,000 ppm on day 6 through day 16 post coitum (136, 400, and 1060 mg/kg-day) Signs of maternal toxicity at 136 mg/kg-day included decreased body weight and feed consumption, hematuria (23/25 rats), indrawn flanks (7/25 rats), and piloerection (1/25 rats). No adverse effects on gestational parameters and no signs of developmental toxicity were noted. Maternal toxicity: NOAEL: 400 LOAEL: 1,060 mg/kg-day (decreased body weight and feed consumption) Developmental toxicity: NOAEL ≥1,060 mg/kg-day; highest dose tested LOAEL: Not established	Hellwig et al., 1996; ECHA, 2013	Limited study details reported in a secondary source; test material as cited in study report: Melamine (mixture of Melamine from Agrolinz and BASF at a ratio of 1:1); analytical purity: about 100%.
	Postnatal Development			No data located.

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Prenatal and Postnatal Development			No data located.
	Developmental Neurotoxicity			No data located.
	Other	Potential for developmental toxicity based on a structural alert for aromatic amines. (Estimated)	Professional judgment	Estimated based on a structural alert for aromatic amines and professional judgment.
Neurotoxicity		**LOW: Potential for neurotoxicity is expected to be low.**		
	Neurotoxicity Screening Battery (Adult)			No data located.
	Other	Potential for neurotoxicity is expected to be low (Estimated)	Expert judgment	Estimated based on expert judgment.

Melamine CASRN 108-78-1				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Repeated Dose Effects		**MODERATE: Based on repeated oral exposure to melamine in rats. Bladder stones were reported at a dose of 72 mg/kg-day in a 90-day dietary study in rats. In addition, decreased body weight gain and feed consumption was reported. NOAELs of 167.5 and 140 mg/kg bw-day were reported in 7 day and 14 day oral studies in rats, respectively. A NOAEL of 0.0005 mg/L was reported in a 4-month inhalation study in rats based on no general toxic or gonadotoxic symptoms. Nephrotoxicity was noted in a 3-month oral study in monkeys at 200 mg/kg-day (NOAEL = 60 mg/kg-day). The formation of calculi, hyperactive regeneration of renal tubular epithelium, tubular cell debris, crystal deposition, bladder ulcers and bladder stones, epithelial cell atypia, hyperplasia of the urinary bladder, clinical signs, changes in clinical chemistry, and decreased body weight gain were reported in laboratory animals following repeated oral doses > 100 mg/kg-day. In addition, there is estimated potential for systemic effects based on a structural alert for amine groups and an estimated potential for nephrotoxicity based on a structural alert for amines.**		
		Rat 90-day dietary toxicity study: One male rat receiving 18,000 ppm and two males receiving 6,000 ppm died. Mean body weight gain and feed consumption were reduced. Stones and diffuse epithelial hyperplasia in the urinary bladders were observed in male rats of all treatment groups. Focal epithelial hyperplasia was observed in only 1 male. A second and third 13-week repeated dose toxicity study was conducted in rats at a dose range of 750 to 18,000 ppm; bladder stones were observed at all dose levels. At 18,000 ppm, stones occurred in diets with and without the addition of ammonium chloride to drinking water. NOAEL: Not established LOAEL: 750 ppm (72 mg/kg-day; bladder stones); lowest dose tested	NTP, 1983; Melnick et al., 1984	Sufficient study details reported.

Melamine CASRN 108-78-1				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		In a 7-day oral study, male and female F344 rats were fed melamine and cyanuric acid (co-exposure) in the diet at concentrations of 0, 7, 23, 69, 229, or 694 ppm (0, 0.9, 2.8, 8.6, 17.6, or 29.8 mg/kg-day). Rats were also fed Melamine or cyanuric acid alone at a concentration of 1388 ppm (167.5 mg/kg-day). Histopathological alterations consistent with nephrotoxicity at 229 and 694 ppm (co-exposure); renal injury as evidenced by alterations in the expression of KIM-1, TIMP1, clusterin, osteopontin, and NGAL genes in kidney tissue. There were no statistically significant gene expression changes in rats fed melamine or cyanuric acid only. Crystals were present in the renal tubules in 5/12 rats fed melamine only. NOAEL: 1388 ppm (167.5 mg/kg-day; only dose tested) LOAEL: Not established	Camacho et al., 2011; Jacob et al., 2011	Study details reported in a primary source. Toxicity was a result of co-exposure of melamine and cyanuric acid. No toxicity was evident in rats fed melamine in the absence of cyanuric acid; only one melamine-only dose tested.
		Rat 28-day dietary toxicity study: Incidence and size of bladder stones were directly related to the amount of substance administered. The larger stones were found to be unchanged melamine in a matrix of protein, uric acid and phosphate.	American Cyanamid Company, 1984	Sufficient study details were not available.

Melamine CASRN 108-78-1				
PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
		Lowest effect dose (LED): 1,500 ppm (~125 mg/kg-day) in males.		
		In a 3-month oral study, monkeys were administered melamine via nasal-gastric gavage at doses of 0, 60, 200 or 700 mg/kg-day. Effects at 700 mg/kg-day included turbid and whitish urine, urine crystals, red blood cell changes, increased serum alanine aminotransferase and kidney and/or liver weights, nephrotoxicity, pericarditis and increased hematopoiesis. Nephrotoxicity was also evident at 200 mg/kg-day. NOAEL: 60 mg/kg-day LOAEL: 200 mg/kg-day (nephrotoxicity)	Early et al., 2013	Study details reported in a primary source.
		Rat 28-day dietary toxicity study: Clinical signs included a dose-related increase in pilo-erection, lethargy, bloody urine spots in the cage and on the pelage of animals, and chromodacryorrhea. The incidence of urinary bladder calculi and urinary bladder hyperplasia in treated animals was dose dependent, with a significant relationship between the calculi and hyperplasia. Calculi composition indicated the presence of an organic matrix containing melamine, phosphorus, sulfur, potassium, and chloride. Crystals of dimelamine	RTI, 1983	Sufficient study details reported

Melamine CASRN 108-78-1				
PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
		monophosphate were identified in the urine. NOAEL: 2,000 ppm (240 mg/kg-day), excluding the observed increase in water consumption and the incidence of crystalluria. LOAEL: 4,000 ppm (475 mg/kg-day) based on the formation of calculi.		
		In a 14-day oral study, rats were administered melamine at doses of 0, 140, 700, and 1,400 mg/kg-day (lowered to 1,000 mg/kg-day subsequently due to mortality). A 5-day study was also conducted with genomic biomarkers on kidney tissues. Doses were 0, 350 and 1,050 mg/kg-day. Effects (14-day study) at 700 mg/kg-day included clinical signs of toxicity (red urine), decreased body weight, changes in clinical chemistry parameters (increased serum urea nitrogen and creatinine), and kidney effects (renal tubular cell debris, crystal deposition, and hyperactive regeneration of renal tubular epithelium) Systemic effects from the 5-day study were similar to the 14-day study. Significant up-regulation of Kim-1, Clu, Spp1, A2m, Lcn2, Tcfrsf12a, Gpnmb, and CD44 and significant	Early et al., 2013	Study details reported in a primary source.

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PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
		down-regulation of Tff3. NOAEL: 140 mg/kg-day LOAEL: 700 mg/kg-day (clinical signs, changes in clinical chemistry, tubular cell debris, crystal deposition, and hyperactive regeneration of renal tubular epithelium)		
		Mouse 90-day dietary toxicity study: a single female mouse died after receiving 9,000 ppm. Mean body weight gain relative to controls was depressed. The incidence of mice with bladder stones was dose-related and was greater in males than in females. Sixty percent of mice having bladder ulcers also had urinary bladder stones. Bladder ulcers were multifocal or associated with inflammation (cystitis). Epithelial hyperplasia and bladder stones were observed together in 2 mice. Also, epithelial cell atypia was seen. NOAEL: 6,000 ppm (600 mg/kg-day). LOAEL: 9,000 ppm (900 mg/kg-day; decreased body weight gain, bladder ulcers and bladder stones, epithelial cell atypia)	NTP, 1983; Melnick et al., 1984	Sufficient study details reported.
		Increased incidence of acute and chronic inflammation and epithelial hyperplasia of the urinary bladder was observed in mice following oral (feed)	NTP, 1983	Repeated dose effects reported in a carcinogenicity bioassay study.

Melamine CASRN 108-78-1				
PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
		exposure for up to 103 weeks to 2,250 or 4,500 ppm. There was also increased incidence of bladder stones in male mice. NOAEL: Not established LOAEL: 2,250 ppm in the diet (lowest concentration tested; hyperplasia of the urinary bladder, bladder stones in males)		
		Rat 24- to 30-month dietary toxicity study: A dose related trend for dilated glands in glandular gastric mucosa and inflammation in non glandular gastric mucosa was observed. Urinary bladder calculi formation was not observed.	Wolkowski, 1983	Sufficient study details were not available.
		Rat 30-month dietary toxicity study: Neither accumulation of calculi nor any treatment-related urinary bladder lesions were found.	Mast et al., 1982a	Sufficient study details were not available.
		Rabbit and dog 28-day dietary toxicity study: no significant rise in the body temperature of rabbits was noted. Gross histological examination of the heart, lung, liver, spleen, thyroid, pancreas, intestines, kidneys and bladder did not show pathological changes. A zone of fat was found in the inner part of the renal cortex in two dogs, but also in the kidneys of 3 control dogs.	Lipshitz and Stokey, 1945	Sufficient study details were not available.
		Dog 1-year dietary toxicity study: crystalluria started 60 to 90 days into	American Cyanamid Company, 1955	Sufficient study details were not available.

Melamine CASRN 108-78-1				
PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
		treatment, and persisted during the study period. No other effects attributable to melamine were observed.		
		Melamine may cause kidney stone formation when ingested chronically in dogs. In addition, pediatric patients may be at increased risk for stone formation when melamine is combined with cyanuric acid in formula.	Skinner et al., 2010	Study details reported in a primary source.
		In a 42-day study, Broiler hens (20/group) were fed diets containing melamine only, melamine in combination with cyanuric acid (CYA) or CYA only. Group 1: control; group II: 10 mg/kg MEL and 3.3 mg/kg CYA; group III: 30 mg/kg MEL and 10 mg/kg CYA; group IV: 100 mg/kg MEL and 33.3 mg/kg CYA; group V: 100 mg/kg MEL only; group VI: 33.3 mg/kg CYA only. No clinical signs of toxicity. Melamine alone had no effect on growth, but co-administration and CYA alone had adverse effects. Average daily weight gain of group II was reduced and food consumption was decreased in group III. No pathological changes in the livers of hens in group II. Swelling of some hepatic cells and granular degeneration in hens co-administered melamine and CYA (severity increased with dose). Lesions in the	Ding et al., 2012	Study details reported in a primary source. It appears that effects from melamine-only exposures are minimal and that toxicity is a result of co-administration with cyanuric acid.

Melamine CASRN 108-78-1				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		kidney were similar and correlated with dose. Increased rate of renal apoptosis in the melamine-only group on day 42; rate was increased for CYA-only group on days 21 and 42.		
		In a 4-month study, male rats were exposed via inhalation to melamine at concentrations of 0, 0.011, 0.058 and 0.50 mg/m^3. No general toxic or gonadotoxic symptoms. NOAEL: 0.50 mg/mg^3 (0.0005 mg/L); highest concentration tested LOAEL: Not established	ECHA, 2013	Insufficient description of the study. It is not clear if a vapor, dust or aerosol was applied. The study is not considered to be reliable.
		Potential for nephrotoxicity based on a structural alert for amines	Professional judgment	Estimated based on a structural alert for amine groups and professional judgment.
		Potential for systemic toxicity based on a structural alert for amine groups	Professional judgment	Estimated based on a structural alert for amine groups and professional judgment.
Skin Sensitization		**LOW: Melamine is not a skin sensitizer to guinea pigs.**		
	Skin Sensitization	Non-sensitizing to guinea pigs	ECHA, 2013	Adequate study reported in a secondary source. Study was conducted in accordance with OECD Guideline 406 and GLP.
		Non-sensitizing to guinea pigs	Fasset and Roudabush, 1963; Trochimowicz et al., 2001	Sufficient study details were not available.
Respiratory Sensitization		**No data located.**		
	Respiratory Sensitization			No data located.

Melamine CASRN 108-78-1				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Eye Irritation		**LOW: Melamine was mildly irritating to rabbit eyes.**		
	Eye Irritation	Non-irritating to rabbit eyes	BASF, 1969	Sufficient study details were not available.
		Non-irritating to rabbit eyes following 0.5 mL of 10% melamine	American Cyanamid Company, 1955; Trochimowicz et al., 2001	Sufficient study details were not available.
		Mild irritant to rabbit eyes following exposure to 30 mg of dry powder	American Cyanamid Company, 1955; Trochimowicz et al., 2001	Sufficient study details were not available.
		Slightly irritating to rabbit eyes	Marhold, 1972	Sufficient study details were not available.
Dermal Irritation		**VERY LOW: Melamine was not irritating to rabbit skin.**		
	Dermal Irritation	Not irritating to rabbit skin	Rijcken, 1995	OECD 404 guideline study.
		Not irritating to rabbit skin	BASF, 1969	Sufficient study details were not available.
		Not irritating to rabbit skin	American Cyanamid Company, 1955; Trochimowicz et al., 2001	Sufficient study details were not available.
		Not irritating to rabbit skin	Fasset and Roudabush, 1963; Trochimowicz et al., 2001	Sufficient study details were not available.
Endocrine Activity		**There was limited data located for the endocrine endpoint. Melamine showed no estrogenic activity (no change in B-galactosidase activity) in an *in vitro* yeast two-hybrid assay in *Saccharomyces cerevisiae* Y 190.**		
		Showed no estrogenic activity (no change in B-galactosidase activity) in an *in vitro* yeast two-hybrid assay in *Saccharomyces cerevisiae* Y 190.	ECHA, 2011	Reported in a secondary source. Non-guideline study.

Melamine CASRN 108-78-1				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Immunotoxicity		**There was limited data located for the immunotoxicity endpoint. Melamine did not inhibit the mitogenesis of B- and T- lymphocytes in an *in vitro* mouse lymphocyte mitogenesis test. It is unclear how well a mitogenesis test assesses immunotoxicity of chemicals. The available data are not sufficient to determine the hazard potential for this endpoint.**		
	Immune System Effects	Did not inhibit the mitogenesis of B- and T- lymphocytes in an *in vitro* mouse lymphocyte mitogenesis test.	ECHA, 2011	Reported in a secondary source. Unclear how well mitogenesis test assesses immunotoxicity of chemicals.
ECOTOXICITY				
ECOSAR Class		Melamines		
Acute Aquatic Toxicity		**LOW: Based on experimental acute aquatic values > 100 mg/L in fish, daphnia, and algae. Estimated toxicity values indicate No Effects at Saturation (NES).**		
Fish LC_{50}		*Oryzias latipes* 48-hour LC_{50} = 1,000 mg/L (Experimental)	OECD-SIDS, 1999	Study details reported in a secondary source.
		Freshwater fish (*Leuciscus idus melanotus*) 48-hour LC_{50} >500 mg/L (Experimental)	OECD-SIDS, 1999; ECHA, 2013	Study details reported in a secondary source.
		Poecilia reticulata 96-hour LC_{50} >3,000 mg/L (Experimental)	OECD-SIDS, 1999; ECHA, 2013	Study details reported in a secondary source.
		Freshwater fish (*Oncorhynchus mykiss*) 96-hour LC_{50} >3,000 mg/L NOEC = 3,000 mg/L semi-static; 0, 750, 1,500 and 3,000 ppm (nominal) (Experimental)	ECHA, 2013	Adequate study reported in a secondary source. Study was conducted in accordance to a method similar to present guidelines; non-GLP.
		Poecilia reticulata 4,400 mg/L dose lethal to <10% (Experimental)	OECD-SIDS, 1999; ECHA, 2013	Study details reported in a secondary source.

Melamine CASRN 108-78-1			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	Freshwater fish 96-hour LC_{50}: > 100 mg/L (ECOSAR class: Anilines, amino-meta); > 100 mg/L (ECOSAR class: Melamines); > 100 mg/L (ECOSAR class: Neutral organics) (Estimated)	ECOSAR v1.11	The estimated effect levels for the ECOSAR Anilines, amino-meta and Neutral organics classes exceed the water solubility of 3,230 mg/L. NES are predicted for these endpoints. Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.
Daphnid LC_{50}	*Daphnia magna* 48-hour LC_{50} > 1,000 mg/L 48-hour EC_{50} (mobility and behavior) = 200 mg/L static test conditions; 0, 56, 100, 180, 320, 560, and 1,000 mg/L (nominal) (Experimental)	ECHA, 2013	Adequate study reported in a secondary source. Study was conducted according to EPA Office of Pesticide Programs (OPP) 72-2, EU Method C.2 and GLP.
	Daphnia magna 48-hour LC_{50} >2,000 mg/L 48-hour EC_{50}(behavior) < 180 mg/L static test conditions; 180, 320, 560, 1,000, 1,800 and 2,000 mg/L (nominal) (Experimental)	ECHA, 2013	Adequate study reported in a secondary source. Study was conducted according to EPA OPP 72-2, EU Method C.2 and GLP.
	Daphnia magna 48-hour LC_{50}: 17 mg/L	ECOSAR v1.11	The estimated effect level for the ECOSAR Neutral organics class

Melamine CASRN 108-78-1			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	(ECOSAR class: Anilines, amino-meta); 510 mg/L (ECOSAR class: Melamines); 46,000 mg/L (ECOSAR class: Neutral organics) (Estimated)		exceeds the water solubility of 3,230 mg/L. NES are predicted for these endpoints. Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.
Green Algae EC_{50}	Green algae (*Selenastrum capricornutum*) 96-hour EC_{50} = 325 mg/L NOEC = 98 mg/L static test conditions; 0, 10, 32, 100, 320 and 1,000 ppm (nominal) (Experimental)	ECHA, 2013	Study details reported in a secondary source. Study was conducted in accordance with guideline PRO/FT Algae-AC090-6 and GLP.
	Green algae (*Scenedesmus pannonicus*) 4-day EC_{50} = 940 mg/L 4-day NOEC = 320 mg/L static test conditions; 0, 10, 32, 100, 320, 560, 1,000 and 2,000 mg/L (nominal) (Experimental)	OECD-SIDS, 1999; ECHA, 2013	Study details reported in a secondary source. Study was conducted in accordance with Dutch draft Standard Method NEN 6506, 1979.
	Green algae 96-hour EC_{50}: 6.1 mg/L (ECOSAR class: Anilines, amino-meta); > 100 mg/L (ECOSAR class:	ECOSAR v1.11	NES are predicted for these endpoints. Narcosis classes (neutral organics) are provided for

Melamine CASRN 108-78-1			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	Melamines); > 100 mg/L (ECOSAR class: Neutral organics) (Estimated)		comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.
Chronic Aquatic Toxicity	**LOW: Based on experimental data in fish, daphnia, and algae indicating a Low chronic aquatic toxicity hazard.**		
Fish ChV	*Salmo gairdneri* NOEC (macroscopic) = 500 mg/L; NOEC (microscopic) <125 mg/L (Experimental)	OECD-SIDS, 1999	Study details reported in a secondary source, study details and test conditions were not provided.
	Jordanella floridae 35-day NOEC ≥ 1,000 mg/L (Experimental)	OECD-SIDS, 1999	Study details reported in a secondary source, study details and test conditions were not provided.
	Freshwater fish ChV: > 10 mg/L (ECOSAR class: Anilines, amino-meta); > 10 mg/L (ECOSAR class: Melamines); > 10 mg/L (ECOSAR class: Neutral organics) (Estimated)	ECOSAR v1.11	The estimated effect levels for the ECOSAR Melamines and Neutral organics classes exceed the water solubility of 3,230 mg/L. NES are predicted for these endpoints. The toxicity value for the ECOSAR Anilines, amino-meta class was estimated through application of acute-to-chronic ratios per methods outlined in the ECOSAR Methodology Document. Narcosis classes (neutral organics) are provided for comparative purposes; DfE

Melamine CASRN 108-78-1			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
			assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.
Daphnid ChV	*Daphnia magna* 21-day LC_{50} = 32-56 mg/L, 21-day LC_{100} = 56 mg/L, 21-day NOEC = 18 mg/L (Experimental)	OECD-SIDS, 1999; ECHA, 2013	Study details reported in a secondary source, study details and test conditions were not provided.
	Daphnia magna ChV: 0.16 mg/L (ECOSAR class: Anilines, amino-meta); > 10 mg/L (ECOSAR class: Melamines); > 10 mg/L (ECOSAR class: Neutral organics) (Estimated)	ECOSAR v1.11	The toxicity value for the ECOSAR Melamines class was estimated through application of acute-to-chronic ratios per methods outlined in the ECOSAR Methodology Document. Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.

Melamine CASRN 108-78-1			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
Green Algae ChV	Green algae (*Selenastrum capricornutum*) 96-hour EC_{50} = 325 mg/L NOEC = 98 mg/L static test conditions; 0, 10, 32, 100, 320 and 1,000 ppm (nominal) (Experimental)	ECHA, 2013	Study details reported in a secondary source. Study was conducted in accordance with guideline PRO/FT Algae-AC090-6 and GLP.
	Green algae (*Scenedesmus pannonicus*) 4-day EC_{50} = 940 mg/L 4-day NOEC = 320 mg/L static test conditions; 0, 10, 32, 100, 320, 560, 1,000 and 2,000 mg/L (nominal) (Experimental)	OECD-SIDS, 1999; ECHA, 2013	Study details reported in a secondary source. Study was conducted in accordance with Dutch draft Standard Method NEN 6506, 1979.
	Green algae ChV: 1.3 mg/L (ECOSAR class: Anilines, amino-meta); > 10 mg/L (ECOSAR class: Melamines); > 10 mg/L (ECOSAR class: Neutral organics) (Estimated)	ECOSAR v1.11	The toxicity values for the ECOSAR Anilines, amino-meta and Melamines classes were estimated through application of acute-to-chronic ratios per methods outlined in the ECOSAR Methodology Document. Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.

Melamine CASRN 108-78-1				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
ENVIRONMENTAL FATE				
Transport		**Level III fugacity models incorporating available physical and chemical property data indicate that at steady state, melamine is expected to be found primarily in soil and to a lesser extent, water. Melamine is expected to have high mobility in the soil, based on its calculated K_{OC}. Melamine will not volatilize from moist soil and water surfaces based on its Henry`s Law constant. Volatilization from dry surfaces is not expected based on its vapor pressure. In the atmosphere, melamine is expected to exist almost entirely in the particulate phase. Particulates may be removed from air by wet or dry deposition.**		
	Henry's Law Constant (atm-m^3/mole)	<10^{-8} at 20°C (Estimated)	EPI v4.11	Estimated from experimental water solubility and vapor pressure.
	Sediment/Soil Adsorption/Desorption - K_{oc}	32 (Estimated)	EPI v4.11	
	Level III Fugacity Model	Air = 0.01% Water = 25% Soil = 74.9% Sediment = 0.1% (Estimated)	EPI v4.11	
Persistence		**HIGH: Experimental data indicate melamine undergoes slow degradation under stringent guideline conditions, although melamine is readily degraded in acclimated treatment systems. Pure culture studies have shown biodegradation of melamine by enzymatic hydrolytic deamination in less than 10 days. However, an original MITI test detected less than 30% degradation after 14 days and two separate guideline OECD 302B studies observed no degradation after 28 days and 16% degradation after 20 days. The environmental persistence half-life of melamine is therefore expected to be between 60 and 180 days based on the guideline biodegradation studies, consistent with a High hazard designation. Melamine was found to hydrolyze in strong alkaline and acidic solutions but hydrolysis is not expected under neutral conditions. Melamine is not expected to be susceptible to direct photolysis by sunlight. The atmospheric half-life of vapor-phase melamine is estimated to be 16 days.**		
Water	**Aerobic Biodegradation**	Passes Ready Test: No Test method: Original MITI test <30% after 14 days (Measured)	OECD-SIDS, 1998	Guideline study reported in a secondary source.
		Study results: 16%/20 days Test method: 302B: Inherent - Zahn-	OECD-SIDS, 1998	Guideline study reported in a secondary source.

Melamine CASRN 108-78-1				
PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
		Wellens/EMPA Test Elimination of 10% after 14 days; not inherently degradable (Measured)		
		Study results: 0%/28 days Test method: 302B: Inherent - Zahn-Wellens/EMPA Test (Measured)	OECD-SIDS, 1998	Guideline study reported in a secondary source.
		Study results: 14±10% /100 days Test method: Activated sludge treatment systems Local municipal WWTP; 100 day adaptation; average melamine removal 14±10% with the Modified Ludzack-Ettinger process and 20±15% with the continuous stirred tank reactor (Measured)	Xu et al., 2013	
		Study results: 100%/<10 days Test method: Other: Pure culture study Bacterium, *Nocardioides sp.* strain ATD6 rapidly degraded melamine and accumulated cyanuric acid and ammonium, via the intermediates ammeline and ammelide. (Measured)	Takagi et al., 2012	Melamine degradation was found to occur in species specific biodegradation studies.
	Volatilization Half-life for Model River	>1 year (Estimated)	EPI v4.11	
	Volatilization Half-life for Model Lake	>1 year (Estimated)	EPI v4.11	

Melamine CASRN 108-78-1				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Soil	**Aerobic Biodegradation**	Study results: 100%/4 days Test method: Other: Pure culture study Bacterium, *A. citrulli* strain B-12227 rapidly degraded melamine and accumulated cyanuric acid, ammeline and ammelide, via the intermediates ammeline and ammelide. (Measured)	Shiomi and Ako, 2012	Melamine degradation was found to occur in species specific biodegradation studies.
		A set of soil bacteria has been identified whose members rapidly metabolize melamine as their source of nitrogen to support growth; these bacteria contain an enzyme which hydrolytically deaminate melamine (Measured)	Cook and Hutter, 1981, 1984	Melamine degradation was found to occur in species specific biodegradation studies.
	Anaerobic Biodegradation	Not probable (Anaerobic-methanogenic biodegradation probability model)	EPI v4.11	
	Soil Biodegradation with Product Identification			No data located.
	Sediment/Water Biodegradation			No data located.
Air	**Atmospheric Half-life**	16 days (Estimated)	EPI v4.11	
Reactivity	**Photolysis**			No data located.
	Hydrolysis	Melamine hydrolysis proceeds stepwise, with loss of one to three amino groups; hydrolysis occurs by reaction with mineral acid or inorganic alkali; Hydrolysis products include ammeline (CASRN 645-92-1), ammelide (CASRN 645-93-2) and cyanuric acid (CASRN 108-80-5) (Measured)	OECD-SIDS, 1998	Reported in a secondary source.

Melamine CASRN 108-78-1				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		Melamine is hydrolyzed in strong alkaline and acidic solutions. The rate constants at 100°C: $k(s^{-1}) = 3.8E\text{-}6\ [OH^-]$ $k(s\text{-}1) = 1.25E10\text{-}4\ [H^+]$. Hydrolysis products are ammeline, ammelide and cyanuric acid. (Measured)	OECD-SIDS, 1998	Reported in a secondary source. Study was conducted in the extreme pH ranges at high temperatures. This study is not relevant for environmental conditions.
Environmental Half-life		2-3 years in soil (Measured)	OECD-SIDS, 1998	Reported in a secondary source.
		75 days (Estimated)	PBT Profiler	Half-life estimated for the predominant compartment (soil), as determined by EPI methodology.
Bioaccumulation		**LOW: Measured BCF and estimated BAF values are below 100, the Low bioaccumulation designation criteria.**		
	Fish BCF	<3.8 *Cyprinus carpio* for 0.2 mg/L <0.38 for 2 mg/L; according to OECD 305C (Measured)	OECD-SIDS, 1998	Guideline study reported in a secondary source.
	Other BCF			No data located.
	BAF	0.9 (Estimated)	EPI v4.11	
	Metabolism in Fish			No data located.
ENVIRONMENTAL MONITORING AND BIOMONITORING				
Environmental Monitoring		Melamine has been detected in river water and sediments in Japan (ECHA, 2013).		
Ecological Biomonitoring		Melamine has been reported in fish in Japan (ECHA, 2013).		
Human Biomonitoring		Melamine was not included in the NHANES biomonitoring report (CDC, 2009).		

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Oligomeric ethyl ethylene phosphate

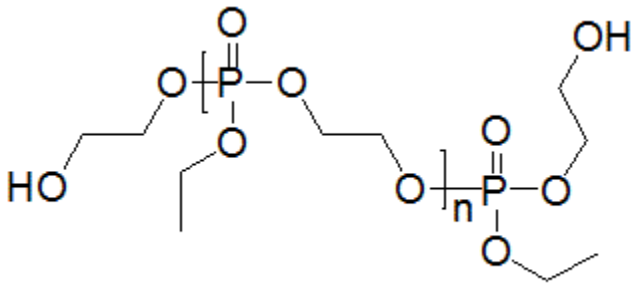
Screening Level Toxicology Hazard Summary

This table contains hazard information for each chemical; evaluation of risk considers both hazard and exposure. Variations in end-of-life processes or degradation and combustion by-products are discussed in the report but not addressed directly in the hazard profiles. The caveats listed below must be taken into account when interpreting the information in the table.

VL = Very Low hazard L = Low hazard M = Moderate hazard H = High hazard VH = Very High hazard – Endpoints in colored text (VL, L, M, H, and VH) were assigned based on empirical data. Endpoints in black italics *(VL, L, M, H,* and *VH*) were assigned using values from estimation software and professional judgment [(Quantitative) Structure Activity Relationships "(Q)SAR"].

[d] This hazard designation would be assigned MODERATE for a potential for lung overloading if >5% of the particles are in the respirable range as a result of dust forming operations.

Chemical	CASRN	Human Health Effects											Aquatic Toxicity		Environmental Fate	
		Acute Toxicity	Carcinogenicity	Genotoxicity	Reproductive	Developmental	Neurological	Repeated Dose	Skin Sensitization	Respiratory Sensitization	Eye Irritation	Dermal Irritation	Acute	Chronic	Persistence	Bioaccumulation
Oligomeric ethyl ethylene phosphate	184538-58-7	L	*L*	*M*	*L*	*M*	*M*	*L*[d]	*L*		M	L	*L*	*L*	*VH*	*L*



Representative structure

CASRN: 184538-58-7

MW: Product MW_N range from 300 to 4,000

MF: $(C_6H_{15}O_4P \cdot C_2H_4O \cdot O_5P_2)_n$

Physical Forms: Liquid
Neat:

Use: Flame retardant

SMILES: C(COP(=O)(OCC)OCC)OP(=O)(OCC)OCC (Representative structure used for n=1 estimations)
The polymeric components with MW >1,000 oligomers (n≥6) are not amenable to SMILES notation.

Synonyms: Phosphoric acid, triethyl ester, polymer with oxirane and phosphorus oxide (P2O5); Oxirane, polymer with phosphorus oxide (P2O5) and triethyl phosphate; Phosphorus oxide (P2O5), polymer with oxirane and triethyl phosphate; Alkylphosphate oligomer; Oligomeric ethyl ethylene phosphate
Trade names: Fyrol PNX; Fyrol PNX-LE; Modified oligomeric ethyl ethylene phosphate; Exolit 550;

Chemical Considerations: This alternative is a polymer consisting of oligomers with MWs above and below 1,000 daltons according to publicly available patents and commercial product literature. A typical phosphorus content of 19% was reported from these sources. Residual monomers, unreacted starting material (triethyl phosphate) and low MW oligomers are expected to be present at a level requiring their assessment. The n≥6, oligomers have a MW >1,000 and are assessed using the available polymer assessment literature. The n≤5 oligomers are those with a MW <1,000 and are assessed with EPI v4.11 and ECOSAR v1.11 estimates due to an absence of publically available experimental physical/chemical, environmental fate and aquatic toxicity values (Hardy and Jaffe, 1983; Boethling and Nabholz, 1997; Akzo Nobel and Wuestenenk, 2005).

Polymeric: Yes
Oligomeric: The oligomers are produced by reacting phosphorus pentoxide with triethyl phosphate to form a polyphosphate ester that is in turn reacted with ethylene oxide. The repeating phosphate ester units, represented between the brackets where n = 2 to 20 units, although n=500 has been reported in one patent. Both linear and cross-linked polymers may be formed during polymerization. The polymers may be terminated with either an ethyl or hydroxyl ethyl group (Hardy and Jaffe, 1983; Akzo Nobel and Wuestenenk, 2005; Professional judgment).

Metabolites, Degradates and Transformation Products: None identified; although biodegradation or hydrolysis pathways may yield diethyl phosphate, ethyl phosphate, ethanol, phosphate and ethylene glycol (Professional judgment)

Analog: None
Endpoint(s) using analog values: Not applicable

Analog Structure: Not applicable

Structural Alerts: Organophosphates, neurotoxicity (EPA, 2012).

Risk Phrases: Not classified by Annex VI Regulation (EC) No 1272/2008 (ESIS, 2012).

Hazard and Risk Assessments: None identified.

Oligomeric ethyl ethylene phosphate CASRN 184538-58-7			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
PHYSICAL/CHEMICAL PROPERTIES			
Melting Point (°C)			No data located.
Boiling Point (°C)	>300 for n≥1 (Estimated)	EPI v4.11; Professional judgment; EPA, 1999	Estimate based on representative oligomers where n=1-5 with MW < 1,000. Also estimated for oligomers where n≥6 with MWs >1,000. Cutoff value according to HPV assessment guidance and cutoff value used for large, high MW solids.
Vapor Pressure (mm Hg)	$3.6x10^{-6}$ at 25°C for n=1 $2.1x10^{-8}$ for n=2-5 (Estimated)	EPI v4.11	Estimates based on representative oligomers where n=1-5.
	$<10^{-8}$ for the n≥6 oligomers (Estimated)	Professional judgment; Boethling and Nabholz, 1997	Cutoff value for large, high MW polymers.
Water Solubility (mg/L)	3375 mg/L for n=1 933 mg/L for n=2 233 mg/L for n=3 1 mg/L for n=6 (Estimated)	EPI v4.11	Estimates based on representative oligomers where n=1-6.
	Soluble (Measured)	ICL, 2010	Non-quantitative value from a MSDS for the commercial product Fyrol PNX LE containing 95-100% pure material.
	Miscible (Measured)	Submitted confidential study	Non-quantitative value with limited details reported.
Log K_{ow}	-0.58 (Measured)	Submitted confidential study	Limited study details provided in a confidential source.
	0.42 for n=1 -0.03 for n=2 -0.48 for n=3 -1.33 for n=6 (Estimated)	EPI v4.11	Estimates based on representative oligomers where n=1-6.
	<-1	ICL, 2010	From a MSDS for the commercial product Fyrol

Oligomeric ethyl ethylene phosphate CASRN 184538-58-7				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		(Measured)		PNX LE containing 95-100% pure material.
Flammability (Flash Point)		Not flammable (Measured)	ICL, 2010	From a MSDS for the commercial product Fyrol PNX LE containing 95-100% pure material.
Explosivity		Not explosive (Measured)	ICL, 2010	From a MSDS for the commercial product Fyrol PNX LE containing 95-100% pure material.
Pyrolysis				No data located.
pH		Not applicable (Estimated)	Professional judgment	Does not contain functional groups that are expected to ionize under environmental conditions.
pK_a		Not applicable (Estimated)	Professional judgment	Does not contain functional groups that are expected to ionize under environmental conditions.
HUMAN HEALTH EFFECTS				
Toxicokinetics		**For low MW components (n < 6), absorption is estimated to be low for all routes based on confidential analogs. For high MW components, no absorption is expected through the skin and gastrointestinal tract. Poor absorption is estimated in the lungs because the polymer is dispersible due to its physical chemical properties.**		
Dermal Absorption *in vitro*				No data located.
Absorption, Distribution, Metabolism & Excretion	**Oral, Dermal or Inhaled**			No data located.
	Other	For low MW components (n < 6), absorption is expected to be low for all routes based on confidential analogs. For high MW components, no absorption is expected through the skin and gastrointestinal tract. Poor absorption is expected in the lungs because the polymer is dispersible due to its physical chemical properties. (Estimated)	Professional judgment	Estimated based on analogy to a confidential analog, physical chemical properties, and professional judgment.

Oligomeric ethyl ethylene phosphate CASRN 184538-58-7				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Acute Mammalian Toxicity		**LOW: Based on oral and dermal LD_{50} values > 2,000 mg/kg for the polymeric mixture that included LMW components. No data were located for the inhalation route of exposure. The higher MW components of this polymer (MW >1,000) are expected to have limited bioavailability and have low potential for acute toxicity.**		
Acute Lethality	**Oral**	Rat oral LD_{50} = 5,000 mg/kg	Submitted confidential study	Data reported in a confidential study submitted to EPA for the polymeric mixture that included LMW components.
	Dermal	Rabbit dermal LD_{50} > 2,000 mg/kg	Submitted confidential study	Data reported in a confidential study submitted to EPA for the polymeric mixture that included LMW components.
	Inhalation			No data located.
Carcinogenicity		**LOW: Estimated based on predictions for the polymer containing lower MW components. The risk for carcinogenicity is estimated to be low considering that the residual monomers do not contain substituted terminal double bonds, and reactive-functional-group-bearing side chains. The higher MW components of this polymer (MW >1,000) are expected to have limited bioavailability and have low potential for carcinogenicity. No experimental data were located.**		
	OncoLogic Results	Based on estimates considering that the residual monomers do not contain substituted terminal double bonds; the low MW species do not contain reactive-functional-group-bearing side chains; the polymer is cross-linked, is not linear, and has a MW of less than 100,000.	OncoLogic, 2008	Estimated for the polymer containing lower MW components.
	Carcinogenicity (Rat and Mouse)			No data located.
	Combined Chronic Toxicity/Carcinogenicity			No data located.
	Other			No data located.

Oligomeric ethyl ethylene phosphate CASRN 184538-58-7				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Genotoxicity		**MODERATE: There is uncertain concern for mutagenicity based on the structure, ethyl substituted phosphate. This substance did not cause gene mutations in bacteria; however, there is uncertainty due to the lack of experimental data for this endpoint. Complete data requirements for this endpoint are both gene mutation and chromosomal aberration assays. For instances of incomplete or inadequate mutagenicity/genotoxicity data, a Low hazard designation cannot be given. The higher MW components of this polymer (MW >1,000) are expected to have limited bioavailability and have low potential for genotoxicity.**		
	Gene Mutation *in vitro*	Uncertain concern for mutagenicity (Estimated)	Professional judgment	Estimated for the low MW component due to ethyl substituted phosphate.
		Negative for gene mutation in an Ames test in *S.typhimurium* and *E. coli*.	Submitted confidential study	Data reported in a submitted confidential study.
	Gene Mutation *in vivo*			No data located.
	Chromosomal Aberrations *in vitro*			No data located.
	Chromosomal Aberrations *in vivo*			No data located.
	DNA Damage and Repair			No data located.
	Other			No data located.
Reproductive Effects		**LOW: Estimated to have a low potential for reproductive effects based on expert judgment and a lack of structural alert for this endpoint. No experimental data were located. The higher MW components of this polymer (MW >1,000) are expected to have limited bioavailability and have low potential for reproductive toxicity.**		
	Reproduction/Developmental Toxicity Screen			No data located.
	Combined Repeated Dose with Reproduction/ Developmental Toxicity Screen			No data located.
	Reproduction and Fertility Effects			No data located.

Oligomeric ethyl ethylene phosphate CASRN 184538-58-7				
PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
	Other	There is low potential for reproductive effects (Estimated)	Expert judgment	Estimated based on expert judgment and the lack of structural alerts.
Developmental Effects		**MODERATE: There were no experimental data for the developmental toxicity endpoint. There were no structural alerts identified for this endpoint. The higher MW components of this polymer (MW >1,000) are expected to have limited bioavailability and have low potential for developmental toxicity.** **There were also no experimental data located for the developmental neurotoxicity endpoint. There is uncertain potential for developmental neurotoxicity for this substance based on a structural alert for organophosphates for the neurotoxicity endpoint; decreased cholinesterase activity in pregnant lab animals has been shown to have a negative impact on fetal brain development. As a result, an estimated Moderate designation is assigned.**		
	Reproduction/ Developmental Toxicity Screen			No data located.
	Combined Repeated Dose with Reproduction/ Developmental Toxicity Screen			No data located.
	Prenatal Development			No data located.
	Postnatal Development			No data located.
	Prenatal and Postnatal Development			No data located.
	Developmental Neurotoxicity	Uncertain concern for developmental neurotoxicity based on the potential for Cholinesterase (ChE) inhibition in dams that may result in alterations of fetal neurodevelopment. (Estimated)	Professional judgment	Estimated based on a structural alert for organophosphates for the neurotoxicity endpoint.
	Other	There is low potential for developmental effects (Estimated)	Expert judgment	Estimated based on expert judgment and the lack of structural alerts.

Oligomeric ethyl ethylene phosphate CASRN 184538-58-7				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Neurotoxicity		**MODERATE: Estimated to have uncertain potential for neurotoxic effects based on a structural alert and professional judgment. No data were located. In the absence of experimental data, a Moderate hazard designation is assigned. The higher MW components of this polymer (MW >1,000) are expected to have limited bioavailability and have low potential for acute toxicity.**		
	Neurotoxicity Screening Battery (Adult)			No data located.
	Other	There is potential for neurotoxic effects based on a structural alert for organophosphates. (Estimated)	Professional judgment	Estimated based on a structural alert and professional judgment.
		Uncertain concern for neurotoxicity (Estimated)	Professional judgment	Estimated for the low MW component due to ethyl substituted phosphate.
Repeated Dose Effects		**LOW: Estimated to have low potential for repeated dose effects for the low MW components of this substance based on expert judgment. This substance may contain polymer components with a MW >1,000. In this case, it is expected to have limited bioavailability; however, there is the possibility of lung overloading. No experimental data were located.**		
		Estimated to have low potential for repeated dose effects for the low MW components of this substance. This substance may contain polymer components with a MW >1,000. In this case, it is expected to have limited bioavailability; however, there is the possibility of lung overloading. (Estimated)	Professional judgment	Estimated based on professional judgment.

Oligomeric ethyl ethylene phosphate CASRN 184538-58-7				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Skin Sensitization		**LOW: Estimated to have low potential for skin sensitization based on expert judgment. There were no experimental data located.**		
	Skin Sensitization	There is low potential for skin sensitization (Estimated)	Expert judgment	Estimated based on expert judgment.
Respiratory Sensitization		**No data located.**		
	Respiratory Sensitization			No data located.
Eye Irritation		**MODERATE: This substance was moderately to slightly irritating to rabbit eyes.**		
	Eye Irritation	Moderate to slight eye irritation in rabbits; conjunctival irritation with redness and discharge; cleared within 96 hours.	Submitted confidential study	Data reported in a confidential study submitted to EPA.
Dermal Irritation		**LOW: This substance is slightly irritating to rabbit skin with irritation clearing within 3 days.**		
	Dermal Irritation	Slightly irritating to rabbit skin	Submitted confidential study	Data reported in a confidential study submitted to EPA
		Mild and transient dermal irritation in rabbits; cleared within 3 days.	Submitted confidential study	Data reported in a confidential study submitted to EPA.
Endocrine Activity		**The potential for endocrine activity for the low MW components of this substance is uncertain. The higher MW components of this polymer (MW >1,000) are expected to have limited bioavailability and have low potential for endocrine activity.**		
				No data located.
Immunotoxicity		**Estimated to have a low potential for immunotoxic effects based on expert judgment. The higher MW components of this polymer (MW >1,000) are expected to have limited bioavailability and have low potential for immunotoxicity.**		
	Immune System Effects	There is low potential for immunotoxic effects (Estimated)	Expert judgment	Estimated based on expert judgment.

Oligomeric ethyl ethylene phosphate CASRN 184538-58-7			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
ECOTOXICITY			
ECOSAR Class			
Acute Aquatic Toxicity	**LOW: Based on estimated acute aquatic toxicity values for representative oligomers. Experimental data in fish also indicate a Low hazard; experimental data was not located for daphnia or algae.**		
Fish LC_{50}	*Danio rerio* (Zebrafish) 96-hour LC_{50} > 1,000 mg/L according to OECD 203 (Experimental)	Clariant, 2011	Data reported in a confidential study submitted to EPA; the toxicity value is well above the water solubility for this substance; therefore NES is predicted.
	Freshwater fish 96-hour LC_{50} = > 100 mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	Estimate based on representative oligomer n=1-6. Estimates for the Esters class are provided for comparative purposes. See Section 5.5.1.
Daphnid LC_{50}	Daphnia magna 48-hour LC_{50} > 100 mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	Estimate based on representative oligomers n=1-6. Estimates from the Esters class are provided for comparative purposes. See Section 5.5.1.
Green Algae EC_{50}	Green algae 96-hour EC_{50} > 100 mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	Estimate based on representative oligomers n=1-6. Estimates from the Esters class are provided for comparative purposes. See Section 5.5.1.

Oligomeric ethyl ethylene phosphate CASRN 184538-58-7			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
Chronic Aquatic Toxicity	**LOW: An estimated chronic aquatic toxicity value derived using an acute-to-chronic ratio (ACR) for the phosphate ester class and was applied to the available experimental acute data for this chemical and indicated a Low hazard. ECOSAR estimates for the Esters class also indicated Low hazard. There were no experimental data available for daphnia or algae.**		
Fish ChV	Freshwater fish ChV ≥ 41.7 mg/L (Estimated)	Professional judgment	An ACR of 24 was derived for the phosphate ester class based on experimental data for Tris (p-t-butylphenyl) phosphate (TBPP). The acute-to-chronic ratio was applied to available experimental acute fish data for oligomeric ethyl ethylene phosphate (ChV = >1000 mg/L /24 = 41.7 mg/L)
	Freshwater fish ChV > 10 mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	Estimate based on representative oligomer n=1-6. Estimates for the Esters class are provided for comparative purposes. See Section 5.5.1.
Daphnid ChV	Daphnia magna ChV = > 10 mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	Estimate based on representative oligomer n=1-6. Estimates for the Esters class are provided for comparative purposes. See Section 5.5.1.
Green Algae ChV	Green algae ChV > 10 mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	Estimate based on representative oligomer n=1-6. Estimates for the Esters class are provided for comparative purposes. See Section 5.5.1.

Oligomeric ethyl ethylene phosphate CASRN 184538-58-7				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
ENVIRONMENTAL FATE				
Transport		**The environmental fate for the lower MW oligomers where n is 1-5, with MW<1,000 are based on the estimated moderate water solubility and low vapor pressure indicating that the lower MW oligomers are anticipated to partition predominantly to soil. The higher MW oligomers where n≥6, with MW>1,000 are expected to have negligible water solubility and negligible vapor pressure indicating that the higher MW oligomers are anticipated to partition predominantly to soil and sediment. The estimated Henry's Law Constant of $<10^{-8}$ atm-m^3/mole indicates that the lower MW and higher MW oligomers are not expected to volatilize from water to the atmosphere. The estimated K_{OC} of >11,000 indicates that the lower MW and higher MW oligomers are not anticipated to migrate through soil to groundwater and also have the potential to adsorb to sediment.**		
	Henry's Law Constant (atm-m^3/mole)	$<10^{-8}$ for n≥1 (Estimated)	EPI v4.11; Professional judgment; Boethling and Nabholz, 1997	Estimates based on representative oligomers where n=1-5; cutoff values for nonvolatile compounds. Estimated by the HENRYWIN Group SAR Method with no measured chemical property inputs. Estimates based on representative oligomers where n≥6; cutoff value used for large, high MW polymers. High MW polymers are expected to have low vapor pressure and are not expected to undergo volatilization.
	Sediment/Soil Adsorption/Desorption - K_{oc}	11,000 for n=1 >30,000 for n≥2 (Estimated)	EPI v4.11; Professional judgment	Using MCI Method KOCWIN v2.00, estimate based on representative oligomers where n=1-5. Also estimated for oligomers where n≥6 with MWs >1,000 based on professional judgment.
	Level III Fugacity Model	Air = 0% Water = 0.55% Soil = 52% Sediment = 47% (Estimated)	EPI v4.11	Estimate based on representative oligomer where n=6.
		Air = 0% Water = 15% Soil = 80% Sediment = 4.8% (Estimated)	EPI v4.11	Estimate based on representative oligomer where n=1.

Oligomeric ethyl ethylene phosphate CASRN 184538-58-7				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Persistence		**VERY HIGH: The persistence designation for this polymer is based on its higher MW components (MW >1,000). The lower MW oligomers (MW <1,000; n ≤ 5) of this polymer are expected to have lower persistence because of their higher water solubility and increased bioavailability to microorganisms. The higher MW components are expected to have higher persistence because of their low water solubility and poor bioavailability, indicating that neither biodegradation nor hydrolysis are expected to be important environmental fate processes. This is supported by experimental studies with the commercial product. In a ready test using the OECD guideline 301D, 0% biodegradation occurred after 28 days and 2% biodegradation was achieved after 140 days. In a nonguideline study with limited details, slow hydrolysis was reported for the commercial product at normal temperatures in acidic and alkaline aqueous solutions. Additionally, this polymer does not contain functional groups that would be expected to absorb light at environmentally significant wavelengths. Experimental values for commercial products and evaluation of the higher MW components of this polymer suggest an environmental half-life of >180 days.**		
Water	**Aerobic Biodegradation**	Passes Ready Test: No Test method: OECD TG 301D: Closed Bottle Test This commercial product biodegraded 0% at day 28 and 2% at day 140 (Measured)	ICL, 2010	From a MSDS for the commercial product Fyrol PNX LE containing 95-100% pure material.
		Hours-days (Primary Survey Model) Weeks (Ultimate Survey Model) (Estimated)	EPI v4.11	Estimate based on representative oligomers where n=1-2.
	Volatilization Half-life for Model River	>1 year for n≥1 (Estimated)	EPI v4.11	Estimate based on representative oligomers where n=1-6.
	Volatilization Half-life for Model Lake	>1 year for n≥1 (Estimated)	EPI v4.11	Estimate based on representative oligomers where n=1-6.
Soil	**Aerobic Biodegradation**			No data located.
	Anaerobic Biodegradation	Probable (Anaerobic-methanogenic biodegradation probability model)	EPI v4.11	Estimate based on representative oligomers where n=1.

Oligomeric ethyl ethylene phosphate CASRN 184538-58-7				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Soil Biodegradation with Product Identification			No data located.
	Sediment/Water Biodegradation			No data located.
Air	**Atmospheric Half-life**	0.086 days for n=1 0.056 days for n=2 0.042 days for n=3 0.025 days for n=6 (Estimated)	EPI v4.11	Estimate based on representative oligomers where n=1-6.
Reactivity	**Photolysis**	Not a significant fate process (Estimated)	Professional judgment; Mill, 2000	The substance does not contain functional groups that would be expected to absorb light at wavelengths >290 nm.
	Hydrolysis	Hydrolyzes slowly at normal temperatures in acidic or alkaline aqueous solutions (Measured)	ICL, 2010	Non-quantitative value from a MSDS for the commercial product Fyrol PNX LE containing 95-100% pure material.
		50%/340 days at pH 5-8 50%/320 days at pH 9 for n=6 (Estimated)	EPI v4.11	Estimate based on representative oligomer where n=6.
		50%/3.3 years at pH 5-8 50%/3 years at pH 9 for n=1 (Estimated)	EPI v4.11	Estimate based on representative oligomer where n=1.
Environmental Half-life		>180 days (Estimated)	Professional judgment	The n≥6 oligomers with a MW >1,000 are not anticipated to be assimilated by microorganisms. Therefore, biodegradation is not expected to be an important removal process. The higher MW oligomers are also not expected to be removed by other degradation processes under environmental conditions because of limited water solubility and limited partitioning to air.
		30 (Estimated)	EPI v4.11; PBT Profiler	Half-life estimated for the predominant compartment (Soil) for the oligomer where n=1, as

Oligomeric ethyl ethylene phosphate CASRN 184538-58-7				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
				determined by EPI and the PBT Profiler methodology.
Bioaccumulation		**LOW: Both the higher MW and lower MW oligomers are estimated to have Low potential for bioaccumulation. The representative oligomers with lower MW, where n=1-5, have estimated BCF values of 3.2 and estimated BAF values below 1. The high MW oligomers, where n≥6 (MW >1,000) are expected to have limited water solubility, poor bioavailability and are not expected to be bioaccumulative.**		
	Fish BCF	3.2 for n=1-5 (Estimated)	EPI v4.11	Estimate based on representative oligomers where n=1-5.
		<100 for the n≥6 oligomers (Estimated)	Professional judgment	The substance has a MW >1,000 and is not anticipated to be taken up by aquatic organisms; therefore, bioconcentration is not expected.
	Other BCF			No data located.
	BAF	0.94 for n=1 0.90 for n=2-5 (Estimated)	EPI v4.11	Estimate based on representative oligomers where n=1-5.
		n≥6 oligomers (Estimated)	Professional judgment	No data located for MW >1,000 oligomers where n≥6.
	Metabolism in Fish			No data located.
ENVIRONMENTAL MONITORING AND BIOMONITORING				
Environmental Monitoring		No data located.		
Ecological Biomonitoring		No data located.		
Human Biomonitoring		This chemical was not included in the NHANES biomonitoring report (CDC, 2013).		

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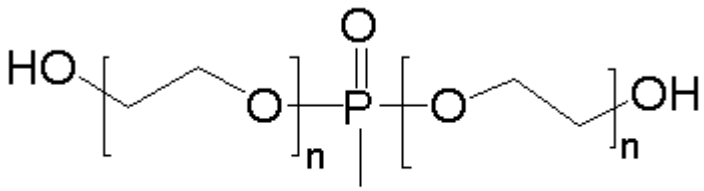
Oligomeric phosphonate polyol

Screening Level Toxicology Hazard Summary

This table contains hazard information for each chemical; evaluation of risk considers both hazard and exposure. Variations in end-of-life processes or degradation and combustion by-products are discussed in the report but not addressed directly in the hazard profiles. The caveats listed below must be taken into account when interpreting the information in the table.

VL = Very Low hazard L = Low hazard M = Moderate hazard H = High hazard VH = Very High hazard – Endpoints in colored text (VL, L, M, H, and VH) were assigned based on empirical data. Endpoints in black italics *(VL, L, M, H,* and *VH*) were assigned using values from estimation software and professional judgment [(Quantitative) Structure Activity Relationships "(Q)SAR"].

		Human Health Effects											Aquatic Toxicity		Environmental Fate	
Chemical	CASRN	Acute Toxicity	Carcinogenicity	Genotoxicity	Reproductive	Developmental	Neurological	Repeated Dose	Skin Sensitization	Respiratory Sensitization	Eye Irritation	Dermal Irritation	Acute	Chronic	Persistence	Bioaccumulation
Oligomeric phosphonate polyol	363626-50-0	L	*M*	*M*	*L*	*M*	*M*	*L*	*L*		L	VL	*L*	*M*	*M*	*L*



CASRN: 363626-50-0

MW: <1,000; MW_N 311

MF: $CH_5O_3P \cdot (C_2H_4O)_n \cdot (C_2H_4O)_n$

Physical Forms: Liquid
Neat: Liquid

Use: Reactive flame retardant

SMILES: C(O)COP(C)(=O)OCCO (Representative structure where n=1; MW = 184)

Synonyms: Poly(oxy-1,2-ethanediyl), α,α`-(methylphosphinylidene)bis[ω-hydroxy-; Bis(polyoxyethylene) methylphosphonate; Polyethylene glycol methylphosphonate
Trade Names: Exolit OP 560

Chemical Considerations: : This alternative is a phosphonate polyol with an average MW of 311 daltons and a typical phosphorus content of 10-13% according to publicly available product literature Representative monomers and oligomers were assessed with EPI v4.11 and ECOSAR 1.11 estimates due to an absence of publicly available experimental physical/chemical, environmental fate and aquatic toxicity values.

This alternative is a reactive flame retardant designed for use in the production of polyurethane foams. It is incorporated into a polymer backbone (i.e. polyurethane) by chemically bonding with raw materials during the polymerization process. Although not all reactive flame retardants have reactive functional groups, all reactive flame retardants are irreversibly incorporated into a polymer during manufacture to improve flame retardancy. Once a reactive flame retardant is incorporated into a polymer, it is unlikely to be released. Additive flame retardants, in contrast, are not reacted or chemically bonded with the manufactured product and have potential to be released under certain conditions (Clariant, 2012; Clariant, 2013).

Polymeric: Yes
Oligomeric: This alternative is a polymer consisting of methylphosphonate substituted with polyethylene glycol.

Metabolites, Degradates and Transformation Products: None identified.

Analog: None **Endpoint(s) using analog values:** Not applicable	**Analog Structure:** Not applicable

Structural Alerts: Organophosphates - neurotoxicity (EPA, 2012).

Risk Phrases: Not classified by Annex VI Regulation (EC) No 1272/2008 (ESIS, 2012).

Hazard and Risk Assessments: None identified.

Oligomeric phosphonate polyol CASRN 363626-50-0			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
PHYSICAL/CHEMICAL PROPERTIES			
Melting Point (°C)	<-30 (Measured)	Clariant, 2012	Cutoff value reported in a Safety Data Sheet with no study details.
Boiling Point (°C)	>150 at 0.76 mm Hg decomposes; using differential thermal analysis (DTA) (Measured)	Clariant, 2012	Cutoff value reported in a Safety Data Sheet with no study details.
	>300 for n=1-7 (Estimated)	EPI v4.11; EPA, 1999	Estimate based on representative structures where n=1-7. Cutoff value for high boiling point compounds according to HPV assessment guidance; decomposition likely occurs before the boiling point is reached.
Vapor Pressure (mm Hg)	n=1: $6.9x10^{-6}$ n=2: $3.6x10^{-8}$ $<10^{-8}$ at 25°C for n≥3-7 (Estimated)	EPI v4.11; EPA, 1999	Estimates based on representative structures where n=1-7. Cutoff value for nonvolatile compounds for n=3-7 oligomers according to HPV assessment guidance.
Water Solubility (mg/L)	Slow hydrolysis in the presence of water (Measured)	Clariant, 2012; Clariant, 2013	No study details and no indication of measured hydrolysis rates were reported in the Safety Data Sheet; rates are expected to be pH dependent.
	$1x10^{6}$ for n=1-7 (Estimated)	EPI v4.11	Estimates based on representative structures where n=1-7. Slow hydrolysis expected in the presence of water based on Safety Data Sheet.
Log K_{ow}	<-2 for n=1-7 (Estimated)	EPI v4.11	Estimated values based on representative structures where n=1-7, indicate high estimated water solubility.
Flammability (Flash Point)	Flash point: 196°C According to Cleveland DIN 51376; open cup (Estimated)	Clariant, 2012	Reported in a product datasheet.
	Not flammable (Estimated)	Professional judgment	No experimental data located; based on its use as a flame retardant.

Oligomeric phosphonate polyol CASRN 363626-50-0				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Explosivity		Not expected to form explosive mixtures with air (Estimated)	Professional judgment	No experimental data located; based on its use as a flame retardant.
Pyrolysis				No data located.
pH		4.5 at 10 g/L (Estimated)	Clariant, 2012; Clariant, 2013	Reported in a Safety Data Sheet.
pK_a				No data located.
Particle Size				No data located.
HUMAN HEALTH EFFECTS				
Toxicokinetics		**There were no experimental data located for any route of exposure. There is potential for absorption from the lungs and poor absorption is expected from the skin and gastrointestinal tract. This substance may undergo metabolic oxidation to form a carboxylic acid.**		
Dermal Absorption *in vitro*				
Absorption, Distribution, Metabolism & Excretion	**Oral, Dermal or Inhaled**			No data located.
	Other	There is potential for absorption via inhalation. Absorption is expected to be poor from the skin and gastrointestinal tract. The most relevant route of exposure is inhalation due to potential worker exposure and because greater bioavailability is expected via the inhalation route of exposure compared to the oral route. This substance may undergo metabolic oxidation to form a carboxylic acid	Professional judgment	Based on these physical chemical properties and professional judgment.

Oligomeric phosphonate polyol CASRN 363626-50-0				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Acute Mammalian Toxicity		**LOW: Based on an oral LD_{50} value >2,000 mg/kg. No data were located for the dermal and inhalation routes of exposure.**		
Acute Lethality	**Oral**	Rat oral LD_{50} >2,000 mg/kg	Clariant, 2012; Submitted confidential study	Limited study details reported in a Safety Data Sheet and in a submitted confidential study.
	Dermal			No data located.
	Inhalation			No data located.
Carcinogenicity		**MODERATE: There is uncertainty due to lack of experimental data for this substance; carcinogenic effects cannot be ruled out.**		
	OncoLogic Results			Structure could not be evaluated by OncoLogic.
	Carcinogenicity (Rat and Mouse)			No data located.
	Combined Chronic Toxicity/Carcinogenicity			No data located.
	Other			No data located.
Genotoxicity		**MODERATE: There is uncertainty due to the lack of experimental data for this endpoint. This substance was not a mutagen in bacteria in one study. DfE criteria for this endpoint require both gene mutation and chromosomal aberration assays. For instances of incomplete or inadequate mutagenicity/genotoxicity data, a Low hazard designation cannot be assigned.**		
	Gene Mutation *in vitro*	Negative for gene mutation in an Ames test.	Clariant, 2012; Submitted confidential study	Limited study details reported in a Safety Data Sheet and in a submitted confidential study.
	Gene Mutation *in vivo*			No data located.
	Chromosomal Aberrations *in vitro*			No data located.
	Chromosomal Aberrations *in vivo*			No data located.
	DNA Damage and Repair			No data located.
	Other			No data located.

Oligomeric phosphonate polyol CASRN 363626-50-0				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Reproductive Effects		**LOW: Estimated based on expert judgment and lack of structural alerts for reproductive toxicity identified for this substance. No experimental data were located.**		
	Reproduction/Developmental Toxicity Screen			No data located.
	Combined Repeated Dose with Reproduction/ Developmental Toxicity Screen			No data located.
	Reproduction and Fertility Effects			No data located.
	Other	There is low potential for reproductive effects (Estimated)	Expert judgment	Estimated based on expert judgment and the lack of structural alerts.
Developmental Effects		**MODERATE: There were no experimental data for the developmental toxicity endpoint. There were no structural alerts identified for this endpoint. There were also no experimental data located for the developmental neurotoxicity endpoint. There is uncertain potential for developmental neurotoxicity for this substance based on a structural alert for organophosphates for the neurotoxicity endpoint; decreased cholinesterase activity in pregnant lab animals has been shown to have a negative impact on fetal brain development. As a result, an estimated Moderate designation is assigned.**		
	Reproduction/ Developmental Toxicity Screen			No data located.
	Combined Repeated Dose with Reproduction/ Developmental Toxicity Screen			No data located.
	Prenatal Development			No data located.
	Postnatal Development			No data located.

Oligomeric phosphonate polyol CASRN 363626-50-0				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Prenatal and Postnatal Development			No data located.
	Developmental Neurotoxicity	Uncertain concern for developmental neurotoxicity based on the potential for Cholinesterase (ChE) inhibition in dams that may result in alterations of fetal neurodevelopment. (Estimated)	Professional judgment	Estimated based on a structural alert for organophosphates for the neurotoxicity endpoint.
	Other	There is low potential for developmental effects (Estimated)	Expert judgment	Estimated based on expert judgment and the lack of structural alerts.
Neurotoxicity		**MODERATE: Estimated to have uncertain potential for neurotoxic effects based on a structural alert for organophosphates and professional judgment. Neurotoxicity is generally decreased for phosphonates compared to phosphate esters and for structures without good leaving groups. However, there were no experimental data located, particularly for the most relevant route of exposure (inhalation). Due to the lack of data, the concern for the structural alert could not be ruled out; therefore, a conservative designation of Moderate is assigned.**		
	Neurotoxicity Screening Battery (Adult)			No data located.
	Other	There is potential for neurotoxic effects based on a structural alert for organophosphates (Estimated)	Professional judgment	Estimated based on a structural alert for organophosphates and professional judgment. Neurotoxicity is generally decreased for phosphonates when compared to phosphate esters and for structures that lack “good” leaving groups; alcohols are not considered “good” leaving groups.

Oligomeric phosphonate polyol CASRN 363626-50-0				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Repeated Dose Effects		**LOW: Estimated based on expert judgment and lack of structural alerts for repeated dose toxicity identified for this substance. No experimental data were located.**		
		Estimated to have low potential for repeated dose effects (Estimated)	Expert judgment	Estimated based on expert judgment and absence of structural alerts.
Skin Sensitization		**LOW: Estimated based on expert judgment and lack of structural alerts for skin sensitization identified for this substance. No experimental data were located.**		
	Skin Sensitization	There is low potential for skin sensitization (Estimated)	Expert judgment	Estimated based on expert judgment and the absence of structural alerts.
Respiratory Sensitization		**No data located.**		
	Respiratory Sensitization			No data located.
Eye Irritation		**LOW: No eye irritation to slight eye irritation was reported.**		
	Eye Irritation	Slight eye irritation	Professional judgment; Submitted confidential study	Data reported in a confidential study submitted to EPA.
		Not an eye irritant in rabbits.	Clariant, 2012	Limited study details reported in a Safety Data Sheet; conducted according to OECD 405.
Dermal Irritation		**VERY LOW: This substance is not a skin irritant.**		
	Dermal Irritation	Not a skin irritant; 4-hour exposure to rabbits.	Clariant, 2012; Submitted confidential study	Limited study details reported in a Safety Data Sheet and a submitted confidential study; conducted according to OECD 404.
Endocrine Activity		**No experimental data were located.**		
				No data located.
Immunotoxicity		**There were no immunotoxicity structural alerts identified for substance. There were no experimental data located.**		
	Immune System Effects	There is low potential for immunotoxic effects (Estimated)	Expert judgment	Estimated based on expert judgment and the absence of structural alerts.

Oligomeric phosphonate polyol CASRN 363626-50-0			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
ECOTOXICITY			
ECOSAR Class			
Acute Aquatic Toxicity	**LOW: Based on estimated acute aquatic toxicity values (Esters class) for representative oligomers (n=1 through n=7). Estimated values were all >100 mg/L. Experimental data in fish also indicated a Low hazard; experimental data were not located for daphnia or algae.**		
Fish LC_{50}	*Brachydanio rerio* (Zebrafish) 96-hour LC_{50} > 100 mg/L (Experimental)	Clariant, 2012; Submitted confidential study	Limited study details reported in a Safety Data Sheet and in a submitted confidential study; conducted according to OECD 203.
	Freshwater fish 96-hour LC_{50} = n=1-7: > 100 mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	Estimates based on representative oligomers where n=1 through n = 7. Estimate for the Esters class was provided for comparative purposes. See Section 5.5.1.
Daphnid LC_{50}	*Daphnia magna* 48-hour LC_{50} = n=1-7: > 100 mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	Estimates based on representative oligomers where n=1 through n=7. Estimate for the Esters class was provided for comparative purposes. See Section 5.5.1.
Green Algae EC_{50}	Green algae 96-hour EC_{50} = n=1-7: > 100 mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	Estimates based on representative oligomers where n=1 through n=7. Estimate for the Esters class was provided for comparative purposes. See Section 5.5.1.

Oligomeric phosphonate polyol CASRN 363626-50-0			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
Chronic Aquatic Toxicity	**MODERATE: The estimated chronic aquatic toxicity value derived using an acute-to-chronic ratio (ACR) for the phosphate esters class and was applied to experimental acute data for this chemical and indicated a Moderate hazard. Estimated values (Esters class) for all oligomers were >10 mg/L. There is potential concern based on estimates and the uncertainty due to the lack of experimental data; therefore a Moderate hazard designation was assigned.**		
Fish ChV	Freshwater fish ChV ≥ 4.17 mg/L (Estimated)	Professional judgment	An ACR of 24 was derived for the phosphate ester class based on experimental data for Tris (p-t-butylphenyl) phosphate (TBPP). The acute-to-chronic ratio was applied to available experimental acute fish data for oligomeric phosphonate polyol (ChV >100 mg/L /24 = 4.17 mg/L)
	Freshwater fish ChV = n=1-7: > 10 mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	Estimates based on representative oligomers where n=1 through n=7. Estimate for the Esters class was provided for comparative purposes. See Section 5.5.1. compound is not currently well represented in ECOSAR v1.11.

Oligomeric phosphonate polyol CASRN 363626-50-0			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
Daphnid ChV	Daphnia magna ChV = n=1-7: > 10 mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	Estimates based on representative oligomers where n=1 through n=7. Estimate for the Esters class was provided for comparative purposes. See Section 5.5.1. judgment indicates that this compound is not currently well represented in ECOSAR v1.11
Green Algae ChV	Green algae ChV = n=1-7: > 10 mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	Estimates based on representative oligomers where n=1 through n=7. Estimate for the Esters class was provided for comparative purposes. See Section 5.5.1.
ENVIRONMENTAL FATE			
Transport	**Level III fugacity models incorporating available physical and chemical property data indicate that at steady state, the polymer is anticipated to be found predominantly in soil, and to a lesser extent, water. The estimated Henry's Law Constant of $<10^{-8}$ atm-m^3/mole based on an estimated high water solubility and low vapor pressure indicates that the polymer is not expected to volatilize from water to the atmosphere. The estimated K_{oc} values in the range of 10-260 indicate that components of the polymer are anticipated to migrate through soil to groundwater.**		

Oligomeric phosphonate polyol CASRN 363626-50-0				
PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
	Henry's Law Constant (atm-m^3/mole)	$<10^{-8}$ for n=1-7 (Estimated)	EPI v4.11; Professional judgment	Estimates based on representative structures where n=1-7. Cutoff values for non-volatile compounds. Estimated by the HENRYWIN Bond SAR Method with no measured chemical property inputs.
	Sediment/Soil Adsorption/Desorption - K_{oc}	n=1-6: 10 n=7: 260 (Estimated)	EPI v4.11	Using MCI Method KOCWIN v 2.00, estimates based on representative structures where n=1-7.
	Level III Fugacity Model	Air = 0% Water = 12% Soil = 88% Sediment = 0% (Estimated) n=7	EPI v4.11	Estimate based on a representative structure where n=7.
		Air = 0% Water = 31% Soil = 69% Sediment = 0% (Estimated) n=1	EPI v4.11	Estimate based on a representative structure where n=1.

Oligomeric phosphonate polyol CASRN 363626-50-0				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Persistence		**MODERATE: Biodegradation is expected to be an important mechanism of removal. Phosphonates occur naturally in the environment where many strains of bacteria have been isolated that metabolize phosphonates. Although no experimental biodegradation studies were located, estimates using representative components of the polymer indicate that the lower MW components (where n≤2) are expected to have ultimate persistence with a half-life ≥16-<60 days, equivalent to a Moderate hazard designation using a conservative approach. The larger representative oligomers, outside the domain of the biodegradation estimation methods, are anticipated to behave similarly based on the chemical properties. Hydrolysis was reported in a Safety Data Sheet for this polymer. The available study details did not provide key information of the rate of hydrolysis and important test conditions, such as pH. This polymeric mixture does not contain functional groups that would be expected to absorb light at environmentally significant wavelengths; therefore degradation by direct photolysis is not expected.**		
Water	**Aerobic Biodegradation**	n=1: Days (Primary Survey Model) Weeks (Ultimate Survey Model) (Estimated)	EPI v4.11	Estimate based on a representative structure where n=1.
		n=7: Weeks (Primary Survey Model) Months (Ultimate Survey Model) (Estimated)	EPI v4.11	The higher MW oligomer where n=7 is outside the domain of the available estimation methods.
		In nature, phosphonates are found in cell membranes of plants and animals. Bacterial metabolism of phosphonates with the C-P lyase enzyme plays a major role in biodegradation of phosphonates and the phosphorus cycle in the environment. The C-P lyase enzyme, converts alkylphosphonates to the corresponding alkane and inorganic phosphate and is found in many strains of bacteria with broad specificity. Phosphonates are considered to be inherently	Ghisalba et al., 1987; Nowack, 2003	Supporting information about the bacterial biodegradation of this class of compounds.

Oligomeric phosphonate polyol CASRN 363626-50-0				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		biodegradable. (Estimated)		
	Volatilization Half-life for Model River	>1 year for n=1-7 (Estimated)	EPI v4.11	Estimates based on representative structures where n=1-7.
	Volatilization Half-life for Model Lake	>1 year for n=1-7 (Estimated)	EPI v4.11	Estimates based on representative structures where n=1-7.
Soil	**Aerobic Biodegradation**			No data located.
	Anaerobic Biodegradation	Probable (Anaerobic-methanogenic biodegradation probability model)	EPI v4.11	Estimate based on representative structure where n=1-2. Estimates indicate anaerobic biodegradation is not probable for representative structures where n=3-7.
	Soil Biodegradation with Product Identification			No data located.
	Sediment/Water Biodegradation			No data located.
Air	**Atmospheric Half-life**	n=1: 0.19 n=2: 0.13 n=3: 0.10 n=7: 0.05 (Estimated)	EPI v4.11	Estimates based on representative structures where n=1-7. The substance is expected to have limited volatility; therefore, this is not expected to be an important removal pathway.
Reactivity	**Photolysis**	Not a significant fate process (Estimated)	Professional judgment; Mill, 2000	The substance does not contain functional groups that would be expected to absorb light at wavelengths >290 nm.
	Hydrolysis	Slow hydrolysis in the presence of water (Measured)	Clariant, 2012; Clariant, 2013	No study details and no indication of hydrolysis rate were reported in the Safety Data Sheet; rates are expected to be pH dependent.
		n=1-7: >1 year at pH 5 to 9 (Estimated)	EPI v4.11	Estimates based on representative structures where for n=1-7.
Environmental Half-life		30 (Estimated)	PBT Profiler v1.301; EPI v4.11	Half-life estimated for the predominant compartment (Soil) for a representative structure where n≥1-2, as determined by EPI and the PBT

Oligomeric phosphonate polyol CASRN 363626-50-0				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
				Profiler methodology.
		>75 days (Estimated)	PBT Profiler v1.301; EPI v4.11	The higher MW oligomers where n=3-7, are outside the domain of the available estimation methods; the half-life estimated for the predominant compartment is anticipated to be shorter than the estimated output.
Bioaccumulation		**LOW: Estimated based on BCF values of 3.2 and BAF values of <1 for the representative structures of the polymeric mixture.**		
	Fish BCF	n=1-7: 3.2 (Estimated)	EPI v4.11	Estimates based on representative structures where n=1-7.
	Other BCF			No data located.
	BAF	n=1-7: 0.9 (Estimated)	EPI v4.11	Estimates based on representative structures where n=1-7.
	Metabolism in Fish			No data located.
ENVIRONMENTAL MONITORING AND BIOMONITORING				
Environmental Monitoring		No data located.		
Ecological Biomonitoring		No data located.		
Human Biomonitoring		This chemical was not included in the NHANES biomonitoring report. (CDC, 2013).		

CDC (2013) Fourth national report on human exposure to environmental chemicals, updated tables, March 2013. http://www.cdc.gov/exposurereport/pdf/FourthReport_UpdatedTables_Mar2013.pdf.

Clariant (2012) Safety data sheet in accordance with Regulation (EU) No.453/2010: EXOLIT OP 560. Clariant.

Clariant (2013) Product data sheet - Flame retardants: Exolit OP 560: Phosphorus polyols. Clariant. http://www.clariant.com/bu/additives/PDS_Additives.nsf/www/DS-OSTS-7SHC6G?open.

ECOSAR Ecological Structure Activity Relationship (ECOSAR). Estimation Programs Interface (EPI) Suite for Windows, Version 1.11. Washington, DC: EPIWIN/EPISUITE. U.S. Environmental Protection Agency. http://www.epa.gov/oppt/newchems/tools/21ecosar.htm.

EPA (1999) Determining the adequacy of existing data. High Production Volume (HPV) Challenge. Washington, DC: U.S. Environmental Protection Agency. http://www.epa.gov/hpv/pubs/general/datadeqfn.pdf.

EPA (2012) Using noncancer screening within the SF initiative. Washington, DC: U.S. Environmental Protection Agency. http://www.epa.gov/oppt/sf/pubs/noncan-screen.htm.

EPI Estimation Programs Interface (EPI) Suite, Version 4.11. Washington, DC: EPIWIN/EPISUITE. U.S. Environmental Protection Agency. http://www.epa.gov/opptintr/exposure/pubs/episuitedl.htm.

ESIS (2012) European chemical Substances Information System. European Commission. http://esis.jrc.ec.europa.eu/.

Ghisalba O, Kueenzi M, Ramostombo GM, et al. (1987) Microbial degradation and utilization of selected organophosphorus compounds Strategies and applications. 41:206-214.

Mill T (2000) Photoreactions in surface waters. In: Boethling R, Mackay D, eds. Handbook of Property Estimation Methods for Chemicals, Environmental Health Sciences. Boca Raton: Lewis Publishers.:355-381.

PBT Profiler Persistent (P), Bioaccumulative (B), and Toxic (T) Chemical (PBT) Profiler, Version 1.301. Washington, DC: U.S. Environmental Protection Agency. www.pbtprofiler.net.

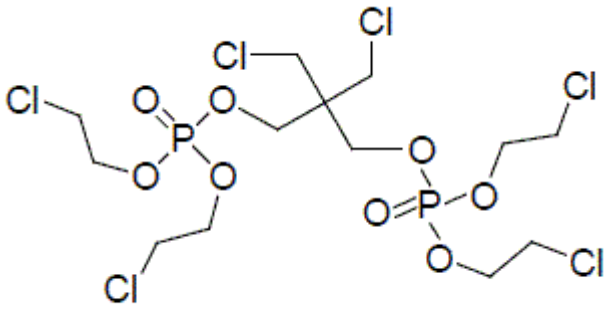
Phosphoric acid, P,P'-[2,2-bis(chloromethyl)-1,3-propanediyl] P,P,P',P'-tetrakis(2-chloroethyl) ester

Screening Level Toxicology Hazard Summary

This table contains hazard information for each chemical; evaluation of risk considers both hazard and exposure. Variations in end-of-life processes or degradation and combustion by-products are discussed in the report but not addressed directly in the hazard profiles. The caveats listed below must be taken into account when interpreting the information in the table.

VL = Very Low hazard L = Low hazard M = Moderate hazard H = High hazard VH = Very High hazard – Endpoints in colored text (VL, L, M, H, and VH) were assigned based on empirical data. Endpoints in black italics *(VL, L, M, H,* and *VH*) were assigned using values from estimation software and professional judgment [(Quantitative) Structure Activity Relationships "(Q)SAR"].

Chemical	CASRN	Human Health Effects										Aquatic Toxicity		Environmental Fate	
		Acute Toxicity	Carcinogenicity	Genotoxicity	Reproductive	Developmental	Neurological	Repeated Dose	Skin Sensitization	Respiratory Sensitization	Eye Irritation	Dermal Irritation	Acute	Chronic	Persistence	Bioaccumulation
Phosphoric acid, P,P'-[2,2-bis(chloromethyl)-1,3-propanediyl] P,P,P',P'-tetrakis(2-chloroethyl) ester	38051-10-4	L	*M*	L	M	H	L	M	L		L	L	M	*M*	H	*L*



CASRN: 38051-10-4

MW: 582.99

MF: $C_{13}H_{24}Cl_6O_8P_2$

Physical Forms: Liquid
Neat:

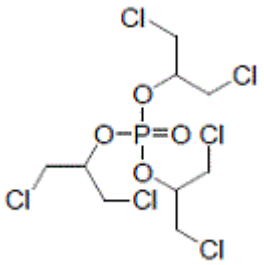
Use: Fire retardant; polyurethane foam additive

SMILES: O=P(OCCCl)(OCCCl)OCC(CCl)(CCl)COP(=O)(OCCCl)OCCCl

Synonyms: V6; Amgard V6; BCMP-BCEP; 2,2-bis(chloromethyl)trimethylene bis(bis(2-chloroethyl) phosphate); tetrekis(2-chlorethyl)dichloroisopentyldiphosphate

Chemical Considerations: This is a discrete organic chemical with a MW below 1,000. EPI v4.11 was used to estimate physical/chemical and environmental fate values due to an absence of experimental data. Commercially available forms of this chemical have a purity of >85-90% (w/w). Impurities anticipated to be present in the commercial product are: 1,2 dichloroethane (CASRN 107-06-2) and 4.5-7.5% TCEP or tris(chloroethyl) phosphate (CASRN 115-96-8) (EU, 2008a; CELLTECH, 2009).

Polymeric: No
Oligomeric: Not applicable

Metabolites, Degradates and Transformation Products: Metabolites: ethylchloride; 2-chloroethanol; parent compound missing a chloroethyl moiety; parent compound with chlorine replaced by an OH group; and parent compound with one chlorine oxidized to a carboxyl group (ECHA, 2012)	
Analog: 2-Propanol, 1,3-dichloro-, phosphate (CASRN 13674-87-8) **Endpoint(s) using analog values:** Carcinogenicity	**Analog Structure:** 
Structural Alerts: Organophosphates, neurotoxicity. The commercial product may contain an impurity, CASRN 115-96-8, that appears on the List of Chemicals Known to the State to Cause Cancer for the State of California: California Proposition 65 cancer (EPA, 2012; California EPA, 2013).	
Risk Phrases: Not classified; although the commercial product is classified based on the amount of TCEP impurity present (ECHA, 2012; ESIS, 2012).	
Hazard and Risk Assessments: A risk assessment was reported by the European Chemicals Industry; a SIDS initial assessment profile was completed under the OECD HPV chemicals program; an environmental risk assessment was completed by the EU in 2008 (EC, 2000; EU, 2008a; OECD, 2009).	

Phosphoric acid, P,P'-[2,2-bis(chloromethyl)-1,3-propanediyl] P,P,P',P'-tetrakis(2-chloroethyl) ester CASRN 38051-10-4			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
PHYSICAL/CHEMICAL PROPERTIES			
Melting Point (°C)	<-50.5 reported as a freezing point; Good laboratory practice (GLP) guideline study OECD 102, EEC Directive 92/69; test substance partially frozen but temperature did not remain constant (Measured)	OECD, 2009; ECHA, 2012	Guideline study reported for the commercial product Antiblaze V6.
	90 (Measured)	van der Veen and de Boer, 2012	Inadequate, reported in a secondary source, insufficient details available to access the quality of this value.
Boiling Point (°C)	252.29 Decomposes According to EU Method A.2, during experiment exotherm occurred resulting in a final pressure of 781.5 psi (Measured)	OECD, 2009; ECHA, 2012	Guideline study reported in a secondary source.
	>200 Decomposes Decomposition products include phosphorus oxides, carbon monoxide and chlorides (Measured)	EC, 2000; ECHA, 2012	Reported in a secondary source.
	620 (Unknown)	van der Veen and de Boer, 2012	Reported in a secondary source; citing another secondary source (ChemSpider, 2011) that could not be verified.
Vapor Pressure (mm Hg)	2.06×10^{-8} at 25°C (Estimated)	EPI v4.11	
	<0.1 at 100°C (Measured)	EC, 2000	Reported in a secondary source; test not applicable due to product decomposition.
	1.7 at 25°C	ECHA, 2012	Reported for a commercial

Phosphoric acid, P,P'-[2,2-bis(chloromethyl)-1,3-propanediyl] P,P,P',P'-tetrakis(2-chloroethyl) ester CASRN 38051-10-4			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	reported as 22.29 hPa at 25°C; according to GLP guideline study EU Method A.4 (Measured)		product Amgard V6. Value inconsistent with result expected for this chemical; high vapor pressure attributed to volatile impurities in the commercial product.
Water Solubility (mg/L)	2.1 (Measured) at 25°C	van der Veen and de Boer, 2012	Reported in a secondary source.
	232 (Measured) at 20°C, pH 7.65; GLP guideline study OECD 105 and EU Method A.6	OECD, 2009; ECHA, 2012	Reported in a secondary source for the commercial product Antiblaze V6.
	0.31 (Estimated)	EPI v4.11	
	Insoluble in water, at pH 7 (Measured)	EC, 2000	Qualitative value reported in a secondary source with limited details.
Log K_{ow}	2.83 +/- 0.05 at 20°C, pH 8.5 GLP guideline study OECD 107 and EU Method A.8; average of 6 assays ranging from 2.74-2.87 (Measured)	ECHA, 2012	Reported in a secondary source for the commercial product Antiblaze V6.
	3.3 (Estimated)	EPI v4.11	

Phosphoric acid, P,P'-[2,2-bis(chloromethyl)-1,3-propanediyl] P,P,P',P'-tetrakis(2-chloroethyl) ester CASRN 38051-10-4			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
Flammability (Flash Point)	Flash point: 191°C Closed cup; GLP study in compliance with EU Method A.9 of Commission Directive 92/69/EEC and OECD/GD(92)32 literature value of >230°C using Cleveland Open Cup, atmospheric pressure 100.39 kPa, corrected flash point 191.215°C (Measured)	EC, 2000; ECHA, 2012	Reporting in a Secondary source for the commercial product Amgard V6.
	Auto flammability: >400°C at 100 kPa GLP study in compliance with EU Method A.15 of Commission Directive 92/96/EEC and OECD (92)32; performed at 15-20°C, atmospheric pressure 100.30 to 100.99 kPa (Measured)	EC, 2000; ECHA, 2012	Reported in a secondary source.
Explosivity	Not expected to form explosive mixtures with air (Estimated)	Professional judgment	No experimental data located; based on its use as a flame retardant.
Pyrolysis			No data located.
pH	Not applicable (Estimated)	Professional judgment	Does not contain functional groups that are expected to ionize under environmental conditions.
pK_a	Not applicable (Estimated)	Professional judgment	Does not contain functional groups that are expected to ionize under environmental conditions.

Phosphoric acid, P,P'-[2,2-bis(chloromethyl)-1,3-propanediyl] P,P,P',P'-tetrakis(2-chloroethyl) ester CASRN 38051-10-4				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
HUMAN HEALTH EFFECTS				
Toxicokinetics		**Absorption of Phosphoric acid, P,P'-[2,2-bis(chloromethyl)-1,3-propanediyl] P,P,P',P'-tetrakis(2-chloroethyl) ester (V6) from the gastrointestinal tract is nearly 100% following oral exposure in rats. V6 and metabolites are distributed throughout the body. Excretion occurred via the biliary route (60%), in urine (20%) and as exhaled $^{14}CO_2$. Absorption of V6 via the dermal route in human skin membranes was low (0.51% and 6% for undiluted V6 or in an ethanol vehicle, respectively). No inhalation studies were located.**		
Dermal Absorption *in vitro*		*In vitro* dermal absorption study in human skin membranes; the delivery of undiluted V6 and V6 in ethanol (0.2 mg/cm$^{3)}$ was 0.51% and 6%, respectively.	EU, 2008b; OECD, 2009	Study details reported in a secondary source. Study was conducted in accordance with OECD Guideline 428 and to GLP.
Absorption, Distribution, Metabolism & Excretion	**Oral, Dermal or Inhaled**	Oral administration of ^{14}C labeled Phosphoric acid, P,P'-[2,2-bis(chloromethyl)-1,3-propanediyl] P,P,P',P'-tetrakis(2-chloroethyl) ester (V6) in the rat. Bioavailability was ≥ 100% at the low dose (15 mg/kg) and ~ 50% at the high dose (600 mg/kg). Complete absorption from the gastrointestinal tract at 15 mg/kg. Elimination half-life was 99 - 113 hours; excretion via the biliary route (60%) and urine (20%) with the remainder exhaled as $^{14}CO_2$. V6 and metabolites were distributed throughout the body (no target organs); four major metabolites were identified in feces.	EU, 2008b; OECD, 2009	Study details reported in a secondary source. Study was conducted in accordance with OECD Guideline 417 and to GLP.
	Other			No data located.

Phosphoric acid, P,P'-[2,2-bis(chloromethyl)-1,3-propanediyl] P,P,P',P'-tetrakis(2-chloroethyl) ester CASRN 38051-10-4				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Acute Mammalian Toxicity		**LOW: Phosphoric acid, P,P'-[2,2-bis(chloromethyl)-1,3-propanediyl] P,P,P',P'-tetrakis(2-chloroethyl) ester (V6) is not acutely toxic via the oral or inhalation routes of exposure in rats or via the dermal route of exposure in rabbits.**		
Acute Lethality	**Oral**	Rat oral LD_{50} = between 2,000 – 5,000 mg/kg Mortality (all within 48 hours of dosing) was 1/10 at the low dose and 8/10 at the high dose	EU, 2008b (as cited in OECD, 2009)	Study details reported in a secondary source. Study conformed to OPPTS or OECD guidelines except that survivors were not necropsied.
		Rat oral LD_{50} >2,000 mg/kg	Submitted confidential study	Test substance purity and composition not specified; conducted according to OECD 401.
	Dermal	Rabbit dermal LD_{50} >2,000 mg/kg	Submitted confidential study (as cited in EU, 2008b; OECD, 2009)	Study details reported in a secondary source. Study was conducted to OECD Guideline 402.
	Inhalation	Rat inhalation (snout only) 4-hour LC_{50} >1.65 mg/L (highest attainable aerosol concentration)	Submitted confidential study (as cited in EU, 2008b; OECD, 2009)	Study details reported in a secondary source and in a confidential study submitted to EPA. Study was conducted in accordance with OECD Guideline 403.
Carcinogenicity		**MODERATE: Based on the weight of evidence. There were no carcinogenicity studies located for Phosphoric acid, P,P'-[2,2-bis(chloromethyl)-1,3-propanediyl] P,P,P',P'-tetrakis(2-chloroethyl) ester (V6), however; there was no evidence of mutagenicity from genotoxicity studies. The OncoLogic program estimated a Low-Moderate concern for carcinogenicity and there was an increase in benign tumors of the adrenal cortex and liver in a 2-year study with an analog chemical 2-Propanol, 1,3-dichloro-, phosphate (CASRN 13674-87-8). Due to concerns based on structure and analogs, a moderate hazard designation is warranted.**		
	OncoLogic Results	Low-moderate concern	OncoLogic, 2008	
	Carcinogenicity (Rat and Mouse)			No data located.

Phosphoric acid, P,P'-[2,2-bis(chloromethyl)-1,3-propanediyl] P,P,P',P'-tetrakis(2-chloroethyl) ester CASRN 38051-10-4				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Combined Chronic Toxicity/Carcinogenicity	In a 2-year combined oral chronic toxicity and carcinogenicity assay, Sprague-Dawley rats (60/sex/group) were fed diets that provided doses of containing 0, 5, 20, and 80 mg/kg-day of the analog 2-Propanol, 1,3-dichloro-, phosphate. Increased benign tumors of the adrenal cortex in high-dose females, and hepatocellular adenomas in high-dose males and females, interstitial cell tumors in the testes of high-dose males, and renal cortical adenomas in mid- and high-dose males and females.at 20 and 80 mg/kg-day. (Estimated by analogy)	Freudenthal and Henrich, 2000	Estimated based on analogy to 2-Propanol, 1,3-dichloro-, phosphate (CASRN 13674-87-8). The NRC (2000) concluded that this study provides sufficient evidence of carcinogenicity of TDCPP in rats following chronic oral exposure. Test substance purity: 95%; The mode of action for carcinogenicity could not be determined.
	Other			No data located.
Genotoxicity		**LOW: Based on no evidence of mutagenicity in either *in vitro* or *in vivo* genotoxicity studies.**		
	Gene Mutation *in vitro*	Negative, gene mutations in mouse lymphoma cells with and without metabolic activation.	King, 1993 (as cited in OECD, 2009)	Study was conducted in accordance with OECD Guideline 476; however, no information was provided regarding positive controls.
		Negative, *Salmonella typhimurium* strains TA98 and TA100 with or without metabolic activation	EC, 2000; OECD, 2009	Study details reported in a secondary source. Study was conducted in accordance with OECD Guideline 471 and GLP.
		Negative, *Salmonella typhimurium* strains TA 1535, TA1537, TA98 and TA100 with or without metabolic activation	Submitted confidential study	Study details reported in a confidential study submitted to EPA; test substance purity: 92.3%
	Gene Mutation *in vivo*			No data located.

Phosphoric acid, P,P'-[2,2-bis(chloromethyl)-1,3-propanediyl] P,P,P',P'-tetrakis(2-chloroethyl) ester CASRN 38051-10-4				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Chromosomal Aberrations *in vitro*	Negative, chromosomal aberrations in cultured human lymphocytes with and without metabolic activation; Positive controls yielded expected responses.	EC, 2000; OECD, 2009	Study details reported in a secondary source. Study was conducted in accordance with OECD Guideline 473and GLP.
	Chromosomal Aberrations *in vivo*	Negative, micronucleus formation in bone marrow of mice exposed by to two oral treatments (oral gavage) at a 24-hour interval to 500, 1,000, or 2,000 mg/kg-day (males); 437.5, 875, 1,750 mg/kg-day. Positive controls yielded expected responses.	Submitted confidential study (as cited in OECD, 2009)	Study details reported in a secondary source and in a submitted confidential study. Study was conducted in accordance with OECD Guideline 474.
	DNA Damage and Repair			No data located.
	Other			No data located.
Reproductive Effects		**MODERATE: Based on weight of evidence from multiple studies. Phosphoric acid, P,P'-[2,2-bis(chloromethyl)-1,3-propanediyl] P,P,P',P'-tetrakis(2-chloroethyl) ester (V6) did not produce reproductive toxicity in an oral 2-generation reproductive study or in a 4-week gavage study in rats at doses up to 600 mg/kg-day (LOAELs were not established). Data using the analog 2-Propanol, 1,3-dichloro-, phosphate reported a LOAEL of 5 mg/kg-day (NOAEL not established) for atrophy and decreased secretory product of the seminal vesicle in an oral two-year combined chronic toxicity and carcinogenicity assay in rats. A 12-week fertility study in rabbits using the analog 2-Propanol, 1,3-dichloro-, phosphate reported a NOAEL of 200 mg/kg-day; there is uncertainty if reproductive effect could occur at a dose up to 250 mg/kg-day (the cutoff for the Moderate hazard designation criteria range).**		
	Reproduction/Developmental Toxicity Screen			No data located.
	Combined Repeated Dose with Reproduction/ Developmental Toxicity Screen			No data located.

Phosphoric acid, P,P'-[2,2-bis(chloromethyl)-1,3-propanediyl] P,P,P',P'-tetrakis(2-chloroethyl) ester CASRN 38051-10-4				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Reproduction and Fertility Effects	In an oral 2-generation reproductive toxicity study, rats (28/sex) were fed diets containing the test chemical Phosphoric acid, P,P'-[2,2-bis(chloromethyl)-1,3-propanediyl] P,P,P',P'-tetrakis(2-chloroethyl) ester (0, 29, 86 or 262 mg/kg-day for males and 0, 33, 97 or 302 mg/kg-day for females). No effects on the male and female reproductive systems up to the highest doses tested. NOAEL (fertility): 262 and 302 mg/kg-day for males and females, respectively (highest dose tested) LOAEL: Not established	EU, 2008a; OECD, 2009	Study details reported in a secondary source. Study was conducted in accordance with OECD Guideline 416; however, corpora lutea were not counted at scheduled sacrifice, which represented a deviation from the guideline.
		In a 12-week oral fertility study, rabbits (10 males/dose) were gavaged with 0, 2, 20, or 200 mg/kg-day of the analog 2-Propanol, 1,3-dichloro-, phosphate. Males were treated for 12 weeks, then mated with untreated females. There were no alterations in mating behavior, fertility, or sperm quantity or quality. Neither gross necropsy nor microscopic examinations showed significant alterations in the reproductive tract. NOAEL: 20 mg/kg-day LOAEL: 200 mg/kg-day (highest dose tested) (Estimated by analogy)	Wilczynski et al., 1983; ATSDR, 2012	Study details were available in the secondary source. Estimated by analogy to 2-Propanol, 1,3-dichloro-, phosphate (CASRN 13674-87-8). Data not sufficient to satisfy the reproductive toxicity endpoint since it was described only in an abstract and there was a lack of information in female animals. This limits the usefulness of the study for risk assessment.

Phosphoric acid, P,P'-[2,2-bis(chloromethyl)-1,3-propanediyl] P,P,P',P'-tetrakis(2-chloroethyl) ester CASRN 38051-10-4				
PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
	Other	A confidential, 4-week repeated-dose oral gavage study in rats was submitted. No histopathology was found in the reproductive organs in either sex at a NOAEL of 600 mg/kg-day of the test chemical; however, the study duration was relatively short and reproductive function was not tested. NOAEL: 600 mg/kg-day (highest dose tested) LOAEL: Not established	Submitted confidential study	Study was conducted in accordance with OECD Guideline 407
		Rat, oral, 2-year combined chronic toxicity and carcinogenicity assay; Rats (60/sex/group) were administered 0, 5, 20, 80 mg/kg-day (in the diet) of the analog 2-Propanol, 1,3-dichloro-, phosphate for 2 years. Ten rats/sex/dose were randomly chosen for termination at 12 months; the remainder at 24 months. Reproductive effects in males included effects on seminal vesicles (atrophy, decreased secretory product) at = 5 mg/kg-day, testes (eosinophilic material in lumen, periarteritis nodosa) at = 20 mg/kg-day, and epididymis (oligospermia and degenerated seminal product) at 80 mg/kg-day. NOAEL: Not established LOAEL: 5 mg/kg-day	Freudenthal and Henrich, 2000	Estimated by analogy to 2-Propanol, 1,3-dichloro-, phosphate (CASRN 13674-87-8); Fertility was not assessed in the study. The authors reported the lowest dose of 5 mg/kg-day as a NOAEL and the mid-dose of 20 mg/kg-day as a LOAEL. However, as evaluated in NRC (2000), the lowest dose of 5 mg/kg-day was a LOAEL for atrophy and decreased secretory product of the seminal vesicle; test substance purity: 95%; These effects for reproductive tissues are reported from a 2-year combined chronic toxicity and carcinogenicity assay, and not from a study designed to test reproductive effects specifically; other reproductive parameters were not examined.

Phosphoric acid, P,P'-[2,2-bis(chloromethyl)-1,3-propanediyl] P,P,P',P'-tetrakis(2-chloroethyl) ester CASRN 38051-10-4				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Developmental Effects		**HIGH: Based on a NOAEL of 29 mg/kg-day (LOAEL of 86 mg/kg-day) for increased number of runts and decreased pup weight in an oral 2-generation study in rats. No developmental NOAEL/LOAEL could be established in a prenatal toxicity study in rats due to low survival of dams. There were no data located for the developmental neurotoxicity endpoint. Uncertain concern for the developmental neurotoxicity based on the potential for Cholinesterase (ChE) inhibition in dams that may result in alterations of fetal neurodevelopment.**		
	Reproduction/ Developmental Toxicity Screen			No data located.

Phosphoric acid, P,P'-[2,2-bis(chloromethyl)-1,3-propanediyl] P,P,P',P'-tetrakis(2-chloroethyl) ester CASRN 38051-10-4				
PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
	Combined Repeated Dose with Reproduction/ Developmental Toxicity Screen	In an oral 2-generation reproductive toxicity study, rats were fed diets containing Phosphoric acid, P,P'-[2,2-bis(chloromethyl)-1,3-propanediyl] P,P,P',P'-tetrakis(2-chloroethyl) ester (the overall intake of V6 was (0, 29, 86 or 262 mg/kg-day for males and 0, 33, 97 or 302 mg/kg-day for females). Increased number of runts on post-natal day one and decrease in pup weights in mid- and high-dose groups of both generations. Decreased absolute spleen weight in high dose F0 pups and in all treated F1 pups; decreased relative spleen weight (high dose F1 pups), decreased absolute brain weight but increase in relative liver weights (all treated F1 pups), decreased absolute thymus weights (low and high dose F1 pups). Maternal toxicity: NOAEL: 33 mg/kg-day LOAEL: 97 mg/kg-day Developmental toxicity: NOAEL: 29 and 33 mg/kg-day for males and females, respectively LOAEL: 86 and 97 mg/kg-day for males and females, respectively (based on increased number of runts and decreased pup weight)	EU, 2008b; OECD, 2009	Study details reported in a secondary source. Study was conducted in accordance with OECD Guideline 416; however, corpora lutea were not counted at scheduled sacrifice, which represented a deviation from the guideline.

Phosphoric acid, P,P'-[2,2-bis(chloromethyl)-1,3-propanediyl] P,P,P',P'-tetrakis(2-chloroethyl) ester CASRN 38051-10-4				
PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
	Prenatal Development	Pregnant rats (5/group) were orally gavaged with 0, 100, 200, 400, 800, and 1,600 mg/kg-day Phosgard 2XC20 (CASRN 38051-10-4) on GD 6-19. Uterine examinations were conducted on GD 20. Maternal toxicity occurred at the three highest doses. One rat at 800 mg/kg and all rats at 1,600 mg/kg died between GD 7 and 9, the cause of death was not determined. Clinical signs of toxicity in dams included dry red matter around the nose and forepaws (400 and 800 mg/kg-day) and staining of the anogenital area (800 mg/kg-day). Reduced maternal body weight (800 mg/kg-day). No biologically significant differences in the mean numbers of viable fetuses, post implantation loss, early or late resorption, total implantations or corpora lutea. A slight increase in mean post implantation losses at 800 mg/kg-day was similar to historical controls. Maternal toxicity: NOAEL: 400 mg/kg-day LOAEL: 800 mg/kg-day (based on clinical signs and increased mortality) Fetal toxicity: NOAEL: 800 mg/kg-day LOAEL:1,600 mg/kg-day	Condray, 1990	Limited study details of a pilot rat teratology study provided in secondary source (no quantitative data were shown). Adequate primary source. The small group size (four surviving dams) prevents the identification of fetal NOAEL/LOAEL values. In addition, the only fetal effect (marginal increase in postimplantation loss) occurred at a maternally toxic dose.
		Pregnant Sprague-Dawley rats (20/dose)	Kapp et al., 1981	Estimated by analogy to 2-

Phosphoric acid, P,P'-[2,2-bis(chloromethyl)-1,3-propanediyl] P,P,P',P'-tetrakis(2-chloroethyl) ester CASRN 38051-10-4				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		were gavaged with 0, 25, 100, and 400 mg/kg-day of analog 2-Propanol, 1,3-dichloro-, phosphate on GD 6-15. Dams were sacrificed on Gd 19. No effect on implantation efficiency or mean number of corpora lutea. Increased the number of resorptions and reduced fetal viability at the high dose. Maternal toxicity: NOAEL: 25 mg/kg-day LOAEL: 100 mg/kg-day (clinical signs and transient reduction in body weight gain) Fetal toxicity: NOAEL: 100 mg/kg-day LOAEL: 400 mg/kg-day (increased resorption and fetal mortality) (Estimated by analogy)		Propanol, 1,3-dichloro-, phosphate (CASRN 13674-87-8)
	Postnatal Development			No data located.
	Prenatal and Postnatal Development			No data located.
	Developmental Neurotoxicity	Uncertain concern for developmental neurotoxicity based on the potential for Cholinesterase (ChE) inhibition in dams that may result in alterations of fetal neurodevelopment (Estimated)	Professional judgment	Estimated based on a structural alert for organophosphates for the neurotoxicity endpoint.
	Other			No data located.

Phosphoric acid, P,P'-[2,2-bis(chloromethyl)-1,3-propanediyl] P,P,P',P'-tetrakis(2-chloroethyl) ester CASRN 38051-10-4				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Neurotoxicity		**LOW: Phosphoric acid, P,P'-[2,2-bis(chloromethyl)-1,3-propanediyl] P,P,P',P'-tetrakis(2-chloroethyl) ester (V6) was not neurotoxic to rats in a 4-week gavage study at doses up to 600 mg/kg-day (LOAEL not established). The only effect in several acute studies in rats was depressed serum cholinesterase activity following oral gavage of 250-1,500 mg/kg-day. In addition, no changes indicative of neurotoxicity were observed in an acute and a 90-day delayed neurotoxicity study in hens gavaged with analog chemical 2-Propanol, 1,3-dichloro-, phosphate (CASRN 13674-87-8).**		
	Neurotoxicity Screening Battery (Adult)	In a 4-week repeated-dose oral gavage study in rats included a neurotoxicity screening battery. No behavioral effects or neurohistopathology were found at the highest dose tested. NOAEL: 600 mg/kg-day (the highest dose tested) LOAEL: Not established	Submitted confidential study; EU, 2008b	Study details reported in a secondary source. Study conducted to OECD guideline 424 (neurotoxicological investigation).
	Other	In several acute rat studies, cholinesterase activity was depressed following oral gavage of 250 – 1,500 mg/kg test substance. In rabbits dermally administered 2,000 mg/kg test substance, no significant suppression of cholinesterase activity was measured in serum, whole blood or the brain within 24 hours. NOAEL: Not established LOAEL: 250 mg/kg (by oral gavage) based on cholinesterase activity	Submitted confidential study; EU, 2008b	Limited study details reported.
		In an acute oral and a 90-day delayed neurotoxicity study in hens gavaged with 2-Propanol, 1,3-dichloro-, phosphate, there was no inhibition of brain neurotoxic esterase (NTE) activity at a	Morey et al., 1978	Estimated by analogy to 2-Propanol, 1,3-dichloro-, phosphate (CASRN 13674-87-8).

Phosphoric acid, P,P'-[2,2-bis(chloromethyl)-1,3-propanediyl] P,P,P',P'-tetrakis(2-chloroethyl) ester CASRN 38051-10-4				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		dose of 10,000 mg/kg-day and no behavioral effects or histopathological changes indicative of neurotoxicity at doses up to 100 mg/kg-day. NOAEL: Not established LOAEL: 10,000 mg/kg-day (Estimated by analogy)		
Repeated Dose Effects		**MODERATE: Based on a NOAEL of 29 mg/kg-day (LOAEL= 86 mg/kg-day) for liver and thyroid weight changes and associated histopathology in an oral 2-generation study in rats. Liver effects were also observed in rats at a dose of 150 mg/kg-day following oral administration for 28 days (NOAEL = 15 mg/kg-day). No neurological effects were reported in a 4-week repeated-dose oral study in rats at a dose of 600 mg/kg-day (highest dose tested). In a 2-year combined oral chronic toxicity and carcinogenicity study in rats using analog chemical, 2-Propanol, 1,3-dichloro-, phosphate (CASRN 13674-87-8), a LOAEL of 5 mg/kg-day (lowest dose tested) was established for anomalies of the liver, kidneys, testes, renal cortex, and adrenal cortex.**		

Phosphoric acid, P,P'-[2,2-bis(chloromethyl)-1,3-propanediyl] P,P,P',P'-tetrakis(2-chloroethyl) ester CASRN 38051-10-4				
PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
		In an oral 2-generation reproductive toxicity study, rats (28/sex) were fed diets containing Phosphoric acid, P,P'-[2,2-bis(chloromethyl)-1,3-propanediyl] P,P,P',P'-tetrakis(2-chloroethyl) ester over 2 successive generations (approximately 0, 29, 86 or 262 mg/kg-day for males and 0, 33, 97 or 302 mg/kg-day for females). Increased absolute and relative thyroid weight, accompanied by follicular hypertrophy and a reduction in colloid in males (F0 generation, mid- and high dose); increased absolute and relative liver weight (both generations) accompanied by hepatocyte hypertrophy (F0 generation). NOAEL (parental): 29 and 33 mg/kg-day for males and females, respectively LOAEL (parental): 86 and 97 mg/kg-day for males and females, respectively (based on liver and thyroid weight changes and histopathology in mid- and high-dose groups)	EU, 2008a; OECD, 2009	Study details reported in a secondary source. Study was conducted in accordance with OECD Guideline 416.
		In a 28-day oral study, V6 was administered to rats via gavage at doses of 0, 15, 150, or 600 mg/kg-day. Increased relative and absolute liver weight, hepatocellular hypertrophy and centrilobular hypertrophy (150 and 600 mg/kg-day); significantly increased cholesterol levels, increases in absolute	Submitted confidential study (as cited in EU, 2008b; OECD, 2009)	Study details reported in a secondary source with more details provided in a submitted confidential study. Study was conducted in accordance with OECD Guideline 407 and 424 (neurotoxicological investigation).

Phosphoric acid, P,P'-[2,2-bis(chloromethyl)-1,3-propanediyl] P,P,P',P'-tetrakis(2-chloroethyl) ester CASRN 38051-10-4				
PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
		and relative thyroid weight, increased prothrombin time (600 mg/kg-day); NOAEL: 15 mg/kg-day LOAEL: 150 mg/kg-day (based on liver effects)		
		A 4-week repeated-dose oral gavage study in rats included a neurotoxicity screening battery. No behavioral effects or neurohistopathology were found at the highest dose tested. NOAEL: 600 mg/kg-day (the highest dose tested) LOAEL: Not established	Submitted confidential study; EU, 2008b	Study details reported in a secondary source. Study conducted to OECD guideline 424 (neurotoxicological investigation)
		In a 2-year combined oral chronic toxicity and carcinogenicity assay, Sprague-Dawley rats (60/sex/group) were fed diets containing 0, 5, 20, and 80 mg/kg-day of analog 2-Propanol, 1,3-dichloro-, phosphate. Increased mortality, decreased body weight, anomalies of the liver, kidneys, testes, renal cortex, and adrenal cortex. NOAEL: Not established LOAEL: 5 mg/kg-day (based on atrophy and decreased secretory product of the seminal vesicle; hyperplasia of convoluted tubule epithelium in males at 24 months) (Estimated by analogy)	Freudenthal and Henrich, 2000	Estimated by analogy to 2-Propanol, 1,3-dichloro-, phosphate (CASRN 13674-87-8)

Phosphoric acid, P,P'-[2,2-bis(chloromethyl)-1,3-propanediyl] P,P,P',P'-tetrakis(2-chloroethyl) ester CASRN 38051-10-4				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Skin Sensitization		**LOW: Phosphoric acid, P,P'-[2,2-bis(chloromethyl)-1,3-propanediyl] P,P,P',P'-tetrakis(2-chloroethyl) ester (V6) did not produce dermal sensitization in guinea pigs or in human volunteers. A single submitted confidential study reported mild skin sensitization in 17% of tested guinea pigs; however, these data could not be validated.**		
	Skin Sensitization	In a maximization test in guinea pigs (20 test animals and 10 controls) treated intradermally with diluted V6, induced topically with neat material, and challenged with both neat and diluted test material, V6 lacked significant skin sensitization potential.	EU, 2008b; OECD, 2009	Study details reported in a secondary source. Study was conducted in accordance with OECD Guideline 406.
		Not sensitizing to humans following 6 days of treatment and a 48-hour challenge application	Submitted confidential study	Limited study details reported.
		Mild skin sensitization, guinea pigs (17% of animals showing positive results, no further details provided) in a Magnusson and Kligman Maximization study; intradermal induction: 5% w/v in 6% acetone v/v in arachis oil B.P.; topical induction: undiluted as supplied; topical challenge: undiluted as supplied and 75% v/v in acetone., no further details provided)	Submitted confidential study	Study details from reported in a confidential study; purity of supplied test substance not specified.
Respiratory Sensitization		**No data were located.**		
	Respiratory Sensitization			No data located.

Phosphoric acid, P,P'-[2,2-bis(chloromethyl)-1,3-propanediyl] P,P,P',P'-tetrakis(2-chloroethyl) ester CASRN 38051-10-4				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Eye Irritation		**LOW: Phosphoric acid, P,P'-[2,2-bis(chloromethyl)-1,3-propanediyl] P,P,P',P'-tetrakis(2-chloroethyl) ester (V6) produced slight conjunctival irritation in rabbits which resolved within 24 or 48 hours.**		
	Eye Irritation	Not irritating, rabbits (n=3). Monitoring of ocular damage/irritation was done for up to 72 hours after instillation of 0.1 mL of V6. No corneal or iridial response; slight conjunctival redness in one rabbit 24 hours post-instillation which was reversible within 48 hours.	EC, 2000	Study details reported in a secondary source. Study was conducted in accordance with OECD Guideline 405 and GLP.
		Not irritating, rabbits (n=3). Monitoring of ocular damage/irritation was done for up to 72 hours after instillation of 0.1 mL of V6. No corneal or iridial response. Minimal conjunctival irritation was noted in all treated eyes 1 hour post-instillation. All treated eyes appeared normal 24 hours post-treatment. classified as non-irritating	Submitted confidential study (as cited in EU, 2008b)	Study details reported in a submitted confidential study; conducted according to OECD 405; test substance purity not specified.
Dermal Irritation		**LOW: Phosphoric acid, P,P'-[2,2-bis(chloromethyl)-1,3-propanediyl] P,P,P',P'-tetrakis(2-chloroethyl) ester (V6) produced slight irritation (erythema, but no edema) in rabbits which resolved within 48 or 72 hours.**		
	Dermal Irritation	Slightly irritating to the intact skin of rabbits (n=3) after semi-occluded application of 0.5 mL V6 for 4 hours.	EU, 2008b	Study details reported in a secondary source. Study was conducted in accordance with OECD Guideline 404 and GLP.
		Slight irritation (erythema but no edema) in rabbits following a 4-hour semi-occluded exposure to 0.5 g of V6. All treated skin sites had returned to normal by 24 hours post-treatment	Submitted confidential study (as cited in EU, 2008b)	Study details reported in a secondary source and a submitted confidential study. Study was conducted in accordance with OECD Guideline 404 and GLP.
		4-hour semi-occluded application to 0.5 g of V6;	Submitted confidential study (as cited in EU, 2008b)	Study details reported in a submitted confidential study and a

Phosphoric acid, P,P'-[2,2-bis(chloromethyl)-1,3-propanediyl] P,P,P',P'-tetrakis(2-chloroethyl) ester CASRN 38051-10-4				
PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
		Not irritating, rabbits. Barely perceptible irritation (erythema) was detected in 2/3 females at 26 hours, but in none at 72 hours classified as mild irritant Produced a primary irritation index of 1.2 and was classified as a mild irritant to rabbit skin according to the Draize classification scheme. No corrosive effects were noted.		secondary source; conducted according to OECD 404; The test material did not produce positive criteria in any rabbit according to the EEC labeling regulations and was classified as Non-irritant to rabbit skin. No symbol and risk phrase are required; test substance purity and formulation was not reported.

Phosphoric acid, P,P'-[2,2-bis(chloromethyl)-1,3-propanediyl] P,P,P',P'-tetrakis(2-chloroethyl) ester CASRN 38051-10-4			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
Endocrine Activity	**There were thyroid weight changes and associated histopathology in an oral 2-generation study in rats and there was an increase in benign tumors of the adrenal cortex and liver in a 2-year study with an analog chemical 2-Propanol, 1,3-dichloro-, phosphate (CASRN 13674-87-8).**		
	In an oral 2-generation reproductive toxicity study, rats (28/sex) were fed diets containing Phosphoric acid, P,P'-[2,2-bis(chloromethyl)-1,3-propanediyl] P,P,P',P'-tetrakis(2-chloroethyl) ester over 2 successive generations (approximately 0, 29, 86 or 262 mg/kg-day for males and 0, 33, 97 or 302 mg/kg-day for females). Increased absolute and relative thyroid weight, accompanied by follicular hypertrophy and a reduction in colloid in males (F0 generation, mid- and high dose); increased absolute and relative liver weight (both generations) accompanied by hepatocyte hypertrophy (F0 generation). NOAEL (parental): 29 and 33 mg/kg-day for males and females, respectively LOAEL (parental): 86 and 97 mg/kg-day for males and females, respectively (based on liver and thyroid weight changes and histopathology in mid- and high-dose groups).	EU, 2008b	Study details reported in a secondary source. Study was conducted in accordance with OECD Guideline 416.
	In a 28-day oral study, V6 was administered to rats via gavage at doses of 0, 15, 150, or 600 mg/kg-day. Increased relative and absolute liver weight, hepatocellular hypertrophy and centrilobular hypertrophy (150 and 600 mg/kg-day); significantly increased	Submitted confidential study (as cited in EU, 2008b; OECD, 2009)	Study details reported in a secondary source with more details provided in a submitted confidential study. Study was conducted in accordance with OECD Guideline 407 and 424 (neurotoxicological investigation).

Phosphoric acid, P,P'-[2,2-bis(chloromethyl)-1,3-propanediyl] P,P,P',P'-tetrakis(2-chloroethyl) ester CASRN 38051-10-4			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	cholesterol levels, increases in absolute and relative thyroid weight, increased prothrombin time (600 mg/kg-day); NOAEL: 15 mg/kg-day LOAEL: 150 mg/kg-day (based on liver effects)		
	In a 2-year combined oral chronic toxicity and carcinogenicity assay, Sprague-Dawley rats (60/sex/group) were fed diets containing 0, 5, 20, and 80 mg/kg-day 2-Propanol, 1,3-dichloro-, phosphate. Increased mortality, decreased body weight, anomalies of the liver, kidneys, testes, renal cortex, and adrenal cortex. NOAEL: Not established LOAEL: 5 mg/kg-day (based on atrophy and decreased secretory product of the seminal vesicle; hyperplasia of convoluted tubule epithelium in males at 24 months) (Estimated by analogy)	Freudenthal and Henrich, 2000	Estimated by analogy to 2-Propanol, 1,3-dichloro-, phosphate (CASRN 13674-87-8).
	In an oral 2-generation reproductive toxicity study, rats (28/sex) were fed diets containing Phosphoric acid, P,P'-[2,2-bis(chloromethyl)-1,3-propanediyl] P,P,P',P'-tetrakis(2-chloroethyl) ester over 2 successive generations (approximately 0, 29, 86 or 262 mg/kg-day for males and 0, 33, 97 or 302 mg/kg-day for females). Increased absolute and relative thyroid weight, accompanied by follicular hypertrophy and a reduction in colloid in males (F0 generation, mid- and high dose); increased absolute and relative	EU, 2008a; OECD, 2009	Study details reported in a secondary source. Study was conducted in accordance with OECD Guideline 416.

Phosphoric acid, P,P'-[2,2-bis(chloromethyl)-1,3-propanediyl] P,P,P',P'-tetrakis(2-chloroethyl) ester CASRN 38051-10-4			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	liver weight (both generations) accompanied by hepatocyte hypertrophy (F0 generation). NOAEL (parental): 29 and 33 mg/kg-day for males and females, respectively LOAEL (parental): 86 and 97 mg/kg-day for males and females, respectively (based on liver and thyroid weight changes and histopathology in mid- and high-dose groups)		
	In a 2-year combined oral chronic toxicity and carcinogenicity assay, Sprague-Dawley rats (60/sex/group) were fed diets that provided doses of containing 0, 5, 20, and 80 mg/kg-day 2-Propanol, 1,3-dichloro-, phosphate. Increased benign tumors of the adrenal cortex in high-dose females, and hepatocellular adenomas in high-dose males and females, interstitial cell tumors in the testes of high-dose males, and renal cortical adenomas in mid- and high-dose males and females at 20 and 80 mg/kg-day. (Estimated by analogy)	Freudenthal and Henrich, 2000	Estimated by analogy to 2-Propanol, 1,3-dichloro-, phosphate (CASRN 13674-87-8).

Phosphoric acid, P,P'-[2,2-bis(chloromethyl)-1,3-propanediyl] P,P,P',P'-tetrakis(2-chloroethyl) ester CASRN 38051-10-4				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Immunotoxicity		**Decreased absolute and relative spleen weights and decreased absolute thymus weights were observed in pups in an oral 2-generation reproductive toxicity study in rats.**		
	Immune System Effects	In an oral 2-generation reproductive toxicity study, rats were fed diets containing Phosphoric acid, P,P'-[2,2-bis(chloromethyl)-1,3-propanediyl] P,P,P',P'-tetrakis(2-chloroethyl) ester (the overall intake of V6 was (0, 29, 86 or 262 mg/kg-day for males and 0, 33, 97 or 302 mg/kg-day for females). Decreased absolute spleen weight in high dose F0 pups and in all treated F1 pups; decreased relative spleen weight in high dose F1 pups. Decreased absolute thymus weights in low and high dose F1 pups.	EU, 2008b; OECD, 2009	
ECOTOXICITY				
ECOSAR Class				
Acute Aquatic Toxicity		**MODERATE: Based on experimental fish acute LC_{50} of 52 mg/L and a daphnid EC_{50} of 42 mg/L. Phosphoric acid, P,P'-[2,2-bis(chloromethyl)-1,3-propanediyl] P,P,P',P'-tetrakis(2-chloroethyl) ester (V6) is not acutely toxic to algae according to experimental studies.**		
Fish LC_{50}		Freshwater fish (*Oncorhynchus mykiss*) 96-hour LC_{50} = 52 mg/L 96-hour NOEC=38 mg/L; measured concentrations were generally within 20% of initial concentrations (semi-static test conditions) (Experimental)	Submitted confidential study (as cited in EU, 2008b; OECD, 2009)	Limited study details reported in a secondary source with more study details reported in a submitted confidential study; study was conducted in accordance with OECD Guideline 203 and GLP.
		Freshwater fish (*Oncorhynchus mykiss*) 96-hour LC_{50} > 10 mg/L NOEC > 10 mg/L The study was conducted under	EC, 2000	Limited study details reported in a secondary source. Study was conducted in accordance with OECD Guideline 203 and GLP.

Phosphoric acid, P,P'-[2,2-bis(chloromethyl)-1,3-propanediyl] P,P,P',P'-tetrakis(2-chloroethyl) ester CASRN 38051-10-4			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	semistatic conditions (Experimental)		Analytical monitoring was not performed.
	Freshwater fish 96-hour LC_{50} = 13.46 mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	Estimate for the Esters class was provided for comparative purposes. See Section 5.5.1. The toxicity value exceeds the water solubility by10 times; NES is predicted.
Daphnid LC_{50}	*Daphnia magna* 48-hour EC_{50} > 10 mg/L NOEC > 10 mg/L (Experimental)	EC, 2000; EU, 2008b	Limited study details reported in a secondary source. Study was conducted in accordance with OECD Guideline 202 and GLP. Analytical monitoring was not performed.
	Daphnia magna 48-hour EC_{50} = 42 mg/L 48-hour NOEC=21 mg/L; the test was conducted under static conditions. Measured concentrations were stable within 20% of initial concentrations. (Experimental)	Submitted confidential study (as cited in EU, 2008b; OECD, 2009)	Study details reported in a secondary source with more details provided in a submitted confidential study. Study was conducted in accordance with OECD Guideline 202 and GLP.
	Daphnia magna 48-hour LC_{50} = 24.33 mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	Estimate for the Esters class was provided for comparative purposes. See Section 5.5.1.

Phosphoric acid, P,P'-[2,2-bis(chloromethyl)-1,3-propanediyl] P,P,P',P'-tetrakis(2-chloroethyl) ester CASRN 38051-10-4			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
			The toxicity value exceeds the water solubility by10 times; NES is predicted.
Green Algae EC_{50}	Green algae (*Scenedesmus subspicatus*) 76-hour EC_{50} > 10 mg/L NOEC > 10 mg/L (Experimental)	EC, 2000	Limited study details reported in a secondary source. Study was conducted in accordance with OECD Guideline 201 and GLP. Analytical monitoring was not performed.
	Green algae (*Pseudokirchneriella subcapitata*) 72-hour EC_{50}(growth) = 21 mg/L 72-hour E_rC_{50} (biomass) = 35 mg/L (static test conditions). Measured concentrations were stable within 20% of initial concentrations. (Experimental)	Submitted confidential study (as cited in EU, 2008b; OECD, 2009)	Study details reported in a secondary source with more study details provided in a submitted confidential study; Study was conducted in accordance with OECD Guideline 209 and GLP.
	Green algae 96-hour EC_{50}= 8.42 mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	Estimate for the Esters class was provided for comparative purposes. See Section 5.5.1. The toxicity value exceeds the water solubility by 10 times; NES is predicted.

Phosphoric acid, P,P'-[2,2-bis(chloromethyl)-1,3-propanediyl] P,P,P',P'-tetrakis(2-chloroethyl) ester CASRN 38051-10-4			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
Chronic Aquatic Toxicity	**MODERATE: Based on estimated chronic aquatic toxicity values. An estimated chronic aquatic toxicity value derived using an acute-to-chronic ratio (ACR) for the phosphate esters class was applied to the available experimental acute data for this chemical and indicated a Moderate hazard. An ECOSAR estimate for fish of 1.6 mg/L (ECOSAR class: esters) also indicated a Moderate hazard. Experimental data indicated that phosphoric acid, P, P`-[2,2-bis(chloromethyl)-1,3-propanediyl] P,P,P`,P`-tetrakis(2-chloroethyl) ester (V6) does not produce chronic toxicity to daphnia and algae; in the absence of experimental data for fish, an estimated Moderate hazard designation was assigned.**		
Fish ChV	Freshwater fish ChV ≥ 2.2 mg/L (Estimated)	Professional judgment	An ACR of 24 was derived for the phosphate ester class based on experimental data for Tris (p-t-butylphenyl) phosphate (TBPP). The acute-to-chronic ratio was applied to available experimental acute fish data for phosphoric acid, P,P'-[2,2-bis(chloromethyl)-1,3-propanediyl] P,P,P',P'-tetrakis(2-chloroethyl)ester (ChV >52 mg/L /24 = 2.2 mg/L)
	Freshwater Fish ChV = 0.77mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	Estimate for the Esters class was provided for comparative purposes. See Section 5.5.1. The toxicity value exceeds the water solubility by10 times; NES is predicted.

Phosphoric acid, P,P'-[2,2-bis(chloromethyl)-1,3-propanediyl] P,P,P',P'-tetrakis(2-chloroethyl) ester CASRN 38051-10-4			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
Daphnid ChV	*Daphnia magna* 23-day NOEC ≥ 3.68 mg/L Test duration extended to 23 days in order to achieve validity criteria for control reproduction. Some measured concentrations were not within nominal values, therefore, results analyzed and expressed relative to geometric mean concentrations over 23 days. (Experimental)	Submitted confidential study; EU, 2008b; OECD, 2009	The limited study details reported in a secondary source with more study details provided in a submitted confidential study indicate that the test system may have been compromised, and that the study results may not be valid.
	Daphnia magna ChV ≥ 10 mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	Estimate for the Esters class was provided for comparative purposes. See Section 5.5.1. The toxicity value exceeds the water solubility by10 times; NES is predicted.
Green Algae ChV	Green algae (*Pseudokirchneriella subcapitata*) 72-hour NOEC = 10 mg/L Limit test (Experimental)	Submitted confidential study (as cited in EU, 2008b; OECD, 2009)	Limited study details reported in a secondary source with more study details available in a submitted confidential study; concentrations were not measured; test not subjected to GLP.
	Green algae (*Scenedesmus subspicatus*) 76-hour EC_{50} > 10 mg/L NOEC > 10 mg/L (Experimental)	EC, 2000	Limited study details reported in a secondary source. Study was conducted in accordance with OECD Guideline 201 and GLP. Analytical monitoring was not performed.
	Green algae ChV = 3.30 mg/L (Estimated)	ECOSAR v1.11	Estimate for the Esters class was provided for comparative

Phosphoric acid, P,P'-[2,2-bis(chloromethyl)-1,3-propanediyl] P,P,P',P'-tetrakis(2-chloroethyl) ester CASRN 38051-10-4				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		ECOSAR: Esters		purposes. See Section 5.5.1. The toxicity value exceeds the water solubility by10 times; NES is predicted.
ENVIRONMENTAL FATE				
Transport		**Level III fugacity models incorporating available physical and chemical property data indicate that at steady state, phosphoric acid, P,P`-[2,2-bis(chloromethyl)-1,3-propanediyl] P,P,P`,P`-tetrakis(2-chloroethyl) ester, is expected to be found primarily in soil and sediment. The general partitioning of this chemical is toward solid phases and out of water, with limited degradation in soil and sediment predicted. It is not expected to dissociate at environmentally-relevant pH values. Based on measured and estimated K_{OC} values, it is expected to have negligible mobility in soil. Leaching through soil to groundwater is not expected to be an important transport mechanism. Estimated volatilization half-lives indicate that it will be non-volatile from surface water. Based on its estimated vapor pressure it is expected to exist in the vapor and particulate phase in the atmosphere. Vapor-phase phosphoric acid, P,P`-[2,2-bis(chloromethyl)-1,3-propanediyl] P,P,P`,P`-tetrakis(2-chloroethyl) ester is degraded in the atmosphere by reaction with photochemically-produced hydroxyl radicals. Particulates will be removed from air by wet or dry deposition.**		
	Henry's Law Constant (atm-m^3/mole)	$<10^{-8}$ (Estimated)	EPI v4.11; Professional judgment	Cutoff value for nonvolatile compounds.
	Sediment/Soil Adsorption/Desorption - K_{oc}	11,000 reported as Log K_{oc} = 4.04; test method C.19 of 2001/59/EC (Measured)	EU, 2008b	Secondary source reporting screening study for main component of commercial product V6, purity of test substance not stated.
		>30,000 MCI method (Estimated)	EPI v4.11; EPA, 2005	Cutoff value for nonmobile compounds.
	Level III Fugacity Model	Air = 0% Water = 0.7% Soil = 54%	EPI v4.11	

Phosphoric acid, P,P'-[2,2-bis(chloromethyl)-1,3-propanediyl] P,P,P',P'-tetrakis(2-chloroethyl) ester CASRN 38051-10-4				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		Sediment = 45% (Experimental)		
Persistence		**HIGH: The persistence hazard designation for Phosphoric acid, P,P`-[2,2-bis(chloromethyl)-1,3-propanediyl] P,P,P`,P`-tetrakis(2-chloroethyl) ester (V6) is based on guideline biodegradation studies. There is evidence for biodegradation to occur, at rates resulting in a high hazard designation. 37% removal was found in 28 days with an OECD 302C guideline study. Under aerobic conditions in ready biodegradability test OECD 301B, 5% biodegradation occurred after 28 days. This compound is relatively stable to hydrolysis, with experimental half-lives of >1 year at pH 4, pH 7, and pH 9. This compound is not expected to be susceptible to direct photolysis by sunlight, since it does not absorb light at wavelengths >290 nm. It is expected to be degraded in the atmosphere by reaction with photochemically-produced hydroxyl radicals; the half-life for this reaction in air is estimated to be 0.14 days.**		
Water	**Aerobic Biodegradation**	Passes Ready Test: No Test method: OECD TG 301B: CO_2 Evolution Test Achieved 5% degradation after 28 days in domestic activated sludge. Preliminary test OECD 209 confirmed the test substance did not inhibit growth of the microorganisms in the inoculum at the test concentrations employed in the ready test. (Measured)	EC, 2000; OECD, 2009; ECHA, 2012	Guideline study reported in secondary source for the commercial product Amgard V6.
		Study results: 37%/28 days Test method: 302C: Inherent - Modified MITI Test (II) Achieved 37% of its theoretical oxygen demand after 28 days using an activated sludge inoculum; this chemical was not considered inherently biodegradable. (Measured)	EU, 2008b; ECHA, 2012	Non-GLP guideline study reported in a secondary source for the commercial product Amgard V6.
	Volatilization Half-life for Model River			No data located.

Phosphoric acid, P,P'-[2,2-bis(chloromethyl)-1,3-propanediyl] P,P,P',P'-tetrakis(2-chloroethyl) ester CASRN 38051-10-4				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Volatilization Half-life for Model Lake			No data located.
Soil	**Aerobic Biodegradation**			No data located.
	Anaerobic Biodegradation			No data located; chlorinated alkyl phosphates are outside the domain of the available estimation methods.
	Soil Biodegradation with Product Identification			No data located.
	Sediment/Water Biodegradation			No data located.
Air	**Atmospheric Half-life**	0.14 days based on 12-hour day (Estimated)	EPI v4.11	
Reactivity	**Photolysis**	Not a significant fate process (Estimated)	Professional judgment; Mill, 2000	The substance does not contain functional groups that would be expected to absorb light at environmentally significant wavelengths.
	Hydrolysis	50%/1 year at 25°C, pH 4, 7, and 9; according to a GLP guideline study EU Method C.7 92/69/EEC OECD 111 In a preliminary test hydrolysis was below 10% after 5 days at pH 4,7 and 9, 50°C (Measured)	EU, 2008b; ECHA, 2012	Guideline study reported in a secondary source for the commercial product Antiblaze V6.
		50%/ 99 days pH 10 (Estimated)	EPI v4.11	
		50%/ 111 days pH 9 (Estimated)	EPI v4.11	
		50%/ 113 days pH 8 (Estimated)	EPI v4.11	
		50%/ 113 pH 7 (Estimated)	EPI v4.11	
		50%/113 days pH 6 (Estimated)	EPI v4.11	
		50%/113 days pH 5 (Estimated)	EPI v4.11	

Phosphoric acid, P,P'-[2,2-bis(chloromethyl)-1,3-propanediyl] P,P,P',P'-tetrakis(2-chloroethyl) ester CASRN 38051-10-4				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Environmental Half-life		>1 year Soil (Estimated)	PBT Profiler	Half-life estimated for the predominant compartment, as determined by EPI and the PBT Profiler methodology.
Bioaccumulation		**LOW: Based on estimated BCF and BAF values.**		
	Fish BCF	11 Regression-based method (Estimated)	EPI v4.11	
	Other BCF			No data located.
	BAF	31 Arnot-Gobas method (Estimated)	EPI v4.11	
	Metabolism in Fish			No data located.
ENVIRONMENTAL MONITORING AND BIOMONITORING				
Environmental Monitoring		No data located.		
Ecological Biomonitoring		No data located.		
Human Biomonitoring		No data located.		

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Tricresyl phosphate (TCP)

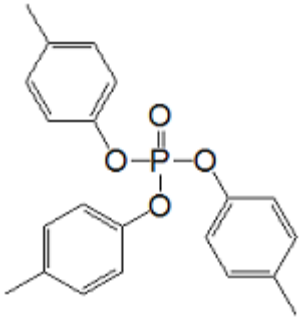
Screening Level Toxicology Hazard Summary

This table contains hazard information for each chemical; evaluation of risk considers both hazard and exposure. Variations in end-of-life processes or degradation and combustion by-products are discussed in the report but not addressed directly in the hazard profiles. The caveats listed below must be taken into account when interpreting the information in the table.

VL = Very Low hazard L = Low hazard M = Moderate hazard H = High hazard VH = Very High hazard – Endpoints in colored text (VL, L, M, H, and VH) were assigned based on empirical data. Endpoints in black italics *(VL, L, M, H,* and *VH*) were assigned using values from estimation software and professional judgment [(Quantitative) Structure Activity Relationships "(Q)SAR"].

Chemical	CASRN	Human Health Effects											Aquatic Toxicity		Environmental Fate	
		Acute Toxicity	Carcinogenicity	Genotoxicity	Reproductive	Developmental	Neurological	Repeated Dose	Skin Sensitization	Respiratory Sensitization	Eye Irritation	Dermal Irritation	Acute	Chronic	Persistence	Bioaccumulation
Tricresyl phosphate (TCP) [1]	1330-78-5	M	L	L	H	M	M	H	*M*		L	L	VH	*H*	M	H

[1] This assessment also includes information for other methylated triphenyl phosphate isomers (phosphoric acid, bis(methylphenyl) phenyl ester (CASRN 26446-73-1) and phosphoric acid, methylphenyl diphenyl ester (CASRN 26444-49-5)).



Representative Structure

CASRN: 1330-78-5; 26446-73-1; 26444-49-5

MW: 368.37

MF: $C_{21}H_{21}O_4P$

Physical Forms: Liquid
Neat:

Use: Flame retardant

SMILES: O=P(Oc1ccc(C)cc1)(Oc2ccc(C)cc2)Oc3ccc(C)cc3 (Representative structure for tricresyl phosphate)
O=P(Oc1ccc(C)cc1)(Oc2ccc(C)cc2)Oc3ccccc3 (Representative structure for dicresyl phenyl phosphate)
O=P(Oc1ccccc1)(Oc2ccccc2)Oc3ccccc3C (Representative structure for monocresyl diphenyl phosphate)

Synonyms: TCP; Phosphoric acid, tris(methylphenyl) ester; Tritolyl phosphate; Phosphoric acid, tritolyl ester; Tri(methylphenyl) phosphate

Chemical Considerations: The alternative, tricresyl phosphate, may contain a mixture of methylated triphenyl phosphate isomers with an unspecified amount of methyl substitution. The composition will be dependent on the manufacturing, purification and processing of the compound. Mono-o-cresyl and di-o-cresyl isomers have well documented toxicity concerns. Efforts are made to minimize the amount of ortho-isomer present in commercial products, to amounts typically less than 0.4% (Weiner and Jortner, 1999). Therefore, preparations will consist mainly of meta- and para-substituted isomers (HSDB, 2013d). The isomers and components expected to be present will be discussed in this report as appropriate when determining hazard designations. Test substance composition was not consistently reported in the literature however a description of the test sample and isomer content is included in the data entries when available. Chemical, fate, and toxicity data for components of the mixture represented by other CASRN were collected in the preparation of this AA and are listed below:

- Phosphoric acid, tris(methylphenyl) ester (CASRN 1330-78-5)
- tri-o-cresyl phosphate (CASRN 78-30-8)
- tri-m-cresyl phosphate (CASRN 563-04-2)
- tri-p-cresyl phosphate (CASRN 78-32-0)
- phosphoric acid, bis(methylphenyl) phenyl ester (CASRN 26446-73-1)
- p-cresyl diphenyl phosphate (CASRN 78-31-9)
- 2-methylphenyl diphenyl phosphate (CASRN 5254-12-6)
- phenyl di(p-tolyl) phosphate (CASRN 34909-69-8)
- phosphoric acid, 3-methylphenyl diphenyl ester (CASRN 69500-28-3)
- (2,4-dimethylphenyl) diphenyl phosphate (CASRN 86864-87-1)
- (2,3-dimethylphenyl) diphenyl phosphate (CASRN 25155-24-2)
- diphenyl xylyl phosphate (CASRN 29660-68-2)

- (2,5-dimethylphenyl) diphenyl phosphate (CASRN 73179-40-5)
- diphenyl 2,4,6-trimethylphenyl ester (CASRN 73179-43-8)
- phosphoric acid, methylphenyl diphenyl ester (CASRN 26444-49-5)

Estimated values using representative structures as indicated in the SMILES section of this assessment, will be used to fill assessment data gaps. EPI v4.11 was used to estimate physical/chemical and environmental fate values due to an absence of experimental data (Weiner and Jortner, 1999; EPA, 2010; van der Veen and de Boer, 2012; HSDB, 2013d).

Polymeric: No
Oligomeric: Not applicable

Metabolites, Degradates and Transformation Products: Degradates include orthophosphate and phenolic moieties; phenol; p-cresyl p-carboxyphenyl phosphate; p-hydroxybenzoic acid; di-p-cresyl phosphate; oxidized triesters di-p-cresyl p-carboxyphenyl phosphate and p-cresyl di-p-carboxyphenyl phosphate; p-hydroxybenzoic acid; dicresylphosphate and cresol.
Metabolites: p-cresyl p-carboxyphenyl phosphate; p-hydroxybenzoic acid; di-p-cresyl phosphate; p-cresyl p-carboxyphenyl phosphate and the oxidized triesters; 2-(2-cresyl)-4h-1-3-2-benzodioxaphosphorin-2-one (CASRN 1222-87-3) (Kurebayashi et al., 1985; WHO, 1990; NTP, 1994; Great Lakes Chemical Corporation, 2001; van der Veen and de Boer, 2012; Schindler et al., 2013).

Analog: Tricresyl phosphate isomers and methyl substituted phenyl phosphate esters anticipated to be present in the commercial product were considered in this evaluation, as described in the chemical considerations section. **Endpoint(s) using analog values:** Not applicable	**Analog Structure:** Not applicable

Structural Alerts: Organophosphates; Neurotoxicity (EPA, 2012).

Risk Phrases: Not classified by Annex VI Regulation (EC) No 1272/2008 (ESIS, 2012).

Hazard and Risk Assessments: This alternative was included in a risk assessment prepared for phosphate ester flame retardants by the Agency for Toxic Substances and Disease Registry. A screening level hazard characterization was prepared for tricresyl phosphate by EPA. HPV Data Summary, Test Plan, SIDS Initial Assessment Profile and SIAM were completed for Diphenyl Cresyl Phosphate (OECD, 1998; Great Lakes Chemical Corporation, 2001; OECD-SIDS, 2002; EPA, 2010; ATSDR, 2012).

Tricresyl phosphate CASRN 1330-78-5			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
PHYSICAL/CHEMICAL PROPERTIES			
Melting Point (°C)	-33 (Measured)	PhysProp, 2012	Reported in a secondary source.
	-35 Crystallizing point (Measured)	HSDB, 2013d	Reported in a secondary source with limited study details.
	-38 (Measured)	van der Veen and de Boer, 2012	Reported in a secondary source for cresyl diphenyl phosphate (CASRN 26444-49-5); purity not stated.
	<-10 (Measured)	OECD-SIDS, 2002	Reported for cresyl diphenyl phosphate (CASRN 26444-49-5).
	25.5 (Measured)	HSDB, 2013b	Reported for tri-m-cresyl phosphate (CASRN 563-04-2).
	11 (Measured)	PhysProp, 2012	Reported for tri-o-cresyl phosphate (CASRN 78-30-8).
	77 (Measured)	van der Veen and de Boer, 2012	Limited study details and test method not stated; inconsistent with other values reported.
Boiling Point (°C)	420 (Measured)	HSDB, 2013d	Reported in a secondary source, with limited study details.
	439 (Measured)	van der Veen and de Boer, 2012	Reported in a secondary source; test method not stated.
	410 (Measured)	PhysProp, 2012	Reported for tri-o-cresyl phosphate (CASRN 78-30-8).
	390 (Measured)	HSDB, 2013a	Reported for cresyl diphenyl phosphate (CASRN 26444-49-5).
	265 (Measured)	PhysProp, 2012	Reported in a secondary source. Similar values reported in other sources at a reduced pressure.
	265 at 10 mmHg (Measured)	Aldrich, 1994	Reported for a 90% mixture of isomers at a reduced pressure.

Tricresyl phosphate CASRN 1330-78-5			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	260 at 15 mmHg (Measured)	HSDB, 2013b	Reported for tri-m-cresyl phosphate (CASRN 563-04-2) at a reduced pressure.
	241 Reported as a range 241-255°C at 0.533 hPa (Measured)	Great Lakes Chemical Corporation, 2001	Reported for tricresyl phosphate (CASRN 1330-78-5) at a reduced pressure.
	245 (Measured)	OECD-SIDS, 2002	Reported for cresyl diphenyl phosphate (CASRN 26444-49-5).
	235 (Measured)	van der Veen and de Boer, 2012	Reported in a secondary source for cresyl diphenyl phosphate (CASRN 26444-49-5) purity not stated.
Vapor Pressure (mm Hg)	$6x10^{-7}$ at 25°C (Extrapolated)	PhysProp, 2012	Reported in a secondary source with limited study details.
	$4.7x10^{-6}$ at 25°C (Measured)	PhysProp, 2012; van der Veen and de Boer, 2012	Reported in a secondary source for cresyl diphenyl phosphate (CASRN 26444-49-5); purity not stated.
	$1.46x10^{-5}$ at 25°C (Extrapolated)	PhysProp, 2012	Reported for tri-o-cresyl phosphate (CASRN 78-30-8).
	$<9x10^{-7}$ at 25°C Reported as $<1.2x10^{-4}$ Pa; OECD TG 104 Dynamic method (Measured)	OECD-SIDS, 2002	Guideline study reported in a secondary source for cresyl diphenyl phosphate (CASRN 26444-49-5); purity of test substance not indicated.
	0.003 at 150°C Reported as 0.0044 hPa at 150°C (Measured)	Great Lakes Chemical Corporation, 2001	Reported in a secondary source at an elevated temperature.
Water Solubility (mg/L)	0.36 (Measured) at 25°C	Saeger et al., 1979 (as cited in EPA, 2010; PhysProp, 2012; HSDB, 2013d); van der Veen and de Boer, 2012	Nonguideline study reported for a mixture of isomers; purity not stated.
	0.24 (Measured)	PhysProp, 2012; van der Veen and de Boer, 2012	Reported in a secondary source for cresyl diphenyl phosphate (CASRN

Tricresyl phosphate CASRN 1330-78-5			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
			26444-49-5); purity not stated.
	0.15 (Measured)	PhysProp, 2012	Reported for bis(methylphenyl) phenyl phosphate (CASRN 26446-73-1).
	0.1 (Measured) at 25°C	HSDB, 2013d	Reported in a secondary source; purity and test method not stated.
	2.4 (Measured) Test method OECD TG 105; at 25°C	OECD-SIDS, 2002	Guideline study reported in a secondary source for cresyl diphenyl phosphate (CASRN 26444-49-5). Purity of test substance not indicated.
	2.6 (Measured) Reported as 0.0026 g/L at 25°C	OECD-SIDS, 2002; HSDB, 2013a	Reported for cresyl diphenyl phosphate (CASRN 26444-49-5); test method and purity of substance not indicated.
Log K_{ow}	5.11 (Measured)	Saeger et al., 1979 (as cited in PhysProp, 2012; HSDB, 2013d); van der Veen and de Boer, 2012	Nonguideline study on a mixture of isomers, purity not stated.
	5.9 (Measured)	HSDB, 2013d; Great Lakes Chemical Corporation, 2001	Reported in a secondary source; purity and test method not stated.
	4.51 (Measured)	Saeger et al., 1979 (as cited in PhysProp, 2012; HSDB, 2013a); van der Veen and de Boer, 2012	Reported in a secondary source for cresyl diphenyl phosphate (CASRN 26444-49-5) for the commercial product mixture Santicizer 140.
	3.7 Test method OECD TG 117; at 25°C (Measured)	OECD-SIDS, 2002	Guideline study reported in a secondary source for cresyl diphenyl phosphate (CASRN 26444-49-5); purity of test substance not indicated.
	5.3 monocresyl diphenyl phosphate; 5.8 for dicresyl phenyl phosphate;	EPI v4.11	Estimated using representative structures indicated in the SMILES section for methylated phenyl phosphate with one, two and three

Tricresyl phosphate CASRN 1330-78-5			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	6.3 for tricresyl phosphate (Estimated)		methyl substituent groups respectively.
Flammability (Flash Point)	Flash point: 212°C (Measured)	van der Veen and de Boer, 2012	Reported in a secondary source for cresyl diphenyl phosphate (CASRN 26444-49-5) with limited details.
	Flash point: 232°C (Measured)	van der Veen and de Boer, 2012	Reported in a secondary source with limited details.
	Auto flammability: 607°C (Measured)	Great Lakes Chemical Corporation, 2001	Reported for tricresyl phosphate.
	Flash point: 225°C closed cup (Measured)	Great Lakes Chemical Corporation, 2001	Reported for tricresyl phosphate.
	Flash point: 242°C open cup (Measured)	OECD-SIDS, 2002	Reported for cresyl diphenyl phosphate (CASRN 26444-49-5).
	Flash point: 240°C open cup (Measured)	OECD-SIDS, 2002	Reported for cresyl diphenyl phosphate (CASRN 26444-49-5).
Explosivity	Not expected to form explosive mixtures with air (Estimated)	Professional judgment	No experimental data located; based on its use as a flame retardant.
Pyrolysis			No data located.
pH	Not applicable (Estimated)	Professional judgment	Does not contain functional groups that are expected to ionize under environmental conditions.
pK_a	Not applicable (Estimated)	Professional judgment	Does not contain functional groups that are expected to ionize under environmental conditions.

Tricresyl phosphate CASRN 1330-78-5				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
HUMAN HEALTH EFFECTS				
Toxicokinetics		**Available information indicates that all three isomers of tricresyl phosphate are well absorbed following oral and dermal exposure. TCP is widely distributed in tissues with highest concentrations in adipose tissue, liver, kidneys, intestine, and stomach. Tri-p-cresyl metabolites were identified in blood, urine, feces, and tissues of the rats up to 72 hours following oral administration. Oxidation that occurred in the liver and hydrolysis in the intestine resulted in urinary metabolites that included hydroxybenzoic acid, di-p-cresyl phosphate, and p-cresyl p-carboxyphenyl phosphate. Major metabolites found in the bile were dip-cresyl phosphate, p-cresyl p-carboxyphenyl phosphate, and the oxidized triesters di-p-cresyl p-carboxyphenyl phosphate and p-cresyl di-p-carboxyphenyl phosphate. The main fecal compound was the parent compound (tri-p-cresyl phosphate). Elimination occurs through urine, feces and expiration. No information was located regarding absorption, distribution, or excretion of inhaled tricresyl phosphate.**		
Dermal Absorption *in vitro*				No data located.
Absorption, Distribution, Metabolism & Excretion	**Oral, Dermal or Inhaled**	Available information indicates that all three isomers of tricresyl phosphate were well absorbed following oral administration to rats. Dermal application of radiolabeled (^{14}C)-tri-o-cresyl phosphate to cats resulted in 28% and 20% of the applied radioactivity being recovered in urine and feces, respectively, during 10 days post application; it was stated that based on similarity of structure and physical properties, other isomeric tricresyl phosphate esters would likely also be absorbed through the skin. Following gavage administration of radiolabeled (^{14}C)-tri-p-cresyl phosphate to rats, radioactivity was widely distributed in the tissues at 24 hours with highest concentrations in adipose tissue, liver, kidneys, intestine, and stomach. At 72 hours, total internal radioactivity was only 25% that observed at 24 hours.	Kurebayashi et al., 1985; NTP, 1994	Study details reported in reliable data sources; Toxicokinetic data for tricresyl phosphate (CASRN 1330-78-5) mainly include results for the tri-ortho isomer (CASRN 78-30-8) and tri-para isomer (CASRN 78-32-0), although limited information is also available for the tri-meta isomer (CASRN 563-04-2).

Tricresyl phosphate CASRN 1330-78-5				
PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
		Parent compound and p-cresyl p-carboxyphenyl phosphate (a metabolite) were present in liver at 24 hours post dosing. Parent compound was also detected in adipose tissue at 24 and 72 hours post dosing and at trace amounts in the kidney at 72 hours post dosing. Tri-p-cresyl metabolites were identified in blood, urine, feces, and tissues of the rats up to 72 hours following oral administration; oxidation occurred in the liver and hydrolysis in the intestine, resulting in urinary metabolites that included p-hydroxybenzoic acid, di-p-cresyl phosphate, and p-cresyl p-carboxyphenyl phosphate. Major metabolites found in the bile were di-p-cresyl phosphate, p-cresyl p-carboxyphenyl phosphate, and the oxidized triesters di-p-cresyl p-carboxyphenyl phosphate and p-cresyl di-p-carboxyphenyl phosphate. The main fecal compound was the parent compound (tri-p-cresyl phosphate). For 3 days post dosing, expiratory excretion of $^{14}CO_2$ amounted to 18% of the total radioactivity. No information was located regarding absorption, distribution, or excretion of inhaled tricresyl phosphate.		
	Other			No data located.

Tricresyl phosphate CASRN 1330-78-5				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Acute Mammalian Toxicity		**MODERATE: Based on an oral LD_{50} of 1,160 mg/kg in rats exposed to tri-o-cresyl phosphate (CASRN 78-30-8). Acute toxicity values for the dermal and inhalation routes of exposure indicate a LOW hazard concern.**		
Acute Lethality	**Oral**	Rat oral LD_{50} = 1,160 mg/kg bw	WHO, 1990	Limited study details reported in a secondary source; test substance: Tri-o-cresyl phosphate (CASRN 78-30-8).
		Rabbit oral LD_{50} >3,000 mg/kg bw	WHO, 1990	Limited study details reported in a secondary source; test substance: Tri-p-cresyl phosphate (CASRN 78-32-0).
		Rabbit oral LD_{50} >3,000 mg/kg bw	WHO, 1990	Limited study details reported in a secondary source; test substance: Tri-m-cresyl phosphate (CASRN 563-04-2).
		Mouse oral LD_{50} = 3,900 mg/kg bw	WHO, 1990	Limited study details reported in a secondary source; test substance: Tricresyl phosphate (mixed isomers); CASRN 1330-78-5.
		Rat oral LD_{50} >4,640 mg/kg/bw	WHO, 1990	Limited study details reported in a secondary source; Test substance: Tricresyl phosphate (mixed isomers); CASRN 1330-78-5).
		Rat oral LD_{50} = 5,190 mg/kg bw	WHO, 1990	Limited study details reported in a secondary source; Test substance: tricresyl phosphate (mixed isomers); CASRN 1330-78-5.
		Rat oral LD_{50} = 6,400 mg/kg bw	OECD-SIDS, 2002	Limited study details reported in a secondary source; test substance: Diphenyl cresyl phosphate (CASRN 26444-49-5).
		Rat oral LD_{50} = 8,400 mg/kg bw	Johannsen et al., 1977	Limited study details reported in a

Tricresyl phosphate CASRN 1330-78-5				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		Single gavage dose (in corn oil) followed by 14-day observation		primary source; test substance: Tri-o-cresyl phosphate (CASRN 78-30-8).
		Rat oral LD_{50} = 10,400 mg/kg bw	Johannsen et al., 1977	Limited study details reported in a primary source; test substance: Cresyl diphenyl phosphate (CASRN 26444-49-5).
		Rat oral LD_{50} range 15,750-31,320 mg/kg bw Single gavage dose; 14-day observation	Great Lakes Chemical Corporation, 2001; EPA, 2010; ATSDR, 2012	Results summarized in reliable secondary sources; Test substance: Phosphoric acid, tris(methylphenyl)ester (CASRN 1330-78-5).
	Dermal	Rabbit dermal LD_{50} = 3,700 mg/kg bw 24-hour occluded dermal application followed by rinsing and 14-day observation	Johannsen et al., 1977	Limited study details reported in a primary source; test substance: Tri-o-cresyl phosphate (CASRN 78-30-8).
		Dermal LD_{50} >5,000 and <20,000 mg/kg Single dermal application followed by 14-day observation period	Great Lakes Chemical Corporation, 2001; EPA, 2010; ATSDR, 2012	Limited study details reported in a secondary sources; Test substance: Phosphoric acid, tris(methylphenyl)ester (CASRN 1330-78-5).
		Rabbit dermal LD_{50} >5,000 mg/kg bw Single 24-hour occluded application followed by rinsing and 14-day observation	Johannsen et al., 1977	Limited study details reported in a primary source; test substance: Cresyl diphenyl phosphate (CASRN 26444-49-5).
		Rabbit dermal LD_{50} >7,900 mg/kg bw Single gavage dose (in corn oil) followed by 14-day observation period	Johannsen et al., 1977	Limited study details reported in a primary source; test substance: Tricresyl phosphate (mixed isomers); CASRN 1330-78-5.
	Inhalation	Rat 4-hour LC_{50} >5.2 mg/L Ten rats/sex exposed to tricresyl phosphate aerosol at 5.2 mg/L for 4 hours, observed for 14 days post exposure	Great Lakes Chemical Corporation, 2001; EPA, 2010	Study considered valid without restriction by secondary source; test substance: Tricresyl phosphate (CASRN 1330-78-5).

Tricresyl phosphate CASRN 1330-78-5				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		No deaths		
		Rats, mice, guinea pigs; no deaths Test conditions: 6-hour exposure to 3,530 mg/m^3 vapors followed by 14-day observation period LC_{50} > 3.5 mg/L	ATSDR, 2012	Limited study details reported in a reliable secondary source; Test substance: Phosphoric acid, tris(methylphenyl)ester (CASRN 1330-78-5).
Carcinogenicity		**LOW: Based on no evidence of carcinogenicity in rats or mice following dietary exposure to a commercial mixture of tricresyl phosphate for 2-years.**		
	OncoLogic Results			No data located.
	Carcinogenicity (Rat and Mouse)			No data located.
	Combined Chronic Toxicity/Carcinogenicity	2-Year dietary study in Fischer 344/N rats (95/sex/concentration) Test substance concentrations: 0, 75, 150, 300 ppm (approximately 0, 3, 6, and 13 mg/kg bw-day for males and 0, 4, 7, and 15 mg/kg bw-day for females) Chronic toxicity: NOAEL = 13 mg/kg bw-day (males); 4 mg/kg bw-day for females LOAEL = 26 mg/kg bw-day (males) and 7 mg/kg bw-day (females) for cytoplasmic vacuolization of adrenal cortex No evidence of carcinogenic activity	NTP, 1994	Study details reported in a reliable primary source; test substance: Tricresyl phosphate (CASRN 1330-78-5) as a commercial product comprised of 18% dicresyl phosphate esters (unconfirmed isomeric composition) and 79% tricresyl phosphate esters (21% confirmed as tri-m-cresyl phosphate, 4% as tri-p-cresyl phosphate, and no detectable tri-o-cresyl phosphate [<0.1%]).
		2-Year dietary study in B6C3F1 mice (95/sex/concentration) Test substance concentrations: 0, 60, 125, 250 ppm (approximately 0, 7, 13, and 27 mg/kg bw-day for males and 0, 8, 18, and 37 mg/kg bw-day for females) chronic toxicity NOAEL = 18 mg/kg bw-day for females, not established for males	NTP, 1994	Study details reported in a reliable primary source; test substance: Tricresyl phosphate (CASRN 1330-78-5) as a commercial product comprised of 18% dicresyl phosphate esters (unconfirmed isomeric composition) and 79% tricresyl phosphate esters (21% confirmed as

Tricresyl phosphate CASRN 1330-78-5				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		LOAEL: 7 mg/kg bw-day (males) and 37 mg/kg bw-day (females) for ceroid pigmentation of adrenal cortex No evidence of carcinogenic activity		tri-m-cresyl phosphate, 4% as tri-p-cresyl phosphate, and no detectable tri-o-cresyl phosphate [<0.1%]).
	Other			No data located.
Genotoxicity		**LOW: Based on negative results for gene mutations in bacteria after treatment with mixed isomers of cresyl diphenyl phosphate or a commercial formulation of tricresyl phosphate and negative results for chromosomal aberrations in CHO cells *in vitro* after treatment with tricresyl phosphate as a commercial formulation. Negative results were also reported in a micronucleus test in Crj:BDF1 mice treated with commercial diphenyl cresyl phosphate by gavage.**		
	Gene Mutation *in vitro*	*Salmonella typhimurium* strains TA98, TA100, TA1535, TA1537 treated with or without metabolic activation Test substance concentrations: 100-10,000 micrograms/plate Negative- test substance not mutagenic with or without metabolic activation	Zeiger et al., 1987	Study details reported in a reliable primary source; test substance: Cresyl diphenyl phosphate (CASRN 26444-49-5; mixed isomers).
		Salmonella typhimurium strains TA98, TA100, TA1535, TA1537 treated with or without metabolic activation Test substance concentrations: 100-10,000 micrograms/plate Negative; test substance not mutagenic with or without metabolic activation	NTP, 1994	Study details reported in a reliable primary source; test substance: Tricresyl phosphate (CASRN 1330-78-5) as a commercial product comprised of 18% dicresyl phosphate esters (unconfirmed isomeric composition) and 79% tricresyl phosphate esters (21% confirmed as tri-m-cresyl phosphate, 4% as tri-p-cresyl phosphate, and no detectable tri-o-cresyl phosphate [<0.1%]).
	Gene Mutation *in vivo*			No data located.

Tricresyl phosphate CASRN 1330-78-5				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Chromosomal Aberrations *in vitro*	CHO cells treated with or without metabolic activation Test substance concentrations: 50-5,000 micrograms/mL Negative; test substance did not cause chromosomal aberrations	NTP, 1994	Study details reported in a reliable primary source; test substance: Tricresyl phosphate (CASRN 1330-78-5) as a commercial product comprised of 18% dicresyl phosphate esters (unconfirmed isomeric composition) and 79% tricresyl phosphate esters (21% confirmed as tri-m-cresyl phosphate, 4% as tri-p-cresyl phosphate, and no detectable tri-o-cresyl phosphate [<0.1%]).
		CHO cells treated with or without metabolic activation Test substance concentrations: 0.05-16 micrograms/mL Negative; test substance did not cause sister chromatid exchanges	NTP, 1994	Study details reported in a reliable primary source; test substance: Tricresyl phosphate (CASRN 1330-78-5) as a commercial product comprised of 18% dicresyl phosphate esters (unconfirmed isomeric composition) and 79% tricresyl phosphate esters (21% confirmed as tri-m-cresyl phosphate, 4% as tri-p-cresyl phosphate, and no detectable tri-o-cresyl phosphate [<0.1%]).
	Chromosomal Aberrations *in vivo*			No data located.
	DNA Damage and Repair			No data located.
	Other	Micronucleus test in Crj:BDF1 mice (5/sex) treated by single gavage Test substance concentrations: 0, 312.5, 625, 1250 mg/kg bw (in olive oil) Negative- test substance did not cause micronucleated polychromatic erythrocytes in bone marrow	OECD-SIDS, 2002	Study details reported in a secondary source; conducted according to OECD Test Guideline 474; test substance: Commercial diphenyl cresyl phosphate (CASRN 26444-49-5; purity 41.9%).

Tricresyl phosphate CASRN 1330-78-5				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Reproductive Effects		**HIGH: Based on a LOAEL of 7 mg/kg-day for ovarian interstitial cell hyperplasia (NOAEL = 4 mg/kg-day) in female rats following a 2-year dietary exposure to tricresyl phosphate as a commercial mixture. A 13-week oral (gavage) exposure to the same tricresyl phosphate mixture resulted in ovarian interstitial cell vacuolization in both rats and mice at a dose of 50 mg/kg-day. Thirteen weeks of dietary exposure to the tricresyl phosphate commercial mixture caused an increased incidence of interstitial cell hypertrophy in rats at 55 mg/kg-day, and ovarian interstitial cell vacuolization in mice at 530 mg/kg-day. Decreased sperm motility was reported in F1 mice that consumed a commercial tricresyl phosphate mixture from the diet at an estimated dose of 62.5 mg/kg-day and whose parents had been exposed at the same estimated dose during mating, gestation, and lactation in a continuous breeding dietary study; cross-over matings at an estimated dose of 250 mg/kg-day revealed decreased numbers of live pups per litter from matings of treated females to control males and treated males to control females. In a 1-generation study of rats, abnormal sperm morphology was also noted following gavage dosing of commercial tricresyl phosphate at 100 mg/kg-day). Decreased fertility was reported in rats following gavage administration of a commercial diphenyl cresyl phosphate mixture at 300 mg/kg-day (NOAEL = 60 mg/kg-day) during premating, mating, gestation, and parturition. Decreased testicular and epididymal weights and increased ovarian weights were observed in rats administered a hydraulic fluid (tricresyl phosphate being the major component) at 400 mg/kg-day from 7 days prior to breeding and throughout 63 days of continuous breeding and 28 days post breeding.**		
	Reproduction/Developmental Toxicity Screen			No data located.
	Combined Repeated Dose with Reproduction/ Developmental Toxicity Screen			No data located.
	Reproduction and Fertility Effects	Continuous breeding protocol using dietary exposure of CD-1 mice (40 breeding pairs in control group, 20 breeding pairs in treatment group) Test substance concentrations: 0, 0.05, 0.1, and 0.2% tricresyl phosphate by weight (continuous breeding phase doses estimated to have been 0, 62.5, 124, and 250 mg/kg-day, respectively); control and 0.2% dose level used for cross-over	Chapin et al., 1988	Well-designed study that followed a continuous breeding protocol; test substance: Tricresyl phosphate (CASRN 1330-78-5); composed of 74.9% tricresyl phosphate (consisting of mixed isomers and 20.6% pure m-cresyl, 3.9% pure para-cresyl, and <0.1% pure o-cresyl isomers), with the remainder composed of dicresyl phenyl and di- and tricresylxylyl

Tricresyl phosphate CASRN 1330-78-5				
PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
		mating phase Test substance treatment period: Continuous breeding phase included 98 days (7 days prior to breeding); cross-over mating phase included 7 days prior to breeding; an additional 7 days of cohabitation treatment (males and females) and throughout gestation (females); last F1 litter of mice continued on treatment of their parents until sexual maturity (postpartum day 74), throughout a 1-week cohabitation period with mice of the same dose group, and necropsied 3 weeks later for assessment of litters and treatment-related gross and histopathological effects Continuous breeding phase results: Significantly decreased fertility at 124 and 250 mg/kg-day; decreased sperm motility in F1 males at 62.5 mg/kg-day Cross-over mating phase results: Significantly decreased numbers of live pups per litter in treated male X control female and treated female X control male groups; significantly decreased proportion of pups born alive in control male X treated female group NOAEL: Not established LOAEL: 62.5 mg/kg-day (based on decreased sperm motility in F1 males)		phosphates; Tricresyl phosphate doses were estimated for the F0 parental mice; the LOAEL of 62.5 mg/kg bw-day for decreased sperm motility in F1 males assumes that the dose to the growing and mating F1 males was the same as that of their parents. EPAHC, 2010 reported a LOAEL of 62.5 mg/kg bw-day for significantly decreased number of litters/pair in the continuous breeding phase; however, the study report noted significantly "increased" number of litters/pair (5.06 versus 4.87 in controls). The LOAEL for the continuous breeding phase should be the mid-dose level (124 mg/kg bw-day) based on significantly increased numbers of dead pups in the 4th and 5th litters and decreased live pup body weight; a NOAEL of 62.5 mg/kg bw-day was identified for the continuous breeding phase of the study.
		One-generation oral (gavage) reproductive toxicity study in Long-Evans rats (12	Carlton et al., 1987	Study details reported in a primary source; test substance: Tricresyl

Tricresyl phosphate CASRN 1330-78-5				
PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
		males/dose, 24 females/dose) Test substance doses (in corn oil): 0, 100, 200 mg/kg/day for males; 0, 200, 400 mg/kg-day for females Dosing period: 56 days prior to mating and during 10 days of mating for males; 14 days prior to mating and through 10 days of mating, gestation, and lactation for females Significantly increased percent abnormal sperm in 100 and 200 mg/kg-day males; decreased sperm concentration, motility and progressive movement and minimal-to-mild significantly increased histopathologic lesions in testes and epididymides of 200 mg/kg-day males; dose-related severely decreased litter size in both groups of dosed females NOAEL: Not established LOAEL: 100 mg/kg bw-day based on abnormal sperm morphology		phosphate (CASRN 1330-78-5); composition: <9% tri-o-cresyl phosphate and remainder a mixture of tri-p-, and tri-m-cresyl phosphate and other tri-cresyl isomers.
		Repeated-dose gavage study of male and female Crj:CD (SD) rats (10/group) administered commercial diphenyl cresyl phosphate (CASRN 26444-49-5; purity 41.9%) for approximately 45 consecutive days (14 days premating, mating, gestation, until postpartum day 3). Dose levels: 0, 12, 60, 300 mg/kg bw-day NOAEL: 60 mg/kg bw-day LOAEL: 300 mg/kg bw-day for decreased	OECD, 1998; OECD-SIDS, 2002	Study details reported in a secondary source; conducted according to OECD guidelines for a Combined Repeated Dose and Reproductive/Developmental Screening Toxicity Test; test substance: commercial diphenyl cresyl phosphate (CASRN 26444-49-5; purity 41.9%).

Tricresyl phosphate CASRN 1330-78-5				
PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
		fertility		
		Modified continuous breeding protocol using gavage treatment in F344 rats (40 breeding pairs in control group, 20 breeding pairs in treatment group) Test substance concentrations: 0, 400 mg/kg-day (served as positive control for a butylated triphenyl phosphate-containing hydraulic fluid) Treatment period: 98 days including 7 days prior to breeding period, 63-day breeding period, 28-day postbreeding period; a second phase (cross-over mating) included a 28-day treatment period Severely decreased numbers of test substance-treated breeding pairs delivering litters (9/20, 0/20, and 0/20 pairs delivering litters 1, 2, and 3, respectively, compared to 40/40, 39/40, and 28/40 control pairs) Cross-over mating trials resulted in 0% fertility among the test-substance-treated males, but no apparent effect on test substance-treated females Test substance-treated rats exhibited significantly decreased testicular and epididymal weights and increased ovarian weights NOAEL: Not established LOAEL: 400 mg/kg bw-day (only dose tested) based on severely decreased numbers of breeding pairs delivering litters, decreased testicular and epididymal	Latendresse et al., 1994	Study details reported in a primary source; only one dose tested; test substance: A mixture of compounds in a hydraulic fluid of which tricresyl phosphate (CASRN 1330-78-5) was a major component; the test substance was composed of mostly p- and o-tricresyl phosphate isomers (62% by weight), cresyl-xylyl (18% by weight), and cresyl-ethyl-phenyl phosphates (18% by weight).

Tricresyl phosphate CASRN 1330-78-5				
PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
		weights, increased ovarian weight		
	Other	2-Year dietary study in Fischer 344/N rats (95/sex/concentration) Test substance concentrations: 0, 75, 150, 300 ppm (approximately 0, 3, 6, and 13 mg/kg bw-day for males and 0, 4, 7, and 15 mg/kg bw-day for females) NOAEL: 4 mg/kg bw-day (females) LOAEL: 7 mg/kg bw-day for ovarian interstitial cell hyperplasia	NTP, 1994	Reliable NTP study; test substance: Tricresyl phosphate (CASRN 1330-78-5) as a commercial product comprised of 18% dicresyl phosphate esters (unconfirmed isomeric composition) and 79% tricresyl phosphate esters (21% confirmed as tri-m-cresyl phosphate, 4% as tri-p-cresyl phosphate, and no detectable tri-o-cresyl phosphate [<0.1%]).
		13-Week gavage study in B6C3F1 mice (10/sex/dose) Test substance concentrations: 0, 50, 100, 200, 400, 800 mg/kg bw-day (in corn oil) Dosing frequency: 1x/d, 5d/w NOAEL: not established LOAEL: 50 mg/kg bw-day for ovarian interstitial cell vacuolization	NTP, 1994	Reliable NTP study; test substance: Tricresyl phosphate (CASRN 1330-78-5) as a commercial product comprised of 18% dicresyl phosphate esters (unconfirmed isomeric composition) and 79% tricresyl phosphate esters (21% confirmed as tri-m-cresyl phosphate, 4% as tri-p-cresyl phosphate, and no detectable tri-o-cresyl phosphate [<0.1%]).
		13-Week gavage study in Fischer 344/N rats (10/sex/dose) Test substance concentrations: 0, 50, 100, 200, 400, 800 mg/kg bw-d (in corn oil) Dosing frequency: 1x/d, 5d/w NOAEL: not established LOAEL: 50 mg/kg bw-day for ovarian interstitial cell vacuolization	NTP, 1994	Reliable NTP study; test substance: Tricresyl phosphate (CASRN 1330-78-5) as a commercial product comprised of 18% dicresyl phosphate esters (unconfirmed isomeric composition) and 79% tricresyl phosphate esters (21% confirmed as tri-m-cresyl phosphate, 4% as tri-p-cresyl phosphate, and no detectable tri-o-cresyl phosphate [<0.1%]).
		13-Week dietary study in Fischer 344/N rats (10/sex/dose)	NTP, 1994	Reliable NTP study; test substance: Tricresyl phosphate (CASRN 1330-

Tricresyl phosphate CASRN 1330-78-5				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		Test substance concentrations: 0, 900, 1700, 3300, 6600, 13,000 ppm (approximately 0, 55, 120, 220, 430, and 750 mg/kg bw-day for males and 0, 65, 120, 230, 430, and 770 mg/kg bw-day for females) NOAEL: not established LOAEL: 55 mg/kg bw-day for ovarian interstitial cell hypertrophy		78-5) as a commercial product comprised of 18% dicresyl phosphate esters (unconfirmed isomeric composition) and 79% tricresyl phosphate esters (21% confirmed as tri-m-cresyl phosphate, 4% as tri-p-cresyl phosphate, and no detectable tri-o-cresyl phosphate [<0.1%]).
		13-Week dietary study in B6C3F1 mice (10/sex/concentration) Test substance concentrations: 0, 250, 500, 1,000, 2,100, 4,200 ppm (approximately 0, 45, 110, 180, 380, and 900 mg/kg bw-day for males and 0, 65, 130, 230, 530, and 1,050 mg/kg bw-day for females) NOAEL: 230 mg/kg bw-day LOAEL: 530 mg/kg bw-day for ovarian interstitial cell vacuolization	NTP, 1994	Reliable NTP study; test substance: Tricresyl phosphate (CASRN 1330-78-5) as a commercial product comprised of 18% dicresyl phosphate esters (unconfirmed isomeric composition) and 79% tricresyl phosphate esters (21% confirmed as tri-m-cresyl phosphate, 4% as tri-p-cresyl phosphate, and no detectable tri-o-cresyl phosphate [<0.1%]).
Developmental Effects		**MODERATE: Based on increased numbers of dead F1 pups per litter were reported among CD-1 mice receiving commercial tricresyl phosphate from the diet at an estimated dose of 124 mg/kg-day (NOAEL = 62.5 mg/kg-day) in a continuous breeding protocol. Decreases in litter size and postnatal pup survival were also reported in a one-generation reproductive toxicity study of rats gavaged at 200 mg/kg-day (lowest dose tested) during premating and mating (males and females) and gestation and lactation (females).** **There were no data located for the developmental neurotoxicity endpoint.**		
	Reproduction/ Developmental Toxicity Screen			No data located.
	Combined Repeated Dose with Reproduction/ Developmental Toxicity Screen			No data located.

Tricresyl phosphate CASRN 1330-78-5				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Prenatal Development	Continuous breeding protocol using dietary exposure of CD-1 mice (40 breeding pairs in control group, 20 breeding pairs in treatment group) Test substance concentrations: 0, 0.05, 0.1, and 0.2% tricresyl phosphate by weight (continuous breeding phase doses estimated to have been 0, 62.5, 124, and 250 mg/kg-day, respectively); control and 0.2% dose level used for cross-over mating phase Test substance treatment period: Continuous breeding phase included 98 days (7 days prior to breeding); cross-over mating phase included 7 days prior to breeding; an additional 7 days of cohabitation treatment (males and females) and throughout gestation (females); last F1 litter of mice continued on treatment of their parents until sexual maturity (postpartum day 74), throughout a 1-week cohabitation period with mice of the same dose group, and necropsied 3 weeks later for assessment of litters and treatment-related gross and histopathological effects Continuous breeding phase results: Significantly decreased fertility at 124 and 250 mg/kg bw-day Cross-over mating phase results: Significantly decreased numbers of live pups per litter in treated male X control female and treated female X control male groups; significantly decreased proportion	Chapin et al., 1988	Well-designed study that followed a continuous breeding protocol; test substance: Tricresyl phosphate (CASRN 1330-78-5); composed of 74.9% tricresyl phosphate (consisting of mixed isomers and 20.6% pure m-cresyl, 3.9% pure para-cresyl, and <0.1% pure o-cresyl isomers), with the remainder composed of dicresyl phenyl and di- and tricresylxylyl phosphates; Tricresyl phosphate doses were estimated for the F0 parental mice; the LOAEL of 62.5 mg/kg bw-day for decreased sperm motility in F1 males assumes that the dose to the growing and mating F1 males was the same as that of their parents. EPAHC, 2010 reported a LOAEL of 62.5 mg/kg bw-day for significantly decreased number of litters/pair in the continuous breeding phase; however, the study report noted significantly "increased" number of litters/pair (5.06 versus 4.87 in controls). The LOAEL for the continuous breeding phase should be the mid-dose level (124 mg/kg bw-day) based on significantly increased numbers of dead pups in the 4th and 5th litters and decreased live pup body weight; a NOAEL of 62.5 mg/kg bw-day was identified for the continuous breeding phase of the study.

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PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
		of pups born alive in control male X treated female group NOAEL: 62.5 mg/kg bw-day LOAEL: 124 mg/kg bw-day based on increased number of dead F1 pups/litter		
		One-generation oral (gavage) reproductive toxicity study in Long-Evans rats (12 males/dose, 24 females/dose) Test substance doses (in corn oil): 0, 100, 200 mg/kg-day for males; 0, 200, 400 mg/kg-day for females Dosing period: 56 days prior to mating and during 10 days of mating for males; 14 days prior to mating and through 10 days of mating, gestation, and lactation for females Dose-related severely decreased litter size and decreased postnatal pup viability in both groups of dosed females NOAEL: Not established LOAEL: 200 mg/kg bw-day based on decreased litter size and postnatal pup viability (lowest dose tested)	Carlton et al., 1987	Study details reported in a primary source; test substance: Tricresyl phosphate (CASRN 1330-78-5); composition: <9% tri-o-cresyl phosphate and remainder a mixture of tri-p-, and tri-m-cresyl phosphate and other tri-cresyl isomers.
		Modified continuous breeding protocol using gavage treatment in F344 rats (40 breeding pairs in control group, 20 breeding pairs in treatment group) Test substance concentrations: 0, 400 mg/kg-day (served as positive control for a butylated triphenyl phosphate-containing hydraulic fluid)	Latendresse et al., 1994	Study details reported in a primary source; only one dose tested; Test substance: A mixture of compounds in a hydraulic fluid of which tricresyl phosphate (CASRN 1330-78-5) was a major component; the test substance was composed of mostly p- and o-tricresyl phosphate isomers (62% by

Tricresyl phosphate CASRN 1330-78-5				
PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
		Treatment period: 98 days including 7 days prior to breeding period, 63-day breeding period, 28-day postbreeding period; a second phase (cross-over mating) included a 28-day treatment period Severely decreased numbers of test substance-treated breeding pairs delivering litters (9/20, 0/20, and 0/20 pairs delivering litters 1, 2, and 3, respectively, compared to 40/40, 39/40, and 28/40 control pairs) NOAEL: Not established LOAEL: 400 mg/kg bw-day (only dose tested) based on reduced number of live pups/litter		weight), cresyl-xylyl (18% by weight), and cresyl-ethyl-phenyl phosphates (18% by weight).
	Postnatal Development			No data located.
	Prenatal and Postnatal Development			No data located.
	Developmental Neurotoxicity	Uncertain concern for developmental neurotoxicity based on the potential for Cholinesterase (ChE) inhibition in dams that may result in alterations of fetal neurodevelopment (Estimated)	Professional judgment	Estimated based on a structural alert for organophosphates for the neurotoxicity endpoint.
	Other			No data located.

Tricresyl phosphate CASRN 1330-78-5				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Neurotoxicity		**MODERATE: Multifocal axonal degeneration was observed in spinal nerve preparations from female mice administered commercial tricresyl phosphate by gavage once per day, 5 days/week for 13 weeks at 100 mg/kg-day; at a dose level of 200 mg/kg-day, male and female rats exhibited decreased grip strength and degenerative effects in spinal cord and sciatic nerve preparations. NOAELs of 100 and 50 mg/kg-day were identified for neurotoxicity of males and females, respectively. Similar effects were reported following a 13-week dietary study with the same commercial product in mice and rats, albeit at dietary concentrations resulting in higher estimated oral doses (≥750 mg/kg-day for rats and ≥380 mg/kg-day for mice)** **Tri-o-cresyl phosphate and other organophosphorus compounds cause a delayed neuropathy that has been termed organophosphate-induced delayed neurotoxicity (OPIDN). Neurological symptoms are typically delayed by 1-3 weeks after initial exposure and begin to be expressed as ataxia and progressive development of paralysis of hind limbs; partial recovery may follow. Chickens and cats are particularly sensitive to organophosphate-induced OPIDN.** **Tri-o-cresyl phosphate occurs as a contaminant in commercial tricresyl phosphate mixtures, but usually in concentrations of <1%.**		
	Neurotoxicity Screening Battery (Adult)			No data located.
	Other	13-Week gavage study in B6C3F1 mice (10/sex/dose) Test substance concentrations: 0, 50, 100, 200, 400, 800 mg/kg bw-day (in corn oil) Dosing frequency: 1x/d, 5d/w NOAEL (males): 100 mg/kg bw-day LOAEL (males): 200 mg/kg bw-day for decreased fore- and hind limb grip strength and degeneration in spinal cord and sciatic nerve NOAEL (females): 50 mg/kg bw-day LOAEL (females): 100 mg/kg bw-day for multifocal axonal degeneration in spinal cord	NTP, 1994	Reliable study, although not designed to comprehensively assess neurological endpoints; test substance: Tricresyl phosphate (CASRN 1330-78-5) as a commercial product comprised of 18% dicresyl phosphate esters (unconfirmed isomeric composition) and 79% tricresyl phosphate esters (21% confirmed as tri-m-cresyl phosphate, 4% as tri-p-cresyl phosphate, and no detectable tri-o-cresyl phosphate [<0.1%]). In addition to the identified LOAEL of 100 mg/kg bw-day for multifocal axonal degeneration in the spinal cord of female mice, significantly decreased grip strength

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PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
				was observed at doses ≥ 200 mg/kg bw-day as well. Degeneration in spinal cord and sciatic nerve preparations was noted in male and female mice at doses ≥ 200 mg/kg bw-day.
		13-Week dietary study in Fischer 344/N rats (10/sex/dose) Test substance concentrations: 0, 900, 1700, 3300, 6600, 13,000 ppm (approximately 0, 55, 120, 220, 430, and 750 mg/kg bw-day for males and 0, 65, 120, 230, 430, and 770 mg/kg bw-day for females) NOAEL (males): 430 mg/kg bw-day LOAEL (males): 750 mg/kg bw-day for reduced hind limb grip strength NOAEL (females): 770 mg/kg bw-day (highest dose tested) LOAEL (females): Not established	NTP, 1994	Reliable study, although not designed to comprehensively assess neurological endpoints; test substance: Tricresyl phosphate (CASRN 1330-78-5) as a commercial product comprised of 18% dicresyl phosphate esters (unconfirmed isomeric composition) and 79% tricresyl phosphate esters (21% confirmed as tri-m-cresyl phosphate, 4% as tri-p-cresyl phosphate, and no detectable tri-o-cresyl phosphate [<0.1%]). Histopathologic evaluations of spinal cord and sciatic nerve preparations revealed no signs of degenerative effects at any dose.
		13-Week dietary study in B6C3F1 mice (10/sex/concentration) Test substance concentrations: 0, 250, 500, 1,000, 2,100, 4,200 ppm (approximately 0, 45, 110, 180, 380, and 900 mg/kg bw-day for males and 0, 65, 130, 230, 530, and 1,050 mg/kg bw-day for females) NOAEL (males): 180 mg/kg bw-day (males)	NTP, 1994	Reliable study, although not designed to comprehensively assess neurological endpoints; test substance: Tricresyl phosphate (CASRN 1330-78-5) as a commercial product comprised of 18% dicresyl phosphate esters (unconfirmed isomeric composition) and 79% tricresyl phosphate esters (21% confirmed as tri-m-cresyl phosphate, 4% as tri-p-cresyl phosphate, and no

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PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
		LOAEL (males): 380 mg/kg bw-day for reduced forelimb grip strength NOAEL (females): 230 mg/kg bw-day LOAEL (females): 530 mg/kg bw-day for reduced fore- and hind limb grip strength		detectable tri-o-cresyl phosphate [<0.1%]). Histopathologic evaluation of spinal cord and sciatic nerve preparations revealed degenerative effects at 530 and 1,050 mg/kg bw-day in females and 900 mg/kg bw-day in males.
		13-Week gavage study in Fischer 344/N rats (10/sex/dose) Test substance concentrations: 0, 50, 100, 200, 400, 800 mg/kg bw-day (in corn oil) Dosing frequency: 1x/d, 5d/w Neurological endpoints included fore- and hind limb grip strength and histopathological evaluations of spinal cord and sciatic nerve NOAEL: 800 mg/kg bw-day (highest dose tested) LOAEL: Not established	NTP, 1994	Reliable study, although not designed to comprehensively assess neurological endpoints; test substance: Tricresyl phosphate (CASRN 1330-78-5) as a commercial product comprised of 18% dicresyl phosphate esters (unconfirmed isomeric composition) and 79% tricresyl phosphate esters (21% confirmed as tri-m-cresyl phosphate, 4% as tri-p-cresyl phosphate, and no detectable tri-o-cresyl phosphate [<0.1%]). There were no effects on grip strength or histopathology of spinal cord or sciatic nerve of treated male rats. Reported decreased hind limb grip strength in female rats at 400- and 800 mg/kg bw-day was of small magnitude (12 and 14% less, respectively, than controls). Furthermore, the 800 mg/kg bw-day group of female rats exhibited significantly lower grip strength than the controls (10% less) at examination prior to the initiation of glutaraldehyde treatment. The 400

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PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
				mg/kg bw-day group of female rats also exhibited 10% less hind limb grip strength than controls (not statistically significant) prior to the initiation of glutaraldehyde treatment. Therefore, the 800 mg/kg bw-day dose level should be considered a NOAEL for neurological effects in the female rats as well.
		Tri-o-cresyl phosphate and other organophosphorus compounds cause a delayed neuropathy that has been termed organophosphate-induced delayed neurotoxicity (OPIDN). Neurological symptoms are typically delayed by 1-3 weeks after initial exposure and begin to be expressed as ataxia and progressive development of paralysis of hind limbs; partial recovery may follow. Chickens and cats are particularly sensitive to organophosphate-induced OPIDN. Neuropathologically, degeneration of spinal cord and peripheral nerve fibers is observed. OPIDN has been elicited in rats as well, but at relatively high repeated oral doses (>840 mg/kg bw-day). Tri-o-cresyl phosphate occurs as a contaminant in commercial tricresyl phosphate mixtures, but usually in concentrations of <1%. Ingestion of preparations contaminated by TOCP by humans may be followed	WHO, 1990	Summary of Tri-o-cresyl phosphate neurological effects.

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		polyneuropathy. Delayed neurotoxic symptoms include pain and paraesthesia in the lower extremities. Muscle weakness can quickly progress to paralysis of the lower extremities and may or may not involve the upper extremities. Axonal degeneration has been reported following histopathological examination. There is variation between individuals both in response to TCP and recovery from the toxic effects of TOCP. Severe symptoms have been reported following the ingestion of 0.15 g of TCP, while other individuals failed to show any toxic effect after ingesting 1-2 g. Some patients show complete recovery while others do not.		
		2-Year dietary study in B6C3F1 mice (95/sex/concentration) Test substance concentrations: 0, 60, 125, 250 ppm (approximately 0, 7, 13, and 27 mg/kg bw-day for males and 0, 8, 18, and 37 mg/kg bw-day for females) Neurological endpoints assessed included grip strength testing and histopathological evaluation of spinal cord and sciatic preparations NOAEL (males): 27 mg/kg bw-day (highest dose tested) LOAEL (males): Not established NOAEL (females): 37 mg/kg bw-day (highest dose tested)	NTP, 1994	Reliable study, although not designed to comprehensively assess neurological endpoints; test substance: Tricresyl phosphate (CASRN 1330.78-5) as a commercial product comprised of 18% dicresyl phosphate esters (unconfirmed isomeric composition) and 79% tricresyl phosphate esters (21% confirmed as tri-m-cresyl phosphate, 4% as tri-p-cresyl phosphate, and no detectable tri-o-cresyl phosphate [<0.1%]). Neurobehavioral evaluations were performed on 15 mice/sex from each exposure group. At 3-month interim evaluation, significantly decreased hind limb grip

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PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
		LOAEL (females): Not established		strength was observed in female mice of the highest treatment level (250 ppm; ca. 7% lower than controls); there was no significant change in grip strength at 9- and 15-month interim evaluations. There was no histopathological evidence of treatment related effects on sciatic nerve or spinal cord. Note: Grip strength was not decreased in male or female mice in 13-week gavage and dietary studies at much higher dose levels; the 13-week studies were performed using the same strains of mice, the same formulation of glutaraldehyde, and the same laboratory as the 2-year dietary study. These results suggest that the finding of decreased hind limb grip strength at the 3-month interim evaluation in the 2-year dietary study are spurious. In that case, the 2-year dietary study identified NOAELs of 27 and 37 mg/kg-day for neurological effects in male and female mice, respectively.
		2-Year dietary study in Fischer 344/N rats (95/sex/concentration) Test substance concentrations: 0, 75, 150, 300 ppm (approximately 0, 3, 6, and 13 mg/kg bw-day for males and 0, 4, 7, and 15 mg/kg bw-day for females) Neurological endpoints assessed included grip strength testing and histopathological	NTP, 1994	Reliable study, although not designed to comprehensively assess neurological endpoints; test substance: Tricresyl phosphate (CASRN 1330-78-5) as a commercial product comprised of 18% dicresyl phosphate esters (unconfirmed isomeric composition) and 79%

Tricresyl phosphate CASRN 1330-78-5				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		evaluation of spinal cord and sciatic preparations NOAEL (males): 13 mg/kg bw-day (highest dose tested) LOAEL (males): Not established NOAEL (females): 15 mg/kg bw-day (highest dose tested) LOAEL (females): Not established		tricresyl phosphate esters (21% confirmed as tri-m-cresyl phosphate, 4% as tri-p-cresyl phosphate, and no detectable tri-o-cresyl phosphate [<0.1%]). Neurobehavioral evaluations were performed on 15 rats/sex from each exposure group. At 3-month interim evaluation, significantly decreased hind limb grip strength was reported for male rats at the two highest treatment levels (300 and 600 ppm; ca. 11% lower than controls) and female rats at the highest treatment level (600 ppm; ca. 7% lower than controls); there was no significant treatment-related effect on grip strength at 9- and 15-month interim evaluations. There was no histopathological evidence of treatment-related effects on spinal cord or sciatic nerve. Note: Grip strength was not decreased in male or female rats in 13-week gavage and dietary studies at much higher dose levels; the 13-week studies were performed using the same strains of rats, the same formulation of glutaraldehyde, and the same laboratory as the 2-year dietary study. These results suggest that the finding of decreased hind limb grip strength at the 3-month interim evaluation in the 2-year dietary study are spurious. In that case, the 2-year dietary study

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
				identified NOAELs of 13 and 15 mg/kg-day for neurological effects in male and female rats, respectively.
		Potential for neurotoxic effects based on a structural alert for organophosphates (Estimated by analogy)	Professional judgment	Estimated based on a structural alert for organophosphates and professional judgment.
Repeated Dose Effects		**HIGH: In addition to the neurotoxicity effects described above, increased incidence of liver lesions was reported in a 2-year dietary study in mice fed commercial tricresyl phosphate at a dose of 13 mg/kg bw-day (NOAEL = 7 mg/kg bw-day); cytoplasmic vacuolization of the adrenal cortex and ovarian interstitial cell hypertrophy were noted at 26 mg/kg bw-day (NOAEL = 13 mg/kg bw-day). Similar effects were reported following a 13-week dietary study with the same commercial product in mice and rats at 50 mg/kg bw-day (lowest dose tested). Furthermore, TCP is immunotoxic in the range of high hazard (see immunotoxicity section).**		
		2-Year dietary study in B6C3F1 mice (95/sex/concentration) Test substance concentrations: 0, 60, 125, 250 ppm (approximately 0, 7, 13, and 27 mg/kg bw-day for males and 0, 8, 18, and 37 mg/kg bw-day for females) NOAEL: 7 mg/kg bw-day (males); 37 mg/kg bw-day (females; highest dose tested) LOAEL: 13 mg/kg bw-day for males based on increased incidences of liver lesions (ceroid pigmentation, clear cell foci, fatty change)	NTP, 1994	Study details reported in a primary source; test substance: Tricresyl phosphate (CASRN 1330.78-5) as a commercial product comprised of 18% dicresyl phosphate esters (unconfirmed isomeric composition) and 79% tricresyl phosphate esters (21% confirmed as tri-m-cresyl phosphate, 4% as tri-p-cresyl phosphate, and no detectable tri-o-cresyl phosphate [<0.1%]).
		2-Year dietary study in Fischer 344/N rats (95/sex/concentration) Test substance concentrations: 0, 75, 150, 300 ppm (approximately 0, 3, 6, and 13 mg/kg bw-day for males and 0, 4, 7, and 15 mg/kg bw-day for females)	NTP, 1994	Study details reported in a primary source; test substance: Tricresyl phosphate (CASRN 1330-78-5) as a commercial product comprised of 18% dicresyl phosphate esters (unconfirmed isomeric composition)

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PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
		NOAEL: 13 mg/kg bw-day (males); 7 mg/kg bw-day (females) LOAEL: 26 mg/kg bw-day (males) and 15 mg/kg bw-day (females) for cytoplasmic vacuolization of adrenal cortex at 3-month interim evaluation		and 79% tricresyl phosphate esters (21% confirmed as tri-m-cresyl phosphate, 4% as tri-p-cresyl phosphate, and no detectable tri-o-cresyl phosphate [<0.1%]).
		13-Week gavage study in B6C3F1 mice (10/sex/dose) Test substance concentrations: 0, 50, 100, 200, 400, 800 mg/kg bw-day (in corn oil) Dosing frequency: 1x/d, 5d/w NOAEL: not established LOAEL: 50 mg/kg bw-day for cytoplasmic vacuolization of the adrenal cortex (males and females), ovarian interstitial cell hypertrophy	NTP, 1994	Study details reported in a primary source; test substance: Tricresyl phosphate (CASRN 1330-78-5) as a commercial product comprised of 18% dicresyl phosphate esters (unconfirmed isomeric composition) and 79% tricresyl phosphate esters (21% confirmed as tri-m-cresyl phosphate, 4% as tri-p-cresyl phosphate, and no detectable tri-o-cresyl phosphate [<0.1%]); EPA HC (2010) suggested that relatively wide range of NOAEL values among less-than-lifetime repeated-dose oral studies may be related to variations in isomeric composition of CASRN 1330-78-5.
		13-Week gavage study in Fischer 344/N rats (10/sex/dose) Test substance concentrations: 0, 50, 100, 200, 400, 800 mg/kg bw-day (in corn oil) Dosing frequency: 1x/d, 5d/w NOAEL: not established LOAEL: 50 mg/kg bw-day for cytoplasmic vacuolization of the adrenal	NTP, 1994	Study details reported in a primary source; test substance: Tricresyl phosphate (CASRN 1330-78-5) as a commercial product comprised of 18% dicresyl phosphate esters (unconfirmed isomeric composition) and 79% tricresyl phosphate esters (21% confirmed as tri-m-cresyl phosphate, 4% as tri-p-cresyl

Tricresyl phosphate CASRN 1330-78-5				
PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
		cortex (males and females)		phosphate, and no detectable tri-o-cresyl phosphate [<0.1%]); EPA HC (2010) suggested that relatively wide range of NOAEL values among less-than-lifetime repeated-dose oral studies may be related to variations in isomeric composition of CASRN 1330-78-5.
		13-Week dietary study in Fischer 344/N rats (10/sex/dose) Test substance concentrations: 0, 900, 1700, 3300, 6600, 13,000 ppm (approximately 0, 55, 120, 220, 430, and 750 mg/kg bw-day for males and 0, 65, 120, 230, 430, and 770 mg/kg bw-day for females) NOAEL: not established LOAEL: 55 mg/kg bw-day (males) for cytoplasmic vacuolization of the adrenal cortex, 65 mg/kg bw-day (females) for cytoplasmic vacuolization of the adrenal cortex and ovarian interstitial cell hypertrophy	NTP, 1994	Study details reported in a primary source; test substance: Tricresyl phosphate (CASRN 1330-78-5) as a commercial product comprised of 18% dicresyl phosphate esters (unconfirmed isomeric composition) and 79% tricresyl phosphate esters (21% confirmed as tri-m-cresyl phosphate, 4% as tri-p-cresyl phosphate, and no detectable tri-o-cresyl phosphate [<0.1%]); EPA HC (2010) suggested that relatively wide range of NOAEL values among less-than-lifetime repeated-dose oral studies may be related to variations in isomeric composition of CASRN 1330-78-5.
		Repeated-dose gavage study of male and female Crj:CD (SD) rats (10/group) administered commercial diphenyl cresyl phosphate (CASRN 26444-49-5; purity 41.9%) for approximately 45 consecutive days (14 days premating, mating, gestation, until postpartum day 3). Dose levels: 0, 12, 60, 300 mg/kg bw-day	OECD-SIDS, 2002	Secondary source indicated the study followed OECD guidelines for a Combined Repeated Dose and Reproductive/Developmental Screening Toxicity Test; test substance: commercial diphenyl cresyl phosphate (CASRN 26444-49-5; purity 41.9%).

Tricresyl phosphate CASRN 1330-78-5				
PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
		NOAEL: 12 mg/kg bw-day LOAEL: 60 mg/kg bw-day for enlargement and vacuolization of adrenal cortex		
		13-Week dietary study in B6C3F1 mice (10/sex/concentration) Test substance concentrations: 0, 250, 500, 1,000, 2,100, 4,200 ppm (approximately 0, 45, 110, 180, 380, and 900 mg/kg bw-day for males and 0, 65, 130, 230, 530, and 1,050 mg/kg bw-day for females) NOAEL: 45 mg/kg bw-day (males); not established for females LOAEL: 110 mg/kg bw-day (males) and 65 mg/kg bw-day (females) for cytoplasmic vacuolization of the adrenal cortex	NTP, 1994	Study details reported in a primary source; test substance: Tricresyl phosphate (CASRN 1330-78-5) as a commercial product comprised of 18% dicresyl phosphate esters (unconfirmed isomeric composition) and 79% tricresyl phosphate esters (21% confirmed as tri-m-cresyl phosphate, 4% as tri-p-cresyl phosphate, and no detectable tri-o-cresyl phosphate [<0.1%]); EPA HC (2010) suggested that relatively wide range of NOAEL values among less-than-lifetime repeated-dose oral studies may be related to variations in isomeric composition of CASRN 1330-78-5.
		3-Month gavage study in Sprague-Dawley rats (5/sex/dose) Test substance concentrations: 30, 100, 300, 1,000 mg/kg bw-day Dosing frequency: 1x/d, 6d/w NOAEL: 300 mg/kg bw-day LOAEL: 1,000 mg/kg bw-day for decreased body weight in males and hypertrophy of the adrenal cortex in both sexes	WHO, 1990; Great Lakes Chemical Corporation, 2001; EPA, 2010	Small group numbers (5 rats/sex/dose); study considered valid with restrictions by secondary source; test substance: Tricresyl phosphate (CASRN 1330-78-5) in 5% gum arabic; test substance purity: 100%; EPA HC (2010) suggested that relatively wide range of NOAEL values among less-than-lifetime repeated-dose oral studies may be related to variations in isomeric

Tricresyl phosphate CASRN 1330-78-5				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
				composition of CASRN 1330-78-5.
		28-Day dietary study in Sprague-Dawley rats (10/sex/dose) Test substance concentrations: 0, 0.1, 0.5, 1.0% (males: 0, 236, 1,281, 1,551 mg/kg bw-day; females: 0, 250, 1,229, 2,130 mg/kg bw-day) NOAEL: 236 mg/kg bw-day (males); 250 mg/kg bw-day (females) LOAEL: 1,281 mg/kg bw-day (males) for mortality; 1,229 mg/kg bw-day (females) for mortality	FMC, 1976	Guideline not specified, but appears to follow OECD test guideline 407; test substance: Tricresyl phosphate (CASRN 1330-78-5); this study was summarized in ATSDR, 2012; Great Lakes Chemical Corporation, 2001; and EPA HC, 2010. However, the estimated low- and mid-dose levels provided by these secondary sources are much lower than the doses calculated using reported body weight and compound consumption data in the primary report (i.e., estimated doses reported in EPAHC (2010) were 0, 50, 250, and 500 mg/kg-day and estimated doses reported in ATSDR (2012) were 0, 140, 938, and 2647 mg/kg-day for the males, and 0, 120, 745, and 2258 mg/kg-day for the females)
Skin Sensitization		**MODERATE: There is uncertain potential for skin sensitization based on a protein binding alert for this compound and professional judgment.**		
	Skin Sensitization	There is uncertain potential for skin sensitization based on a protein binding alert for this compound. (Estimated)	Professional judgment	Estimated based on a protein binding alert (nucleophilic substitution on phosphonates) and professional judgment.
Respiratory Sensitization		**No data located.**		
	Respiratory Sensitization			No data located.

Tricresyl phosphate CASRN 1330-78-5				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Eye Irritation		**LOW: Tricresyl phosphate caused conjuctival effects in 2/6 rabbits that cleared within 48 hours.**		
	Eye Irritation	Eye irritation study in rabbits (n=9) Treated eye of 3/9 rabbits rinsed 4 seconds post application Conjunctival effects at 24 hours in 2/6 rabbits with unrinsed eyes which cleared by 48 hours; no effects in rinsed eyes; results considered to indicate that test substance was not an eye irritant	Great Lakes Chemical Corporation, 2001; EPA, 2010	Study details reported in secondary sources; considered valid; test substance: undiluted phosphoric acid, tris(methylphenyl)ester (CASRN 1330-78-5).
Dermal Irritation		**LOW: Tricresyl phosphate caused erythema in 1/6 rabbits that cleared within 72 hours.**		
	Dermal Irritation	Skin irritation study in rabbits (n=6) Test substance applied to shaved and intact and abraded sites on the back of each rabbit under semi occlusive conditions for 24 hours and observed for up to 7 days post application Erythema on abraded skin of 1/6 rabbits at 24 hours resolved by 72 hours; no edema at any site; results indicated that test substance did not cause skin irritation	Great Lakes Chemical Corporation, 2001; EPA, 2010	Study details reported in secondary sources; considered valid; test substance: undiluted phosphoric acid, tris(methylphenyl)ester (CASRN 1330-78-5).

Tricresyl phosphate CASRN 1330-78-5			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
Endocrine Activity	**Dose-related increasing severity of cytoplasmic vacuolization of the adrenal glands were noted in rats and mice exposed to receiving commercial tricresyl phosphate by repeated gavage dosing or continuously via the diet for 13 weeks at doses in the range of 50-800 mg/kg bw-day. Cytoplasmic vacuolization of the adrenal cortex in male rats at the highest dose level (13 mg/kg bw-day) and female rats at all dose levels (4, 7, and 15 mg/kg bw-day) was observed in a 2-year dietary study, but primarily in the 7 mg/kg bw-day group at the 9- and 15-month interim sacrifice and terminal sacrifice. Ceroid pigmentation of the adrenal cortex occurred in all groups of mice (test substance doses 7-37 mg/kg bw-day) throughout most of the 2-year study.**		
	Thirteen-week oral (gavage) and feeding studies and 2-year feeding studies in F344/N rats and B6C3F1 mice. Results of 13-week studies: Rats and mice exposed to test substance by repeated gavage dosing or continuously via the diet at test substance doses in the range of 50-800 mg/kg bw-day to male and female rats and mice exhibited dose-related increasing severity of cytoplasmic vacuolization of the adrenal glands. Results of 2-year studies: Cytoplasmic vacuolization of the adrenal cortex was noted in male rats at the highest dose level (13 mg/kg bw-day) and female rats at all dose levels (4, 7, and 15 mg/kg bw-day); primarily in the 7 mg/kg bw-day group of female rats at 9- and 15-month interim sacrifice and terminal sacrifice. Ceroid pigmentation of the adrenal cortex occurred in all groups of mice (test substance doses 7-37 mg/kg bw-day) throughout most of the 2-year study, with markedly increased severity in the high-dose females (37 mg/kg bw-day).	NTP, 1994	Study details reported in a reliable primary source; test substance: Tricresyl phosphate (CASRN 1330-78-5) as a commercial product comprised of 18% dicresyl phosphate esters (unconfirmed isomeric composition) and 79% tricresyl phosphate esters (21% confirmed as tri-m-cresyl phosphate, 4% as tri-p-cresyl phosphate, and no detectable tri-o-cresyl phosphate [<0.1%]).
	3-Month gavage study in Sprague-Dawley rats (5/sex/dose) Test substance	WHO, 1990; Great Lakes Chemical Corporation, 2001;	Small group numbers (5 rats/sex/dose); study considered valid

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		concentrations: 30, 100, 300, 1,000 mg/kg bw-day Dosing frequency: 1x/d, 6d/w NOAEL: 300 mg/kg bw-day LOAEL: 1,000 mg/kg bw-day for decreased body weight in males and hypertrophy of the adrenal cortex in both sexes	EPA, 2010	with restrictions by secondary source; test substance: Tricresyl phosphate (CASRN 1330-78-5) in 5% gum arabic; test substance purity: 100%; EPA HC (2010) suggested that relatively wide range of NOAEL values among less-than-lifetime repeated-dose oral studies may be related to variations in isomeric composition of CASRN 1330-78-5.
Immunotoxicity		**Decreased immune response to tetanus antigen significantly reduced at low doses in rats fed technical-grade tricresyl phosphate for 6 weeks. Significant changes in gross immune organ weights and histology were reported at high doses. Significantly decreased thymus weight was noted in male and female mice and rats administered commercial tricresyl phosphate by repeated gavage for 16 days at doses ≥ 1450 mg/kg-day. Other effects seen at 2900 mg/kg bw-day included necrosis of mandibular lymph nodes and spleen and lymphoid depletion in spleen and/or thymus.**		
	Immune System Effects	Rats fed diets containing 0, 20, 50, or 100 ppm tricresyl phosphate and immunized with tetanus toxoid 25 days following initiation of exposure After 6 weeks of treatment, doses of 6 mg/kg bw-day and higher resulted in reduced antibody titer to tetanus toxoid and significantly reduced cell-mediated immune response (at 12 mg/kg bw-day, serum IgM and IgG were significantly reduced). No effects were reported at 2.4 mg/kg bw-day	ATSDR, 2012	Study details reported in a secondary source; test substance: Technical-grade (90% purity) tricresyl phosphate (CASRN 1330-78-5); unspecified mixture of ortho, meta, and para isomers.
		16-day gavage study in mice Test substance concentrations: 0, 360, 730, 1450, or 2900 mg/kg bw-day (in corn oil), 5800 mg/kg bw-day (neat); 5	NTP, 1994	Study details reported in a primary source; test substance: Tricresyl phosphate (CASRN 1330-78-5) as a commercial product comprised of

Tricresyl phosphate CASRN 1330-78-5				
PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
		days/week Significantly decreased thymus weight in males and females at doses of 1450 mg/kg bw-day or more; necrosis of mandibular lymph node and lymphoid depletion in the spleen of males and females at 2900 mg/kg bw-day (but not at 5800 mg/kg bw-day); lymphoid depletion in the thymus of males at 2900 mg/kg bw-day or more; and necrosis and lymphoid depletion in the thymus of females at 2900 mg/kg bw-day (but not at 5800 mg/kg bw-day)		18% dicresyl phosphate esters (unconfirmed isomeric composition) and 79% tricresyl phosphate esters (21% confirmed as tri-m-cresyl phosphate, 4% as tri-p-cresyl phosphate, and no detectable tri-o-cresyl phosphate [<0.1%]).
		16-day gavage study in F344/N rats Test substance concentrations: 0, 360, 730, 1450, or 2900 mg/kg bw-day (in corn oil), 5800 mg/kg bw-day (neat); 5 days/week Significantly decreased thymus weight in males and females at doses of 1450 mg/kg bw-day or more; necrosis of mandibular lymph node in males at 2,900 mg/kg bw-day (but not at 5800 mg/kg bw-day); necrosis of spleen in males at 2900 and 5800 mg/kg bw-day and females at 2900 mg/kg bw-day (but not at 5800 mg/kg bw-day); necrosis and lymphoid depletion in thymus of males and females at 2900 mg/kg bw-day (but not at 5800 mg/kg bw-day).	NTP, 1994	Study details reported in a primary source; test substance: Tricresyl phosphate (CASRN 1330-78-5) as a commercial product comprised of 18% dicresyl phosphate esters (unconfirmed isomeric composition) and 79% tricresyl phosphate esters (21% confirmed as tri-m-cresyl phosphate, 4% as tri-p-cresyl phosphate, and no detectable tri-o-cresyl phosphate [<0.1%]).

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PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
ECOTOXICITY			
ECOSAR Class			
Acute Aquatic Toxicity	**VERY HIGH: Based on experimental acute aquatic toxicity values < 1.0 mg/L in fish, daphnia, and algae. Estimated aquatic toxicity values are also consistent with a Very High hazard designation. Both experimental and estimated toxicity values are at or near the water solubility limit of this compound.**		
Fish LC_{50}	*Lepomis macrochirus* (bluegill) 96-hour LC_{50} = 0.26 mg/L at water hardness 44 mg/L; 0.061 mg/L at water hardness 314 mg/L Flow-through test conditions (Experimental)	EPA, 2013	Limited study details reported in a secondary source; test substance: Phosphoric acid, tris(methylphenyl)ester (CASRN 1330-78-5).
	Oncorhynchus mykiss (rainbow trout) 96-hour LC_{50} range 0.26-0.4 mg/L Flow-through test conditions (Experimental)	EPA, 2013	Limited study details reported in a secondary source; test substance: Phosphoric acid, tris(methylphenyl)ester (CASRN 1330-78-5).
	Danio rerio (Zebra Danio) 96-hour LC_{50} range 0.4-5.9 mg/L Renewal test conditions Solvent: sulfinyl bis(methane) (Experimental)	EPA, 2013	Limited study details reported in a secondary source; test substance: Phosphoric acid, tris(methylphenyl)ester (CASRN 1330-78-5).
	Oncorhynchus mykiss (rainbow trout; *Salmo gairdneri*); 10/group 96-hour LC_{50} = 0.75 mg/L (95% CL 0.54-1.04 mg/L) Static test conditions with solvent controls (solvent not specified) Test substance concentrations: 0.56, 1.00, 1.80, 3.20, 5.60 mg/L (nominal) (Experimental)	Great Lakes Chemical Corporation, 2001; EPA, 2010	Limited study details reported in a secondary source which did not specify a reliability code; test substance: Phosphoric acid, tris(methylphenyl)ester (CASRN 1330-78-5); purity 100%.
	Oryzias latipes (Japanese Medaka) 96-hour LC_{50} = 1.3 mg/L Test substance concentrations: 0.29-3.09	OECD, 1998; OECD-SIDS, 2002	Limited details reported in a secondary source that indicated the study followed OECD Test Guideline

Tricresyl phosphate CASRN 1330-78-5			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	mg/L (nominal); solvent: methanol Semi-static open-system test conditions (Experimental)		203; test substance: Diphenyl cresyl phosphate (CASRN 26444-49-5); Purity: stated as "phenol, m-cresol, p-cresol = 59%, 22%, 12%".
	Oryzias latipes (Japanese Medaka) 96-hour LC_{50} >3.2 <10 mg/L Renewal test conditions (Experimental)	EPA, 2013	Limited study details reported in a secondary source; test substance: Phosphoric acid, tris(methylphenyl)ester (CASRN 1330-78-5).
	Lepomis macrochirus (bluegill) 96-hour LC_{50} range 29-7,000 mg/L Static test conditions (Experimental)	EPA, 2013	Limited study details reported in secondary sources; test substance: Phosphoric acid, tris(methylphenyl)ester (CASRN 1330-78-5).
	Pimephales promelas (fathead minnow); 10/group 96-hour LC_{50} >100 mg/L Static test conditions Test substance concentrations: 10, 18, 32, 56, and 100 mg/L (nominal) (Experimental)	Great Lakes Chemical Corporation, 2001	Limited study details reported in a secondary source which considered the study valid with restrictions; test substance: Phosphoric acid, tris(methylphenyl)ester (CASRN 1330-78-5); purity 100%'
	Brachydanio rerio (Zebrafish) 96-hour LC_o = 8.1 mg/L (not specified whether nominal or analytical) 96-hour LC_{90} = 11.5 mg/L (not specified whether nominal or analytical) Test conditions not specified (Experimental)	OECD-SIDS, 2002	Limited details reported in a secondary source; test substance: Diphenyl cresyl phosphate (CASRN 26444-49-5); purity not specified.
	Fish 96-hour LC_{50}: 0.58 mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	Estimations for monocresyl diphenyl phosphate The estimated log K_{ow} of 5.2 for this chemical exceeds the SAR limitation for log K_{ow} of 5.0; NES are predicted for these endpoints. Dicresyl phenyl phosphate

Tricresyl phosphate CASRN 1330-78-5			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
			and higher alkylated isomers have higher estimated log K_{ow} values; therefore NES are predicted for the higher alkylated isomers also. Estimate for the Esters class was provided for comparative purposes. See Section 5.5.1.
Daphnid LC_{50}	*Daphnia magna* (water flea) 48-hour LC_{50} = 0.27 mg/L Static test conditions Test substance concentrations: 0.06, 0.1, 0.18, 0.32, 0.56 mg/L (nominal) Solvent: Acetone NOEC: 0.1 mg/L (nominal) (Experimental)	Great Lakes Chemical Corporation, 2001; EPA, 2010	Great Lakes Chemical Corporation considered the study valid with restrictions; test substance: Phosphoric acid, tris(methylphenyl)ester (CASRN 1330-78-5).
	Daphnia magna (water flea) 48-hour LC_{50} = 5.6 mg/L Flow-through test conditions (Experimental)	WHO, 1990	Limited study details in secondary source; test substance: Phosphoric acid, tritolyl ester (CASRN 1330-78-5).
	Daphnid 48-hour LC_{50}: 0.85 mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	Estimations for monocresyl diphenyl phosphate The estimated log K_{ow} of 5.2 for this chemical exceeds the SAR limitation for log K_{ow} of 5.0; NES are predicted for these endpoints. Dicresyl phenyl phosphate and higher alkylated isomers have higher estimated log K_{ow} values; therefore NES are predicted for the higher alkylated isomers also. Estimate for the Esters class was

Tricresyl phosphate CASRN 1330-78-5			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
			provided for comparative purposes. See Section 5.5.1.
Green Algae EC_{50}	*Scenedesmus pannonicus* (green algae) 96-hour EC_{50} = 0.56 mg/L (growth rate) (Experimental)	EPA, 2010	Limited study details summarized in reliable secondary source, test substance: Phosphoric acid, tris(methylphenyl)ester (CASRN: 1330-78-5).
	Pseudokirchneriella subcapitata (formerly *Selenastrum capricornutum* ; green algae) 72-hour EC_{50} = 0.99 mg/L (nominal) Test substance concentrations: 0.31-3.24 mg/L (nominal); solvent: methanol (Experimental)	OECD, 1998; OECD-SIDS, 2002	Limited study details reported in secondary source that indicated the study followed OECD Test Guideline 201; Test substance: Diphenyl cresyl phosphate (CASRN 26444-49-5); purity: stated as "phenol, m-cresol, p-cresol = 59%, 22%, 12%".
	Green algae 96-hour EC_{50} range 1.3-3.8 mg/L (growth) Static test conditions (Experimental)	WHO, 1990; EPA, 2013	Limited study details reported in secondary sources; test substance: Phosphoric acid, tris(methylphenyl)ester (CASRN 1330-78-5).
	Green algae 96-hour EC_{50} = 0.04 mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	Estimation for tricresyl phenyl phosphate. Estimate for the Esters class was provided for comparative purposes. See Section 5.5.1.
	Green algae 96-hour EC_{50} = 0.09 mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	Estimation for dicresyl phenyl phosphate. Estimate for the Esters class was

Tricresyl phosphate CASRN 1330-78-5			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
			provided for comparative purposes. See Section 5.5.1.
	Green algae 96-hour EC_{50} = 0.16 mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	Estimation for monocresyl diphenyl phosphate. Estimate for the Esters class was provided for comparative purposes. See Section 5.5.1.
Chronic Aquatic Toxicity	**HIGH: Based on estimated chronic aquatic toxicity values. An estimated chronic aquatic toxicity value derived using an acute-to-chronic ratio (ACR) for the phosphate esters class and was applied to the available experimental acute data for this chemical and indicated a High hazard. Estimated chronic aquatic toxicity values < 0.1 mg/L in fish, daphnia, and algae (Esters class) also indicated a High hazard concern. Experimental studies for *Daphnia magna* and algae indicated a High hazard designation with toxicity values within the 0.1 - 1 mg/L range. No experimental chronic studies were located for fish.**		
Fish ChV	Freshwater fish ChV = 0.01 mg/L (Estimated)	Professional judgment	An ACR of 24 was derived for the phosphate ester class based on experimental data for Tris (p-t-butylphenyl) phosphate (TBPP). The acute-to-chronic ratio was applied to available experimental acute fish data for Phosphoric acid, tris(methylphenyl) ester (CASRN 1330-78-5) (ChV = 0.26 mg/L /24 = 0.01 mg/L)

Tricresyl phosphate CASRN 1330-78-5			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	Fish ChV = 0.004 mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	Estimation for tricresyl phenyl phosphate. Estimate for the Esters class was provided for comparative purposes. See Section 5.5.1.
	Fish ChV = 0.01 mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	Estimation for dicresyl phenyl phosphate. Estimate for the Esters class was provided for comparative purposes. See Section 5.5.1.
	Fish ChV = 0.02 mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	Estimation for monocresyl diphenyl phosphate. Estimate for the Esters class was provided for comparative purposes. See Section 5.5.1.
Daphnid ChV	*Daphnia magna* (water flea) 21-day LC_{50} = 0.35 mg/L (mortality) 21-day EC_{50} = 0.31 mg/L (reproduction) 21-day NOEC = 0.12 mg/L (reproduction) Test substance concentrations: 0.038-3.8 mg/L (nominal); solvent: dimethyl sulfoxide (DMSO) Semi-static open-system test conditions (Experimental)	OECD, 1998; OECD-SIDS, 2002	Secondary source indicated the study followed OECD Test Guideline 202; test substance: Diphenyl cresyl phosphate (CASRN 26444-49-5) Purity: stated as "phenol, m-cresol, p-cresol = 59%, 22%, 12%".
	Daphnia magna (water flea) 21-day EC_{50} range 0.1-1.0	EPA, 2010, 2013	Limited study details reported in secondary sources; test substance:

Tricresyl phosphate CASRN 1330-78-5			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	Renewal test conditions (Experimental)		Phosphoric acid, tris(methylphenyl)ester (CASRN 1330-78-5).
	Daphnid ChV = 0.04 mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	Estimation for tricresyl phenyl phosphate. Estimate for the Esters class was provided for comparative purposes. See Section 5.5.1.
	Daphnid ChV = 0.09 mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	Estimation for dicresyl phenyl phosphate. Estimate for the Esters class was provided for comparative purposes. See Section 5.5.1.
	Daphnid ChV = 0.23 mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	Estimation for monocresyl diphenyl phosphate. Estimate for the Esters class was provided for comparative purposes. See Section 5.5.1.
Green Algae ChV	*Pseudokirchneriella subcapitata* (formerly *Selenastrum capricornutum*; green algae) 72-hour NOEC = 0.55 mg/L (nominal) Test substance concentrations: 0.31-3.24 mg/L (nominal); solvent: methanol (Experimental)	OECD, 1998; OECD-SIDS, 2002	Limited study details reported in secondary source that indicated the study followed OECD Test Guideline 201; Test substance: Diphenyl cresyl phosphate (CASRN 26444-49-5); purity: stated as "phenol, m-cresol, p-cresol = 59%, 22%, 12%".

Tricresyl phosphate CASRN 1330-78-5			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	Green algae ChV = 0.04 mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	Estimation for tricresyl phenyl phosphate. Estimate for the Esters class was provided for comparative purposes. See Section 5.5.1.
	Green algae ChV = 0.08 mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	Estimation for dicresyl phenyl phosphate. Estimate for the Esters class was provided for comparative purposes. See Section 5.5.1.
	Green algae ChV = 0.16 mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	Estimation for monocresyl diphenyl phosphate. Estimate for the Esters class was provided for comparative purposes. See Section 5.5.1.

Tricresyl phosphate CASRN 1330-78-5				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
ENVIRONMENTAL FATE				
Transport		**Level III fugacity models incorporating available physical and chemical property data indicate that at steady state, tricresyl phosphate is expected to be found primarily in soil and to a lesser extent, sediment. Tricresyl phosphate is expected to have negligible to moderate mobility in soil based on both measured and estimated K_{OC} values. Leaching of tricresyl phosphate through soil to groundwater is not expected to be an important transport mechanism. There is slight potential for volatilization from moist soil surfaces based upon the measured Henry`s Law constant; however adsorption to soil is expected to attenuate this process. In the atmosphere, tricresyl phosphate is expected to exist in the vapor and particulate phase. Vapor phase tricresyl phosphate will be degraded in the atmosphere by reaction with photochemically-produced hydroxyl radicals; the half-life for this reaction in air is estimated to be 0.8 days. Particulate phase tricresyl phosphate will be removed from air by wet or dry deposition.**		
	Henry's Law Constant (atm-m^3/mole)	$8x10^{-7}$ (Measured)	PhysProp, 2012	Reported in s a secondary source with limited details.
		$8.3x10^{-5}$ (Measured)	EPA, 2010	Reported for tri-m-cresyl phosphate (CASRN 563-04-2); purity and test method not stated.
		$4x10^{-8}$ for monocresyl diphenyl phosphate; $5x10^{-8}$ for dicresyl phenyl phosphate and tricresyl phosphate Bond method (Estimated)	EPI v4.11	Estimated using representative structures indicated in the SMILES section for methylated phenyl phosphate with one, two and three methyl substituent groups respectively.
	Sediment/Soil Adsorption/Desorption - K_{oc}	Reported as the adsorption coefficient per gram of clay minerals. Kaolin: 0.236 (236 L/kg) Alumina: 0.177 (177 L/kg) Montmorillonite: 4.614 (4614 L/kg) (Measured)	Takimoto et al., 1998	Nonguideline, well-documented study for reagent grade tri-p-cresyl phosphate (CASRN 78-32-0).
		Reported as the adsorption coefficient per gram of clay minerals. Kaolin: 0.196 (196 L/kg) Alumina: 0.144 (144 L/kg)	Takimoto et al., 1998	Nonguideline, well-documented study for reagent grade tri-m-cresyl phosphate (CASRN 563-04-2).

Tricresyl phosphate CASRN 1330-78-5				
PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
		Montmorillonite: 1.361 (1361 L/kg) (Measured)		
		Reported as the adsorption coefficient per gram of clay minerals. Kaolin: 0.158 (158 L/kg) Alumina: 0.118 (118 L/kg) Montmorillonite: 1.550 (1550 L/kg) (Measured)	Takimoto et al., 1998	Nonguideline, well-documented study for reagent grade tri-o-cresyl phosphate (CASRN 78-30-8).
		18,000 for monocresyl diphenyl phosphate; 28,000 for dicresyl phenyl phosphate MCI method (Estimated)	EPI v4.11	Estimated using a representative structure
		>30,000 MCI method (Estimated)	EPI v4.11; EPA, 2005	Estimated using a representative structure for tricresyl phosphate. Cutoff value for nonmobile compounds.
	Level III Fugacity Model	Air = 0.3% Water = 9.9% Soil = 64% Sediment = 26% (Estimated)	EPI v4.11	Estimated using a representative structure for tricresyl phosphate.

Tricresyl phosphate CASRN 1330-78-5				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Persistence		**MODERATE: Based on nonguideline studies that have demonstrated primary and ultimate biodegradation of tricresylphosphate and related components under aerobic conditions. There is evidence of biodegradation resulting in a half-life less than 60 days but greater than 16 days. Both CASRN 563-04-2 and 26444-49-5 did not pass ready biodegradability OECD 301C tests, however some degradation, <43.1%, was observed after 28 days. Other biodegradation tests, including OECD 302A, 302C, CO_2 Evolution and a Die Away test indicated some degradation by this pathway. Experimental data for the direct photolysis of CASRN 26444-49-5 reported a half-life of 4.86 years; therefore, direct photolysis of tricresyl phosphate is not expected to be an important fate process. Experimental half-lives of 27 to 87 minutes for tricresyl phosphate and 2 individual isomers, demonstrate removal by hydrolysis under alkaline conditions.**		
Water	**Aerobic Biodegradation**	Passes Ready Test: No Test method: OECD TG 301C: Modified MITI Test (I) 30.8 and 43.1% degradation in 28 days (Measured)	EPA, 2010	Reported for tri-m-cresyl phosphate (CASRN 563-04-2); purity not stated.
		Passes Ready Test: No Test method: OECD TG 301C: Modified MITI Test (I) Reported as 0, 0, and 0% after 28 days from BOD; 11, 5 and 5% after 28 days from high performance liquid chromatography (HPLC); using GLP (Measured)	OECD-SIDS, 2002	Guideline study in a secondary source for cresyl diphenyl phosphate (CASRN 26444-49-5).
		Passes Ready Test: No Test method: OECD TG 301C: Modified MITI Test (I) Using OECD Test Guideline 301C (100 mg/L concentration of test substance), diphenyl cresyl phosphate had a 0% theoretical BOD after 28 days of incubation. (Measured)	HSDB, 2013a	Reported for diphenyl cresyl phosphate (CASRN 26444-49-5) purity not stated. This study used an initial concentration of compound that was more than 40 times greater than the water solubility.

Tricresyl phosphate CASRN 1330-78-5				
PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
		Study results: 78.6%/7 days Test method: CO_2 Evolution In a modified Sturm test ultimate degradation was measured. At 26.4 mg/L tricresyl phosphate achieved 78.6% of its theoretical CO_2 in 7 days and 82% in 8 days. (Measured)	WHO, 1990; HSDB, 2013d	Nonguideline study reported in secondary sources; purity not indicated.
		Study results: 100%/28 days Test method: 302C: Inherent - Modified MITI Test (II) (Measured)	EPA, 2010	Reported in a secondary source with limited study details for tri-p-cresyl phosphate (CASRN 78-32-0); purity not stated.
		Study results: 65.7%/28 days Test method: 302C: Inherent - Modified MITI Test (II) Inherently biodegradable (Measured)	EPA, 2010	Reported in a secondary source with limited study details for tri-o-cresyl phosphate (CASRN 78-30-8).
		Study results: 82%/22 weeks Test method: 302A: Inherent - Modified SCAS Test Primary degradation measured; influent concentrations of 3 mg/L/day (Measured)	HSDB, 2013a	Reported in a secondary source for diphenyl cresyl phosphate (CASRN 26444-49-5).
		Study results: 100%/4 days Test method: Die-Away River water; complete degradation in 4 days (Measured)	HSDB, 2013a	Reported for diphenyl cresyl phosphate (CASRN 26444-49-5); purity not stated.
		Study results: 75-100%/29 days Test method: Die-Away In die-away tests in Japanese river water	HSDB, 2013d	Nonguideline study reported in secondary sources; purity not indicated.

Tricresyl phosphate CASRN 1330-78-5				
PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
		and Japanese bay water tricresyl phosphate achieved 100% primary degradation after 4 days at 26°C; 75-100% degradation was observed after 29 days at 7°C, a lag-phase of 1-3 days was observed. (Measured)		
		Study results: 82%/28 days Test method: Die-Away In a river die-away test, at a test concentration of 26 mg/L, CO_2 evolution was 79% after 7 days, 82% after 28 days and 86% after 48 days. (Measured)	HSDB, 2013c	Reported for tri-o-cresyl phosphate (CASRN 78-30-8) purity and study details not stated.
		Study results: >97%/4 weeks Test method: Die-Away In a semi-continuous activated sludge test using influent concentrations of 3 and 13 mg/L/day tricresyl phosphate was shown to undergo 97% and >99% primary degradation, respectively, after 4 weeks. (Measured)	Saeger et al., 1979 (as cited in EPA, 2010; HSDB, 2013d)	Nonguideline study reported for a commercial grade mixture of isomers; purity not indicated.
		Study results: 100%/4 days Test method: Die-Away In a river die-away test in water from the Mississippi river St. Louis, MO. Complete primary degradation of tricresyl phosphate was achieved after 4 days following an initial lag-phase of 2 days with 8% degradation. Rapid degradation attributed to microbial adaptation. (Measured)	EPA, 2010; HSDB, 2013d	Nonguideline study reported in a secondary source for a commercial grade mixture of isomers; purity not indicated.
		A die-away study using Lake Ontario	Howard and Deo, 1979 (as cited	Reported for individual isomers.

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PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
		water from Oswego, NY found that the individual isomers exhibited a two-day lag period before degrading rapidly; the ortho- and meta-isomers were completely degraded within 4 days while about half of the para-isomer was degraded in 5 days. (Measured)	in EPA, 2010; HSDB, 2013a, 2013c)	
		Study results: 82.1%/28 days Test method: Screening Test Inherently biodegradable. After 7, 28, and 48 days 78.6, 82.1, and 86.3% theoretical CO_2 evolution was achieved in acclimated bacterial inoculum, respectively. There was a 14-day acclimation period noted. (Measured)	Saeger et al., 1979 (as cited in EPA, 2010)	Reported for a commercial grade sample; mixture of isomers purity not stated.
		Study results: 97%/4 weeks Test method: Other 99% after 7 weeks; activated sludge inoculum and a test substance addition rate of 3 and 13 mg/L per 24 hours. (Measured)	HSDB, 2013c	Reported for tri-o-cresyl phosphate (CASRN 78-30-8); purity and test method not stated.
		Study results: 53.2%/7 days Test method: Other At test concentrations of 23.1 mg/L, this chemical achieved 53.2, 84.5 and 91.3% of its theoretical CO_2 evolution in activated sludge after 7, 28, and 48 days, respectively. (Measured)	HSDB, 2013a	Reported for diphenyl cresyl phosphate (CASRN 26444-49-5) purity and test method not stated.
		Study results: 50%/7.5 hours Test method: Other	Great Lakes Chemical Corporation, 2001	Reported for tri-p-cresyl phosphate (CASRN 78-32-0).

Tricresyl phosphate CASRN 1330-78-5				
PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
		1 µg/ml of ^{14}C-tri-p-cresyl phosphate achieved 70-80% degradation after 24 hours in sewage sludge at 21°C. Degradation was determined by liquid scintillation counting, gas chromatography, and thin layer chromatography. The remaining test material was associated with the sludge solids. The major metabolite was p-hydroxybenzoic acid. (Measured)		
		Study results: 40-60%/48 hour Test method: Other Rapid biodegradation was observed in activated sludge. 40-60% degradation of tricresyl phosphate was achieved in a 48-hour wastewater treatment simulation test. (Measured)	HSDB, 2013d	Nonguideline study reported in a secondary source. Purity of test substance and test details not stated.
		Biodegradable in tests using activated sludge seed. (Measured)	HSDB, 2013b	Reported for tri-m-cresyl phosphate (CASRN 563-04-2) purity and test method not stated.
		Performed in sediment-water incubation systems; Pond sediment half-life: 3.2, 4.1, and 16.3 days at 25, 10, and 2°C, respectively; River sediment half-life: 10.1 days at 25°C. (Measured)	HSDB, 2013b	Reported for tri-m-cresyl phosphate (CASRN 563-04-2) purity not stated.
		Study results: 50%/10 days Test method: Field Test Biodegradation in river water and bottom sediment followed first-order kinetics. The	HSDB, 2013c	Reported for tri-o-cresyl phosphate (CASRN 78-30-8); purity not stated.

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		first-order rate constant in river water ranged from approximately 0.0022 per hour at 14°C to 0.0030 per hour at 25°C; this corresponds to a half-life of about 13 days at 14°C and 10 days at 25°C (Measured)		
		Study results: 0%/8 weeks Test method: Screening Test The meta isomer of tricresyl phosphate did not degrade in 1:10 dilutions of primary anaerobic sludge after 8 weeks. (Measured)	HSDB, 2013d	Nonguideline study reported in a secondary source for tri-m-cresyl phosphate (CASRN 563-04-2); purity not stated.
		River water half-life: approx. 13 days at 14°C; 2.9 days at 20°C Bottom sediment half-life: approx. 8 days at 14°C; 5.4 days at 25°C (Measured)	HSDB, 2013b	Reported for tri-m-cresyl phosphate (CASRN 563-04-2) purity not stated. River water and bottom sediment biodegradation followed first-order kinetics.
	Volatilization Half-life for Model River	58 days (Estimated)	EPI v4.11	Estimated using a representative structure for tricresyl phosphate.
	Volatilization Half-life for Model Lake	>1 year (Estimated)	EPI v4.11	Estimated using a representative structure for tricresyl phosphate.
Soil	**Aerobic Biodegradation**			No data located.
	Anaerobic Biodegradation	Not probable (Anaerobic-methanogenic biodegradation probability model)	EPI v4.11	Tricresyl phosphate (CASRN 1330-78-5); estimated from representative structure: tri-ortho-cresyl-phosphate.
	Soil Biodegradation with Product Identification			No data located.
	Sediment/Water Biodegradation			No data located.
Air	**Atmospheric Half-life**	0.91 days for monocresyl diphenyl	EPI v4.11	Estimated using representative

Tricresyl phosphate CASRN 1330-78-5				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		phosphate; 0.84 for dicresyl phenyl phosphate: 0.78 for tricresyl phosphate (Estimated)		structures indicated in the SMILES section for methylated phenyl phosphate with one, two and three methyl substituent groups respectively.
Reactivity	**Photolysis**	50%/4.86 years Test performed in water using direct sunlight. Concentration: $5x10^{-5}$M; Spectrum: Epsilon = $8.17x10^{3}$ at 300 nm Degradation rate: $2.26x10^{-13}$ mol/l/s Quantum yield = 0.01 (Measured)	OECD-SIDS, 2002	Nonguideline study reported in a secondary source for cresyl diphenyl phosphate (CASRN 26444-49-5) purity of test substance and test method not stated.
	Hydrolysis	50%/47 days at pH 7; 25°C 50%/5.10 days at pH 9 and 25°C (Measured)	OECD-SIDS, 2002	Reported in a secondary source for cresyl diphenyl phosphate (CASRN 26444-49-5).
		50%/27 minutes in 0.03 M $NaBO_3$ at pH 10.3 (Measured)	David and Seiber, 1999	Reported for tri-p-cresyl phosphate (CASRN 78-32-0).
		50%/70 minutes in 0.03 M $NaBO_3$ at pH 10.3 (Measured)	David and Seiber, 1999	Reported for tricresyl phosphate (CASRN 1330-78-5) mixed isomers.
		50%/87 minutes in 0.03 M $NaBO_3$ at pH 10.3 (Measured)	David and Seiber, 1999	Reported for tri-o-cresyl phosphate (CASRN 78-30-8).
		In alkaline medium hydrolysis to dicresylphosphate and cresol occurs; stable in neutral and acidic media. (Measured)	van der Veen and de Boer, 2012	Supporting information reported in a secondary source.
Environmental Half-life		75 (Estimated)	PBT Profiler	Estimation for tricresyl phenyl phosphate, dicresyl phenyl phosphate and monocresyl phenyl phosphate. Half-life estimated for the predominant compartment, as determined by EPI and the PBT Profiler methodology.

Tricresyl phosphate CASRN 1330-78-5				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Bioaccumulation		**HIGH: Multiple experimental BCF and estimated BAF values are above 1,000, the high bioaccumulation designation criteria.**		
	Fish BCF	165 in fathead minnows; flow-through test with 32 day exposure period (Measured)	HSDB, 2013d	Reported in a secondary source, test method not stated.
		169 in Rainbow trout; flow-through test; BCF of 10 for white muscle and 169 for gut and adipose tissue (Measured)	HSDB, 2013d	Reported in a secondary source for a commercial mixture (IMOL S-140) 75% tricresyl phosphate and 18% trixylyl phosphate (CASRN 25155-23-1).
		700 in Zebra fish; flow-through test with 14 day exposure period (Measured)	HSDB, 2013d	Reported in a secondary source, test method not stated.
		928 in fathead minnow; 24-hour static test measured a BCF range of 596-928 based on total ^{14}C; since the ^{14}C measurements include tricresyl phosphate metabolites, the observed BCF values indicate a worse-case estimate only. (Measured)	HSDB, 2013d	Reported in a secondary source with meta- and para-isomers specified, although percent composition of the components and purity not stated.
		980 (Measured)	OECD-SIDS, 2002	Reported in a secondary source for cresyl triphenyl phosphate (CASRN 26444-49-5); test method not stated.
		1,420 in rainbow trout; 24-hour static test measured a BCF range of 784-1420 based on total ^{14}C; since the ^{14}C measurements include tricresyl phosphate metabolites, the observed BCF values indicate a worse-case estimate only. (Measured)	HSDB, 2013d	Reported in a secondary source with meta- and para-isomers specified, although percent composition of the components and purity not stated.
		1,711 (Measured)	van der Veen and de Boer, 2012	Reported in a secondary source for cresyl diphenyl phosphate (CASRN 26444-49-5); purity not stated.
		3,700 in *Gambusia* fish; reported as an ecological magnification factor; static test using a model ecosystem. Tri-p-cresyl	Boethling and Cooper, 1985 (as cited in HSDB, 2013d)	Reported in a secondary source.

Tricresyl phosphate CASRN 1330-78-5				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		phosphate was found to accumulate and persist in all aquatic test systems studied. (Measured)		
	Other BCF			No data located.
	BAF	1381 (Estimated)	EPI v4.11	Estimated using the Arnot-Gobas method with a representative structure for tricresyl phosphate.
		1422 (Estimated)	EPI v4.11	Estimated using the Arnot-Gobas method with a representative structure for dicresyl phenyl phosphate.
		214 (Estimated)	EPI v4.11	Estimated using the Arnot-Gobas method with a representative structure for monocresyl phenyl phosphate.
	Metabolism in Fish			No data located.
ENVIRONMENTAL MONITORING AND BIOMONITORING				
Environmental Monitoring		Tricresyl phosphate has been detected in areas of Japan, Canada, US, UK, Italy, Norway, Sweden, Germany, and Austria in river water, drinking water, rain water and snow, sediments, sea sediment and soil samples. Cresyl diphenyl phosphate was detected in coastal marine sediments in the UK. Tricresyl phosphate has been detected in atmospheric samples, indoor air of theaters, offices, electronic stores, an electronics dismantling facility and airplanes. It has also been detected in fly ash and stack emissions, and various effluents, in dust samples/wipe samples from automobile interiors, aircraft and vegetation samples. In one study, tricresyl phosphate isomers, m-TCP and o-TCP were detected in atmospheric samples, while the para isomer was scarcely detected (Takimoto et al., 1999; OECD-SIDS, 2002; Bacaloni et al., 2008; Takigami et al., 2009; Ibbotson and Ibhadon, 2010; Solbu et al., 2011; HSDB, 2013d; Salamova et al., 2014).		
Ecological Biomonitoring		Tricresyl phosphate has been detected in fish (HSDB, 2013d).		
Human Biomonitoring		Human biomonitoring found small amounts of metabolites of tri-m- and tri-p cresyl phosphates in the urine of aircraft crews. Metabolites of tri-o-cresyl phosphates were not detected above the LOD of the study (Schindler et al., 2013).		

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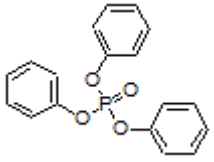
Triphenyl phosphate (TPP)

Screening Level Toxicology Hazard Summary

This table contains hazard information for each chemical; evaluation of risk considers both hazard and exposure. Variations in end-of-life processes or degradation and combustion by-products are discussed in the report but not addressed directly in the hazard profiles. The caveats listed below must be taken into account when interpreting the information in the table.

VL = Very Low hazard L = Low hazard M = Moderate hazard H = High hazard VH = Very High hazard – Endpoints in colored text (VL, L, M, H, and VH) were assigned based on empirical data. Endpoints in black italics *(VL, L, M, H,* and *VH*) were assigned using values from estimation software and professional judgment [(Quantitative) Structure Activity Relationships "(Q)SAR"].

Chemical	CASRN	Human Health Effects											Aquatic Toxicity		Environmental Fate	
		Acute Toxicity	Carcinogenicity	Genotoxicity	Reproductive	Developmental	Neurological	Repeated Dose	Skin Sensitization	Respiratory Sensitization	Eye Irritation	Dermal Irritation	Acute	Chronic	Persistence	Bioaccumulation
Triphenyl phosphate (TPP)	115-86-6	L	*M*	L	L	L	L	H	L		L	VL	VH	VH	L	M



CASRN: 115-86-6

MW: 326.29

MF: $C_{18}H_{15}O_4P$

Physical Forms:
Neat: Solid

Use: Flame retardant

SMILES: O=P(Oc1ccccc1)(Oc1ccccc1)Oc1ccccc1

Synonyms: Phosphoric acid, triphenyl ester; O,O,O-Triphenyl phosphate; TPP

Chemical Considerations: This is a discrete organic chemical with a MW below 1,000. EPI v4.11 was used to estimate physical/chemical and environmental fate values due to an absence of experimental data. Measured values from experimental studies were incorporated into the estimations.

Polymeric: No
Oligomeric: Not applicable

Metabolites, Degradates and Transformation Products: Diphenyl phosphate (CASRN 838-85-7) and phenol (CASRN 108-95-2) (OECD-SIDS, 2002)

Analog: No analog
Endpoint(s) using analog values: Not applicable

Analog Structure: Not applicable

Structural Alerts: Organophosphates; Neurotoxicity (EPA, 2012).

Risk Phrases: R50/53: Very toxic to aquatic organisms. May cause long-term adverse effects in the aquatic environment (OECD-SIDS, 2002).

Hazard and Risk Assessments: DfE Alternatives Assessment for Furniture Flame Retardancy Partnership and Flame Retardant Alternatives for DecaBDE Partnership; Toxicological Profile for Phosphate Ester Flame Retardants, September, 2012; OECD SIDS Initial Assessment Report, October 2002 (OECD-SIDS, 2002; EPA, 2005, 2012; ATSDR, 2009).

Triphenyl phosphate CASRN 115-86-6			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
PHYSICAL/CHEMICAL PROPERTIES			
Melting Point (°C)	50.5 (Measured)	Lide, 2008	Reported in a primary source.
	49 Reported as 49-50°C (Measured)	EC, 2000	Reported in a secondary source; consistent with value reported in primary source.
Boiling Point (°C)	>300 (Estimated)	EPI v4.11; EPA, 1999	Cutoff value for high boiling point compounds according to HPV assessment guidance.
	245 Reported at 11 mm Hg (Measured)	O'Neil et al., 2006	Reported in a primary source.
	220 Reported at 5 mm Hg (Measured)	EC, 2000	Reported in a secondary source; consistent with value reported in primary source.
Vapor Pressure (mm Hg)	6.28×10^{-6} at 25°C (Extrapolated)	Dobry and Keller, 1957	Reported in a secondary source.
	1.5×10^{-6} (Measured)	EC, 2000	Reported in a secondary source.
Water Solubility (mg/L)	1.9 (Measured) Reported at 25°C	Saeger et al., 1979	Reported in a secondary source.
	0.75 (Measured) OECD Guideline 105	EC, 2000	Guideline study reported in a secondary source.
	0.025 (Measured)	EC, 2000	Reported in a secondary source; not consistent with other measured values.
Log K_{ow}	4.59 (Measured)	Hansch et al., 1995	Reported in a primary source.
	4.76 (Measured)	OECD-SIDS, 2002	Reported in a secondary source; consistent with value reported in primary source.
Flammability (Flash Point)	220°C (Measured)	Lewis, 2007	No study details reported.

Triphenyl phosphate CASRN 115-86-6			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
Explosivity	Not expected to form explosive mixtures with air (Estimated)	Professional judgment	No experimental data located; based on its use as a flame retardant.
Pyrolysis			No data located.
pH	Not applicable (Estimated)	Professional judgment	Does not contain functional groups that are expected to ionize under environmental conditions.
pK_a	Not applicable (Estimated)	Professional judgment	Does not contain functional groups that are expected to ionize under environmental conditions.

Triphenyl phosphate CASRN 115-86-6				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
HUMAN HEALTH EFFECTS				
Toxicokinetics		**Triphenyl phosphate is hydrolyzed in the liver to produce diphenyl phosphate as the primary metabolite. TPP can be detected in human breast milk. Experimental data for the FM550 (a mixture made up of a sum total of TBB and TBPH of 50% with additional components identified as IPTPP and TPP) indicate that absorption of at least one component (TBB) can occur in rats following oral exposure from gestation through lactation. TBB was detected in tissues of exposed dams and the pups following exposure to FM550.**		
Dermal Absorption *in vitro*				No data located.
Absorption, Distribution, Metabolism & Excretion	**Oral, Dermal or Inhaled**	Pregnant rats were administered 0, 0.1 or 1 mg/kg-day of FM550 in the diet across gestation and through lactation (GD8 - PND 21) FM550 components including TBPH was detected in adipose, liver, and muscle tissues in Dams at PND 21 with the highest concentration in the adipose tissue (768 ng/g w.w. in high dose, 29.6 ng/g w.w. in low dose, < 7.0 ng/g w.w. in controls). The primary metabolite of TBB (TBBA) was also detected in liver tissue of dams on PND 21. TBB was detected in pooled PND21 pup adipose tissue. TBB was not detected in pooled pup adipose tissue by PND220.	Patisaul et al., 2013	Non guideline study indicates that absorption of this compound can occur in rats through oral exposure; the test substance identified as FM550 is a mixture made up of TBB, TBPH (sum total of TBB and TBPH is approximately 50%), TPP and IPTPP; it is unclear if absorption in pups occurred due to gestational exposure or through lactation.
		Triphenyl phosphate is hydrolyzed in rat liver homogenate to produce the metabolite diphenyl phosphate	OECD-SIDS, 2002; ECHA, 2012	Reported in a secondary source.

Triphenyl phosphate CASRN 115-86-6				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Other	TPP concentrations in milk were analyzed in a human cohort study conducted between 1997 and 2007. Median concentration across all subjects was 8.5 ng/g (min-max values: 3.2 - 11 ng/g).	ECHA, 2012	Limited study details reported in a secondary source
Acute Mammalian Toxicity		**LOW: Oral LD_{50} in rats and mice is >5,000 mg/kg and the dermal LD_{50} in rabbits is >7,900 mg/kg. No adequate data were located to assess the toxicity of inhalation exposure.**		
Acute Lethality	**Oral**	Rat, mouse, oral LD_{50} >5,000 mg/kg	OECD-SIDS, 2002	Reported in a secondary source.
		Rat oral LD_{50} >6,400 mg/kg	ATSDR, 2009	Reported in a secondary source.
		Rat oral LD_{50} >20,000 mg/kg	OECD-SIDS, 2002	Study reported in a secondary source.
		Rat oral LD_{50} = 10,800 mg/kg	OECD-SIDS, 2002	Study reported in a secondary source; number of animals not reported.
		Rat oral LD_{50} = 3,500 mg/kg	OECD-SIDS, 2002	Study reported in a secondary source. Dose range and number of animals is not provided.
	Dermal	Rabbit dermal LD_{50} >7,900 mg/kg	ATSDR, 2009	Reported in a secondary source.
		Rabbit dermal LD_{50} >10,000 mg/kg	OECD-SIDS, 2002	Reported in a secondary source.
	Inhalation	Rat 1-hour LC_{50} >200 mg/L	OECD-SIDS, 2002; ATSDR, 2009	Reported in a secondary source. Insufficient exposure time (1 hour), no data on method or GLP.
Carcinogenicity		**MODERATE: OncoLogic modeling indicates a marginal to low potential for carcinogenicity. No long-term carcinogenicity assays were found.**		
	OncoLogic Results	Marginal; likely to have equivocal carcinogenic activity.	OncoLogic, 2008	
	Carcinogenicity (Rat and Mouse)	Mouse lung adenoma test: Male A/St mice (20/group) received i.p. injections of either 20 mg/kg (18/6 weeks); 40	OECD-SIDS, 2002	Reported in a secondary source. Nonstandard study, limited histopathology and short-

Triphenyl phosphate CASRN 115-86-6				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		mg/kg (3/1 week); or 80 mg/kg. No significant increase in incidence of adenoma compared to negative controls, and positive control (urethane) produced 19.6 tumors/mouse with 100% survival.		duration.
	Combined Chronic Toxicity/Carcinogenicity			No data located.
	Other			No data located.
Genotoxicity		**LOW: Triphenyl phosphate was not mutagenic in bacteria or mammalian cells *in vitro* and did not cause chromosomal aberrations *in vitro*. In addition, triphenyl phosphate did not result in DNA damage in hamster fibroblast cells.**		
	Gene Mutation *in vitro*	Negative, Ames assay in *Salmonella typhimurium* strains TA98, TA100, TA1537, TA1538 with and without metabolic activation	ATSDR, 2009; ECHA, 2013	Reported in a secondary source.
		Negative, forward mutation assay in mouse lymphoma L5178Y cells	OECD-SIDS, 2002; ECHA, 2013	Reported in a secondary source.
	Gene Mutation *in vivo*			No data located.
	Chromosomal Aberrations *in vitro*	Negative in chromosome aberration test in Chinese hamster V79 cells; with and without metabolic activation.	ECHA, 2013	Reported in a secondary source.
	Chromosomal Aberrations *in vivo*			No data located.
	DNA Damage and Repair	Negative, unscheduled DNA synthesis in hamster fibroblast cells	OECD-SIDS, 2002	Reported in a secondary source.
	Other	Negative, mitotic gene conversion assay in *Saccharomyces cerevisiae* with and without activation	OECD-SIDS, 2002	Reported in a secondary source.

Triphenyl phosphate CASRN 115-86-6				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Reproductive Effects		**LOW: Based on a rat oral reproductive/developmental NOAEL = 690 mg/kg-day for reproductive effects (highest dose tested). In addition, no histopathological effects on reproductive organs were reported following 3 weeks of dermal exposure in rabbits. Correlation of TPP in house dust and decreased sperm counts in humans has been reported, however rat studies did not measure the same endpoint, so there is an insufficient data for this effect.**		
	Reproduction/Developmental Toxicity Screen			No data located.
	Combined Repeated Dose with Reproduction/ Developmental Toxicity Screen	Reproductive/developmental dietary study; TPP was administered in the diet for 91 days at concentrations of 0, 0.25, 0.50, 0.75, or 1.0% (~0, 166, 341, 516 or 690 mg/kg-day, respectively). At the completion of this study, females were mated with males from the same group. All remained on the same diet as in the subchronic study until day 20 of gestation when dams were sacrificed. No signs of parental toxicity, no reproductive effects (number pregnant, corpora lutea, implantations, implantation efficiency, resorptions). NOAEL: 690 mg/kg-day (highest dose tested) LOAEL: Not established	OECD-SIDS, 2002; ATSDR, 2009	Reported in a secondary source.
	Reproduction and Fertility Effects	Rabbits, dermal (clipped, intact), 5x/week, 3 weeks, 50% solution in ethanol; no effect on the reproductive organs reported up to the highest dose tested (1,000 mg/kg-day) NOAEL: 1,000 mg/kg-day	OECD-SIDS, 2002	Reported in a secondary source. Organs examined by histopathology; there were no effects at the highest dose tested; dermal repeated-dose study.

Triphenyl phosphate CASRN 115-86-6				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Other	Men living in homes with higher amounts of TPP in house dust had reduced sperm count and altered hormone levels related to fertility and thyroid function. Each interquartile range (IQR) TPP increase in house dust samples was associated with a 19% decrease in sperm concentrations and a 10% increase in prolactin levels.	Betts, 2010; Meeker and Stapleton, 2010	The actual exposure to TPP is unknown; it is not known if TPP or other substances found in the household dust caused or contributed to the reported toxicity.
Developmental Effects		**LOW: Based on a rat oral reproductive/developmental NOAEL = 690 mg/kg-day for fetal effects (highest dose tested). Developmental effects were reported in a study in pregnant Wistar rats administered the analog mixture FM550 (sum total of TBB and TBPH approximately 50%) during gestation though lactation (GD8 - PND21); developmental effects included early female puberty, weight gain, altered exploratory behavior, and increased male left ventricle thickness (LOAEL = 1 mg/kg-day, NOAEL = 0.1 mg/kg-day). It is uncertain which component or components of the FM 550 mixture is driving the reported developmental effects. While the FM 550 mixture data indicates a High hazard potential, it may be the other components driving the reported toxicity. There were no data located for the developmental neurotoxicity endpoint. Decreased cholinesterase activity in pregnant lab animals has been shown to have a negative impact on fetal brain development. As a result, there is uncertain potential for developmental neurotoxicity for this substance.**		
	Reproduction/ Developmental Toxicity Screen			No data located.

Triphenyl phosphate CASRN 115-86-6				
PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
	Combined Repeated Dose with Reproduction/ Developmental Toxicity Screen	Reproductive/developmental dietary study; TPP was administered in the diet for 91 days at concentrations of 0, 0.25, 0.50, 0.75, or 1.0% (~0, 166, 341, 516 or 690 mg/kg-day, respectively). At the completion of this study, females were mated with males from the same group. All remained on the same diet as in the subchronic study until day 20 of gestation when dams were sacrifice. No effects on fetal endpoints (viability, early or late deaths, fetal weight, length or distribution) or skeletal anomalies. Developmental effects: NOAEL: 690 mg/kg-day (highest dose tested) LOAEL: Not established	OECD-SIDS, 2002; ATSDR, 2009; ECHA, 2012	A LOAEL was not identified; there were no effects at the highest dose tested.
	Prenatal Development			No data located.
	Postnatal Development			No data located.
	Prenatal and Postnatal Development	Pregnant Wistar rats were administered 0, 0.1 or 1 mg/kg-day of the analog FM550 in the diet during gestation and through lactation (GD8 - PND 21); Maternal toxicity: Increased serum thyroxine (T4) levels in the high dose dams compared to controls was reported. There was no significant change in triiodothyronine (T3) levels in dam serum. Decreased hepatic carboxylesterease activity was also reported in dams in the high dose	Patisaul et al., 2013	Estimated based on data for FM550 mixture; non guideline study; the test substance identified as FM550 is a mixture made up of TBB, TBPH (sum total of TBB and TBPH is approximately 50%), TPP and IPTPP; it is not clear which component or components of the mixture are driving the reported developmental effects.

Triphenyl phosphate CASRN 115-86-6				
PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
		group. Developmental toxicity: female offspring in the high dose group displayed a significantly earlier vaginal opening when compared to controls. A statistically significant increase in weight was reported in both males and females in the high dose group at PND 120. This effect persisted through PND 180 to PND 220 with high dose males and females having significantly higher weights than same sex controls. A dose-dependent decrease in the number of rats to enter with open arms, (indicating anxiety), was reported in both male and female offspring. Increased blood glucose levels were reported in male offspring in the high-dose group compared to controls. There was no statistically significant difference in heart weight of male or female offspring. Left ventricular (LV) free wall thickness was significantly increased in male offspring in the high dose group; there were no changes in LV thickness in females at any dose. Maternal Toxicity: NOAEL: 0.1 mg/kg-day LOAEL: 1 mg/kg-day Developmental toxicity: NOAEL: 0.1 mg/kg-day LOAEL: 1 mg/kg-day (based on early		

Triphenyl phosphate CASRN 115-86-6				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		vaginal opening in females, increased weight in males and females, decreased open arm behavior, increased blood glucose levels in males and increased LV thickness in males)		
	Developmental Neurotoxicity	There were no data located for the developmental neurotoxicity endpoint. Decreased cholinesterase activity in pregnant lab animals has been shown to have a negative impact on fetal brain development. As a result, there is uncertain potential for developmental neurotoxicity for this substance	Professional judgment	No data located.
	Other			No data located.
Neurotoxicity		**LOW: Based on an adult rat neurotoxicity screening battery NOAEL = 711 mg/kg-day; all other experimental results are consistent with this hazard designation.**		
	Neurotoxicity Screening Battery (Adult)	4-month dietary study, 10 rats/dose, 0.25, 0.5, 0.75 or 1% test concentration (161, 345, 517 or 711 mg/kg-day, respectively), no neurobehavioral effects (open field, accelerating rotarod, forelimb grip strength and negative geotaxis examinations) NOAEL: 711 mg/kg-day (highest dose tested) LOAEL: Not established	ATSDR, 2009	Reported in a secondary source.
	Other	There is potential for neurotoxic effects based on a structural alert for organophosphates (Estimated)	Professional judgment	Estimated based on a structural alert for organophosphates and professional judgment.
		Two female hens/dose in delayed	OECD-SIDS, 2002	Reported in a secondary source.

Triphenyl phosphate CASRN 115-86-6				
PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
		neurotoxicity test, gavage, 2,000, 3,000, 5,000, 8,000, or 12,500 mg/kg, no signs of toxicity in-life or at necropsy NOAEL ≥12,500 mg/kg; highest dose tested LOAEL: Not established		No data on test substance purity.
		Several acute oral studies in hens, administered doses up to 12,500 mg/kg, generally found no signs of paralysis, histopathological changes in examined nerve tissues, or behavior immediately after or during observation periods of up to 36 days. However, blood cholinesterase was decreased by up to 87% in studies where it was measured. NOAEL ≥12,500 mg/kg; highest dose tested LOAEL: Not established	OECD-SIDS, 2002	Reported in a secondary source. No data on test substance purity.
		15-day repeated dose dermal study, rabbits (10/sex/group) were exposed to test compound concentrations of 0, 100, and 1,000 mg/kg-day. No mortality, clinical symptoms, or changes in body weight, hematology, clinical chemistry, necropsy, organ weights and histopathology reported; only decreased acetyl cholinesterase levels in plasma, erythrocytes and brain were reported and not considered	OECD-SIDS, 2002	Reported in a secondary source. Treatment period only 15 days; quantitative data, effect levels, and test substance purity were not presented in the study report.

Triphenyl phosphate CASRN 115-86-6				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		to be of toxicological relevance as there was no clinical or histological correlation.		
Repeated Dose Effects		**HIGH: Based on weight of evidence including reduced body weight in male rats administered triphenyl phosphate in the diet for 28-days. The NOAEL of 23.5 mg/kg-day and the LOAEL of 161.4 mg/kg-day span across the High and Moderate hazard designation ranges (DfE criteria are for 90-day repeated dose studies; criteria values are tripled for chemicals evaluated in 28-day studies making the High hazard range < 30 mg/kg-day and the Moderate hazard range between 30 and 300 mg/kg-day).**		
		28-day repeated dose dietary study, rats were fed test substance at concentrations of 0, 250, 1,000 and 4,000 ppm. Effects on body weights were observed. NOAEL (male): 250 ppm (23.5 mg/kg-day) LOAEL (male): 1,000 ppm (161.4 mg/kg-day)	ECHA, 2012	Reported in secondary source. DfE criteria are for 90-day repeated dose studies. Criteria values are tripled for chemicals evaluated in 28-day studies.
		35-day repeated-dose oral (dietary) study, 5 male rats/group, test compound concentrations of 0, 0.5, and 5.0% (~0, 350, and 3,500 mg/kg-day, respectively), with a 0.1% (~70 mg/kg-day) dose replacing the high dose group after 3 days. Slight reduction in body weight gain and increase in liver weight in 350 mg/kg-day dose group. NOAEL: 70 mg/kg-day LOAEL: 350 mg/kg-day	OECD-SIDS, 2002	Reported in a secondary source. Limited study details provided.
		4-month repeated-dose dietary study, Sprague-Dawley rats (10 rats/dose)	OECD-SIDS, 2002; ATSDR, 2009	Reported in a secondary source.

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PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
		were fed 0.25, 0.5, 0.75 or 1% test concentration (161, 345, 517 or 711 mg/kg-day, respectively). Reduced body weight gain (11%) at 345 mg/kg-day. NOAEL: 161 mg/kg-day LOAEL: 345 mg/kg-day		
		15 day repeated-dose dermal study, rabbits (10/sex/group) were exposed to test compound concentrations of 0, 100, and 1,000 mg/kg-day. No mortality, clinical symptoms, or changes in body weight, hematology, clinical chemistry, necropsy, organ weights and histopathology reported; only decreased acetyl cholinesterase levels in plasma, erythrocytes and brain were reported and not considered to be of toxicological relevance as there was no clinical or histological correlation.	OECD-SIDS, 2002	Reported in a secondary source. Treatment period only 15 days; quantitative data, effect levels, and test substance purity were not presented in the study report.
		In a 3-month study, rats were orally gavaged with test substances at 0, 380 and 1,900 mg/kg-day. No toxic effects were observed. NOEL: 1,900 mg/kg-day; highest dose tested LOEL: Not established	ATSDR, 2009	Limited study details reported in a secondary source. Primary source is an abstract with few experimental details.
	Immune System Effects	120-day dietary study, rats, 0, 0.25, 0.5, 0.75, and 1% of triphenyl phosphate (~0, 161, 345, 517 and 711	ATSDR, 2009	Reported in a secondary source.

Triphenyl phosphate CASRN 115-86-6				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		mg/kg-day); initial, secondary, and tertiary immunizations with sheep red blood cells performed at 60, 81, and 102 days, respectively. No significant effects were reported on the weight and histopathology of the spleen, thymus and lymph nodes, and no significant changes to the humoral response were reported. NOAEL: 711 mg/kg-day (highest dose tested)		
		Rabbits, up to 1,000 mg/kg-day, applied 5 days/week for 3 weeks to intact or abraded skin had no gross or microscopic effects on the spleen, thymus, or lymph nodes. NOAEL: 1,000 mg/kg-day (highest dose tested)	ATSDR, 2009	Reported in a secondary source.
Skin Sensitization		**LOW: Based on an experimental study in guinea pigs indicating that triphenyl phosphate is not a skin sensitizer.**		
	Skin Sensitization	Several human case studies have reported allergic dermatitis; 15 of 23,192 (0.065%) human volunteers patch tested from 1950 to 1962 had positive reactions to cellulose acetate film containing 7-10% triphenyl phosphate and 3-4% phthalic esters	OECD-SIDS, 2002	Reported in a secondary source. Limited study details provided; patch tests conducted with mixtures; unclear which component of mixture caused low incidence of sensitization.
		A confidential skin sensitization study with negative results in guinea pigs	Submitted confidential study	Reported in a confidential study.
		None of the patients tested in two separate studies of 343 and 174	OECD-SIDS, 2002	Reported in a secondary source. Limited study details provided.

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		patients, respectively, had sensitization reactions to triphenyl phosphate		
		Not sensitizing, guinea pig maximization test	OECD-SIDS, 2002	Study reported in a secondary source; conducted according to OECD Guide-line 406
Respiratory Sensitization		**No data located.**		
	Respiratory Sensitization			No data located.
Eye Irritation		**LOW: Triphenyl phosphate is mildly irritating to the eyes with effects clearing within 72 hours.**		
	Eye Irritation	Not irritating, rabbits	OECD-SIDS, 2002	Study reported in a secondary source; conducted according to OECD Guide-line 405
		Mild irritation in rabbit eyes, clearing within 72 hours	OECD-SIDS, 2002	Study reported in a secondary source
Dermal Irritation		**VERY LOW: Triphenyl Phosphate is not a skin irritant in rabbits**		
	Dermal Irritation	Not irritating, rabbits; semi-occlusive or occlusive conditions for 4, 24 or 72 hours	OECD-SIDS, 2002	Study reported in secondary source; conducted according to OECD Guide-line 404
		Non-irritant, rabbit	ATSDR, 2009	Reported in a secondary source.

Triphenyl phosphate CASRN 115-86-6			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
Endocrine Activity	**Triphenyl phosphate was found to be inactive in estrogen-receptor binding assays; however, it was shown to be a moderate androgen-receptor (AR) binder in a competitive binding assay. Triphenyl phosphate was shown to inhibit human AR in the absence of agonist and to inhibit testosterone-induced AR activity. In addition, Triphenyl phosphate significantly impaired reproduction in zebrafish and was correlated with decreased sperm count and altered hormone levels in men. Increased serum thyroxine (T4) levels were reported in the serum of dams following oral administration to FM550 (mixture of 50% sum total of TBB and TBPH with additional components identified as IPTPP and TPP). It is unclear which component or components of the mixture are driving the endocrine activity effects.**		
	21-day reproduction study in zebrafish. Significant decrease in fecundity, significant increases of plasma 17B-estradiol (E2) concentrations, vitellogenin (VTG) levels, and E2/testosterone (T) and E2/11-ketotestosterone (11-KT) ratios. Sex-dependent changes in transcriptional profiles of several genes of the hypothalamus-pituitary-gonad (HPG) axis.	Liu et al., 2013	Adequate primary source
	Study conducted to determine effects of triaryl phosphates on mouse and human nuclear receptors. Mouse constitutively active receptor (CAR) was activated by 1.3-fold following exposure to TPP. Testosterone-induced AR-dependent activity was lowered by 30-40%.	Honkakoski et al., 2004	Adequate primary source
	Exposure to TPP in zebrafish resulted in severe pericardial edema and blocked looping of the atrium and ventricle. TPP-induced cardiotoxicity in zebrafish embryos is mediated	McGee et al., 2013	Adequate primary source

Triphenyl phosphate CASRN 115-86-6			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	through an AHR independent pathway.		
	In a luciferase reporter-gene assay using cultured cells, TPP inhibited the luciferase expression induced by dihydrotestosterone (10^{-9} M). IC_{50} for antiandrogenic activity = 0.000047 - 0.0006 M	Ohyama et al., 2006	Primary source in Japanese with English abstract
	Endocrine disrupting potential was investigated using human cells lines (H295R, MVLN) and zebrafish plasma. TPP was cytotoxic to H295R cells (showing <80% cell viability at ≥ 10 mg/L) and significantly increased E2 and T production. Transcription of CYP19A1 was significantly up-regulated and transcription of SULT1E1 gene was down-regulated. No binding affinity to E2 receptor in MVLN cells, but binding of E2 to ER was reduced in a dose-dependent manner. Plasma E2 was significantly increased in fish plasma and T and 11-KT were decreased (1 mg/L). Changes in transcription of steroidogenic genes and vitellogenin gene were observed.	Liu et al., 2012	Adequate, primary source
	Men living in homes with higher amounts of TPP in house dust had reduced sperm count and altered hormone levels related to fertility and thyroid function. Each interquartile range (IQR) TPP increase in house dust samples was associated with a	Betts, 2010; Meeker and Stapleton, 2010	The actual exposure to TPP is unknown; it is not known if TPP or other substances found in the household dust caused or contributed to the reported toxicity.

Triphenyl phosphate CASRN 115-86-6			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	19% decrease in sperm concentrations and a 10% increase in prolactin levels.		
	Pregnant Wistar rats were administered 0, 0.1 or 1 mg/kg-day of the analog FM550 in the diet during gestation and through lactation (GD8 - PND 21); Increased serum thyroxine (T4) levels (increase of 65%) in the high dose dams compared to controls was reported. There was no significant change in triiodothyronine (T3) levels in dam serum. There was no reported statistically significant change in T4 or T3 levels in pup serum on PND 21 when compared to controls.	Patisaul et al., 2013	Estimated based on data for FM550 mixture; non guideline study; the test substance identified as FM550 is a mixture made up of TBB, TBPH (sum total of TBB and TBPH is approximately 50%), TPP and IPTPP; it is not clear which component or components of the mixture are driving the reported endocrine activity effects.
	Inhibited AR activity in COS-1 cells transfected with human AR both in the absence of agonist, as well as inhibited testosterone-induced AR activity by 30 40%. (Measured)	ATSDR, 2009	Reported in a secondary source.
	Moderate binding in a competitive androgen-receptor (AR) binding assay using recombinant rat protein expressed in *Escherichia coli*.	ATSDR, 2009	Reported in a secondary source.
	Inactive in a binding assay with the rat uteri estrogen receptor from ovariectomized Sprague-Dawley rats	ATSDR, 2009	Reported in a secondary source

Triphenyl phosphate CASRN 115-86-6				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Immunotoxicity		**Oral exposure of rats to triphenyl phosphate for 4 months and dermal exposure of rabbits for 3 weeks produced no effects on immune function parameters.**		
	Immune System Effects	120-day dietary study, rats, 0, 0.25, 0.5, 0.75, and 1% of triphenyl phosphate (~0, 161, 345, 517 and 711 mg/kg-day); initial, secondary, and tertiary immunizations with sheep red blood cells performed at 60, 81, and 102 days, respectively. No significant effects were reported on the weight and histopathology of the spleen, thymus and lymph nodes, and no significant changes to the humoral response were reported.	ATSDR, 2009	Reported in a secondary source.
		Rabbits, up to 1,000 mg/kg-day, applied 5 days/week for 3 weeks to intact or abraded skin had no gross or microscopic effects on the spleen, thymus, or lymph nodes.	ATSDR, 2009	Reported in a secondary source.
ECOTOXICITY				
ECOSAR Class				
Acute Aquatic Toxicity		**VERY HIGH: Based on experimental fish 96-hour LC_{50} values of 0.4 and 0.85 mg/L.**		
Fish LC_{50}		Freshwater fish (*Oncorhynchus mykiss*) 96-hour LC_{50} = 0.4 mg/L (Experimental)	OECD-SIDS, 2002	Reported in a secondary source
		Freshwater fish (*Oncorhynchus mykiss*) 96-hour LC_{50} = 0.85 mg/L (Experimental)	OECD-SIDS, 2002	Reported in a secondary source. Guideline study.
		Freshwater fish (*Lepomis macrochirus*) 96-hour LC_{50} = 290 mg/L (Experimental)	OECD-SIDS, 2002	Limited study details reported in a secondary source. The study does not meet important criteria for standard methods (e.g., test

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PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
			substance concentration at solubility threshold in water).
	Fish 96-hour LC_{50} = 1.34 mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	Estimate for the Esters class was provided for comparative purposes. See Section 5.5.1.
Daphnid LC_{50}	Daphnid 48-hour LC_{50} = 1.28 mg/L (Experimental)	FMC, 1979	Sufficient study details reported.
	Daphnid 48-hour EC_{50} = 1.35 mg/L Static (Experimental)	OECD-SIDS, 2002	Study reported in a secondary source; conducted according to US EPA 660/3-75-009.
	Daphnid 48-hour LC_{50} = 1.0 mg/L (Experimental)	Mayer et al., 1981	Sufficient study details reported.
	Daphnid 48-hour LC_{50} = 2.11 mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	Estimate for the Esters class was provided for comparative purposes. See Section 5.5.1. ECOSAR also provided results for the Esters, and Esters (phosphate) classes; however, professional judgment indicates that this compound is not currently well represented in ECOSAR v1.11.
Other Invertebrate LC_{50}	*Mysidopsis bahia* 96-hour LC_{50} >0.18 - 0.32 mg/L (Experimental)	OECD-SIDS, 2002	Reported in a secondary source.

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PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
Green Algae EC_{50}	Green algae (*Selenastrum capricornutum*) 96-hour EC_{50} = 2.0 mg/L (Experimental)	OECD-SIDS, 2002	Reported in a secondary source.
	Green algae 96-hour EC_{50} = 2.0 mg/L (Experimental)	Mayer et al., 1981	Sufficient study details reported.
	Green algae (*Scenedesmus subspicatus*) 72-hour LOEC = 0.5 - 5 mg/L NOEC = 0.25 - 2.5 mg/L (Experimental)	OECD-SIDS, 2002	Study reported in secondary source; conducted according to OECD guideline 201.
	Green algae 96-hour EC_{50} = 0.6 mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	Estimate for the Esters class was provided for comparative purposes. See Section 5.5.1.
Chronic Aquatic Toxicity	**VERY HIGH: Based on an experimental fish 30-day LOEC = 0.037 mg/L. Experimental data for algae indicate a High hazard concern. No chronic experimental data were available for daphnia.**		
Fish ChV	Freshwater fish (*Oncorhynchus mykiss*) 30-day LOEC = 0.037 mg/L (Experimental)	ECHA, 2013	Reported in a secondary source.
	Fish (*Pimephales promelas*) 30-day LOEC = 0.23 mg/L NOEC = 0.087 mg/L There were no changes in hatchability of eggs, mean total length, and average we weight of fry. There was reduced percentage survival of fry through 30 days post-exposure at 0.23 mg/L. Severe scoliosis was reported in several fry and erratic swimming was reported in all fry at 0.23 mg/L.	OECD-SIDS, 2002	Sufficient study details reported.

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PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	(Experimental)		
	Fish ChV = 0.06 mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	Estimate for the Esters class was provided for comparative purposes. See Section 5.5.1.
Daphnid ChV	Daphnid ChV = 0.69 mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	Estimate for the Esters class was provided for comparative purposes. See Section 5.5.1.
Green Algae ChV	Green algae (*Scenedesmus subspicatus*) 72-hour LOEC = 0.5 - 5 mg/L NOEC = 0.25 - 2.5 mg/L (Experimental)	OECD-SIDS, 2002	Study reported in secondary source; conducted according to OECD guideline 201.
	Green algae ChV = 0.35 mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	Estimate for the Esters class was provided for comparative purposes. See Section 5.5.1.
ENVIRONMENTAL FATE			
Transport	**Level III fugacity models incorporating available physical and chemical property data indicate that at steady state, TPP is expected to be found primarily in soil and to a lesser extent, water. Triphenyl phosphate is expected to have moderate mobility in soil, based on measured K_{oc} values in silty clay, loamy sand and silt loam. Leaching through soil to groundwater may occur, though it is not expected to be an important transport mechanism. Triphenyl phosphate may volatilize from moist soil and water surfaces based on its Henry`s Law constant. Volatilization from dry surface is not expected based on its vapor pressure. In the atmosphere, triphenyl phosphate is expected to exist in both the vapor phase and particulate phase. Particulates may be removed from air by wet or dry deposition.**		
Henry's Law Constant (atm-m^3/mole)	$1.2x10^{-5}$ (Measured)	Huckins et al., 1991	Reported in a primary source.

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PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
	Sediment/Soil Adsorption/Desorption - K_{oc}	2,514 Reported for silty clay (Measured)	Anderson et al., 1993	Reported in a primary source.
		2,736 Reported for silt loam (Measured)	Anderson et al., 1993	Reported in a primary source.
		3,561 Reported for loamy sand. (Measured)	Anderson et al., 1993	Reported in a primary source.
	Level III Fugacity Model	Air = 0.7% Water = 14.5% Soil = 75.8% Sediment = 9.02% (Estimated)	EPI v4.11	Reported in a Level III Fugacity model. Experimental data is consistent with partitioning to sediment.

Triphenyl phosphate CASRN 115-86-6				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Persistence		**LOW: The persistence of triphenyl phosphate is based on experimental data. Under aerobic conditions in a Japanese MITI ready biodegradability test (OECD Test Guidelines (TG) 301C), 90% biodegradation of triphenyl phosphate occurred after 28 days, and 93.8% triphenyl phosphate removal as dissolved organic carbon (DOC) occurred over 20 days in an OECD 303A guideline study. TPP does not meet the criteria for very low persistence because the percent removal in the criteria does not occur within a 10-day window. In loamy sand, a half-life of 37 days was observed under aerobic conditions. Triphenyl phosphate was determined to be inherently biodegradable in a river die-away test, after degrading 100% over 3 days in river water. Triphenyl phosphate may degrade under anaerobic conditions, with primary degradation of 31.1% after 3 days (89.7% after 40 days) in river sediment. However, removal under anaerobic conditions is not anticipated to be an important fate process. Triphenyl phosphate will undergo hydrolysis under alkaline conditions, with half-lives of 3 days at pH 9; it is relatively stable to hydrolysis under neutral and acidic conditions, with half-lives of 28 days at pH 5 and 19 days at pH 7. Triphenyl phosphate is not expected to be susceptible to direct photolysis by sunlight, since it does not absorb light at wavelengths >290 nm. The atmospheric half-live of vapor-phase triphenyl phosphate is estimated to be 12 hours.**		
Water	**Aerobic Biodegradation**	Passes Ready Test: Yes Test method: OECD TG 301C: Modified MITI Test (I) 83-94% biodegradation after 28 days at 100 mg/L of test substance. (Measured)	OECD-SIDS, 2002	Reported in a guideline study.
		Study results: 100%/3 days Test method: Die-Away Reported as inherently biodegradable in a river water/river die-away test (Measured)	OECD-SIDS, 2002	Reported in a secondary source.
	Volatilization Half-life for Model River	4 days (Estimated)	EPI v4.11	Reported in the volatilization from water model.
	Volatilization Half-life for Model Lake	47 days (Estimated)	EPI v4.11	Reported in the volatilization from water model.

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Soil	**Aerobic Biodegradation**	Study results: 93.8%/20 days Test method: 303A: Activated Sludge Units - Simulation Test Removal as DOC, using initial concentration of 5 mg/L with activated sludge. Reported as inherently biodegradable. (Measured)	EC, 2000; OECD-SIDS, 2002	Reported in a guideline study.
		Study results: 77%/28 days Test method: Other Reported as ultimately biodegradable. Monsanto Shake Flask Procedure (precursor to Closed bottle test). (Measured)	OECD-SIDS, 2002	Reported in a secondary source.
		Study results: 82%/28 days Test method: CO_2 Evolution Modified Sturm test. Reported as ultimately biodegradable. Measured in domestic, adapted activated sludge (Measured)	OECD-SIDS, 2002	Reported in a secondary source.
		Study results: 93%/49 days Test method: 302A: Inherent - Modified SCAS Test Reported as inherently biodegradable. (Measured)	OECD-SIDS, 2002	Reported in a guideline study.
	Anaerobic Biodegradation	Study results: 89.7%/40 days Test method: CO_2 Evolution Test Primary degradation: 31.1% after 3 days, 89.7% after 40 days in river sediment. CO_2 evolution: 0.8% after 3 days, and 21.9% after 40 days. (Measured)	OECD-SIDS, 2002	Reported in a secondary source.
	Soil Biodegradation with Product Identification			No data located.

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PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
	Sediment/Water Biodegradation	86.9%/40 days Primary degradation in river sediment. 43.3% after 3 days 86.9% after 40 days (Measured)	OECD-SIDS, 2002	Reported in a secondary source.
Air	**Atmospheric Half-life**	1 day (Estimated)	EPI v4.11	
Reactivity	**Photolysis**	Not a significant fate process (Estimated)	Mill, 2000; Professional judgment	Triphenyl phosphate does not contain functional groups that would be expected to absorb light of wavelengths >290 nm.
		A 0.1 mg/L solution (with acetone) was exposed to a mercury lamp to examine the effect of UV light on the degradation of TPP. High pressure lamp (100W): 100%/20 mins Low pressure lamp (15W): 100%/1 hour (Measured)	EC, 2000	Reported in a secondary source under laboratory conditions.
	Hydrolysis	50%/>28 days Reported at 25°C; pH 5 (Measured)	EC, 2000; OECD-SIDS, 2002	Reported in a secondary source.
		50%/19 days Reported at 25°C; pH 7 (Measured)	OECD-SIDS, 2002	Reported in a secondary source.
		50%/3 days Reported at 25°C; pH 9 (Measured)	EC, 2000; OECD-SIDS, 2002	Reported in a secondary source.
		50%/7.5 days Reported at pH 8.2 in river/lake water (Measured)	EC, 2000	Reported in a secondary source.
		50%/1.3 days Reported at pH 9.5 in river/lake water (Measured)	EC, 2000	Reported in a secondary source.
		100%/10 minutes at pH 13 (Measured)	ECHA, 2013	Reported in secondary source.

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
				Documentation of study details was not sufficient to assess its reliability.
Environmental Half-life		75 days (Estimated)	PBT Profiler	Half-life estimated for the predominant compartment, as determined by the PBT Profiler methodology.
		In loamy sand, observed half-lives of 37 days (aerobic) and 21 days (anaerobic) (Measured)	OECD-SIDS, 2002	Reported in a secondary source.
Bioaccumulation		**MODERATE: There is moderate potential for bioaccumulation based on experimental BCF values.**		
	Fish BCF	132-364 (Rainbow trout) (Measured)	Mayer et al., 1981	Adequate.
		271 Rainbow trout (Measured)	EC, 2000	Reported in a secondary source.
		364 Reported as 132-364 in rainbow trout (Measured)	OECD-SIDS, 2002	Insufficient study details to assess the quality of the reported values.
		193 Reported as 84-193 in Medaka (Measured)	EC, 2000	Reported in a secondary source.
		160 Reported as 68-160 in Fathead minnow (Measured)	EC, 2000	Reported in a secondary source.
		144 Medaka (Measured)	OECD-SIDS, 2002	Reported in a secondary source.
		110 Goldfish (Measured)	OECD-SIDS, 2002	Reported in a secondary source.
	Other BCF			No data located.

Triphenyl phosphate CASRN 115-86-6				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	BAF	The pregnant rats were administered 0, 0.1 or 1 mg/kg-day of FM550 by oral gavage across gestation and through lactation (GD8 - PND 21). (Estimated by analogy)	Patisaul et al., 2013	BAFs were not calculated. This study did not analyze the samples for the presence of TPP. Non guideline study. The test substance identified as FM550 is a mixture made up of TBB, TBPH (CASRN 26040-51-7), IPTPP (CASRN 68937-41-7) and TPP (CASRN 115-86-6).
		73 (Estimated)	EPI v4.11	
	Metabolism in Fish			No data located.
ENVIRONMENTAL MONITORING AND BIOMONITORING				
Environmental Monitoring		Triphenyl phosphate has been detected in drinking water in samples collected by the USGS. It has also been detected in household dust in the United States (at concentrations of (<173-1,798,100 ng/g), Pakistan, New Zealand, Belgium, Spain and Japan. Triphenyl phosphate has been detected in sediment from Taihu Lake in China at concentrations ranging from 0.41-5.54 µg/kg and in sediment in the U.S. It has also been detected in river water, seawater, rainwater, snow, wastewater effluent, ambient air, and indoor air (OECD-SIDS, 2002; Stiles et al., 2008; Stapleton et al., 2009; Betts, 2010; Ali et al., 2012; Cao et al., 2012; van der Veen and de Boer, 2012; HSDB, 2013; Salamova et al., 2014).		
Ecological Biomonitoring		Triphenyl phosphate has been detected in fish tissues. It has also been detected in the blubber of bottlenose dolphins collected from the Gulf of Mexico (Kuehl and Haebler, 1995; Campone et al., 2010).		
Human Biomonitoring		Triphenyl phosphate was detected in human milk, adipose tissue and human plasma. This chemical was not included in the NHANES biomonitoring report (Shah et al., 2006; ECHA, 2012; CDC, 2013).		

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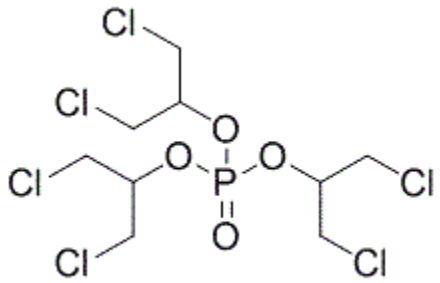
Tris (1,3-dichloro-2-propyl) phosphate (TDCPP)

Screening Level Toxicology Hazard Summary

This table contains hazard information for each chemical; evaluation of risk considers both hazard and exposure. Variations in end-of-life processes or degradation and combustion by-products are discussed in the report but not addressed directly in the hazard profiles. The caveats listed below must be taken into account when interpreting the information in the table.

VL = Very Low hazard L = Low hazard M = Moderate hazard H = High hazard VH = Very High hazard – Endpoints in colored text (VL, L, M, H, and VH) were assigned based on empirical data. Endpoints in black italics *(VL, L, M, H,* and *VH*) were assigned using values from estimation software and professional judgment [(Quantitative) Structure Activity Relationships "(Q)SAR"].

Chemical	CASRN	Human Health Effects											Aquatic Toxicity		Environmental Fate	
		Acute Toxicity	Carcinogenicity	Genotoxicity	Reproductive	Developmental	Neurological	Repeated Dose	Skin Sensitization	Respiratory Sensitization	Eye Irritation	Dermal Irritation	Acute	Chronic	Persistence	Bioaccumulation
Tris (1,3-dichloro-2-propyl) phosphate (TDCPP)	13674-87-8	L	H	M	H	M	L	H	L		L	L	H	H	H	L



CASRN: 13674-87-8

MW: 430.91

MF: $C_9H_{15}Cl_6O_4P$

Physical Forms: Liquid
Neat: Liquid

Use: Flame retardant

SMILES: ClCC(CCl)OP(=O)(OC(CCl)CCl)OC(CCl)CCl

Synonyms: 2-Propanol, 1,3-dichloro-, phosphate (3:1); Tris(1,3-dichloro-2-propyl) phosphate; Tris(1-chloromethyl-2-chloroethyl) phosphate; Tris[2-chloro-1-(chloromethyl)ethyl] phosphate; tris (1,3-dichloroisopropyl) phosphate; 1,3-Dichloro-2-propanol phosphate (3:1); Phosphoric acid, tris(1,3-dichloro-2-propyl)ester; TDCP; TDCPP; Antiblaze 195; Antiblaze TDCP; Amgard TDCP; CRP; Fyrol FR-2; Tolgard TDCP; Tris

Chemical Considerations: This is a discrete organic chemical with a MW below 1,000. EPI v4.11 was used to estimate physical/chemical and environmental fate values due to an absence of experimental data. Measured values from experimental studies were incorporated into the estimations. Commercial formulations of this substance may contain minor amounts of structural isomers such as tris(2,3-dichloro-1-propyl) phosphate (CASRN 78-43-3) (WHO, 1998; NAS, 2000).

Polymeric: No **Oligomeric:** Not applicable	
Metabolites, Degradates and Transformation Products: Metabolites: Bis(1,3-dichloroisopropyl) hydrogen phosphate; bis(1,3-dichloro-2-propyl) phosphate, 1,3-dichloro-2-propanediol, 1,3-dichloro-2-propanol; an unidentified glutathione conjugate; 1,3-dichloro-2-propyl, 1-chloro-2-propanol phosphate; unidentified diester metabolites; dimethyl derivative of 1,3-dichloro-2-propyl phosphate; bis(1,3-dichloro-2-propyl) 1-chloro-2-propanol phosphate; 1-chloro-2-propanol phosphate; bis(1,3-dichloro-2-propyl),1-carboxy-3-cloro-2-propyl phosphate. Thermal Degradation products: carbon monoxide, carbon dioxide, hydrochloric acid, chloromethane, chloroethane, vinyl chloride, 1,2-dichloroethane, chloropropenes, dichloropropenes, 1,2,3-trichloropropane, 2-chloroethanol, 1,3-dichloro-2-propanol, acetaldehyde, acrolein, chloroacetone (Lynn et al., 1981; Nomeir et al., 1981; Sasaki et al., 1984; NICNAS, 2001; BASF, 2007; EU, 2008; Van den Eade et al., 2013).	
Analog: No analogs **Endpoint(s) using analog values:** Not applicable	**Analog Structure:** Not applicable
Structural Alerts: Organophosphates, neurotoxicity. This chemical appears on the List of Chemicals Known to the State to Cause Cancer for the State of California: California Proposition 65 cancer (EPA, 2012; California EPA, 2013).	
Risk Phrases: R40 - limited evidence of a carcinogenic effect. R51/53 - toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment (ECHA, 2012).	
Hazard and Risk Assessments: A risk assessment for this chemical was completed by the European Union (EU) in 2008. This chemical was part of the HPV Data Summary and Test Plan (Akzo Nobel, 2001; EU, 2008).	

Tris (1,3-dichloro-2-propyl) phosphate CASRN 13674-87-8			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
PHYSICAL/CHEMICAL PROPERTIES			
Melting Point (°C)	-58 Using differential scanning calorimetry with a method compliant with OECD Guideline 102. Freezing point reported as -40°C. (Measured)	Akzo Nobel, 2001; EU, 2008	Adequate OECD guideline study reported in a secondary source.
	<-20 GLP study in accordance with Directive 92/69/EC (Measured)	Cuthbert and Mullee, 2002; EU, 2008	Adequate guideline study reported in a secondary source.
	26.66 (Measured)	Akzo Nobel, 2003; EU, 2008	Sufficient details were not available to assess the quality of this study.
	27 This substance exists as a supercooled liquid and can crystallize at temperatures below 27°C. (Measured)	CERI, 1999	Sufficient details were not available to assess the quality of this study.
Boiling Point (°C)	326 GLP study in accordance with Directive 92/69/EC. Decomposition was observed. (Measured)	Cuthbert and Mullee, 2002 (as cited in EU, 2008)	Guideline study reported in a secondary source.
	236 at 5 mmHg Reported as 236-237 at 5 mm Hg (Measured)	WHO, 1998; Budavari, 2001	This value was measured at lowered pressure.
	200 at 4 mmHg Reported as 200 at 4 mmHg	Akzo Nobel, 2003 (as cited in EU, 2008)	This value was measured at lowered pressure.

Tris (1,3-dichloro-2-propyl) phosphate CASRN 13674-87-8			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	(Measured)		
	200 at 4 mmHg Decomposes Reported as 200 at 4 mmHg (Measured)	WHO, 1998	Decomposition may occur before the boiling point is reached. This value was measured at lowered pressure.
	200 Decomposes Reported as gradual decomposition above 200°C (Measured)	HSDB, 2003	Decomposition may occur before the boiling point is reached.
Vapor Pressure (mm Hg)	$4.2x10^{-8}$ at 25°C Reported as $5.6x10^{-6}$ Pa; GLP study in accordance with Directive 92/69/EC vapor pressure balance method. (Measured)	Tremain, 2002 (as cited in EU, 2008)	Adequate OECD guideline study reported in a secondary source.
	0.01 at 30°C Results reported ranged from 0.01 mmHg at 30°C to 0.09 mmHg 20°C. (Measured)	EU, 2008	Values are higher than might be expected for the main component.
	0.01 at 30°C (Measured)	WHO, 1998; Akzo Nobel, 2001	This measured vapor pressure is high relative to the boiling points reported for this chemical.
Water Solubility (mg/L)	18.1 (Measured) Reported as 18.1 ± 1.1 mg/L at 20°C, GLP study in accordance with Directive 92/69/EC	Cuthbert and Mullee, 2002 (as cited in EU, 2008)	Adequate guideline study reported in a secondary source.
	42 (Measured) OECD Guideline 105: Shake-flask method	Akzo Nobel, 2001 (as cited in EU, 2008)	Adequate OECD guideline study reported in a secondary source.
	100 (Measured)	Eldefrawi et al., 1977 (as cited	Adequate guideline study

Tris (1,3-dichloro-2-propyl) phosphate CASRN 13674-87-8			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
		in WHO, 1998; Budavari, 2001; EU, 2008)	reported in a secondary source.
	7 (Measured) Study performed at 24°C	Hollifield, 1979 (as cited in Aston et al., 1996; EU, 2008)	Sufficient details were not available to assess the quality of this study.
	110 (Measured)	CERI, 1999 (as cited in EU, 2008)	Sufficient details were not available to assess the quality of this study.
Log K_{ow}	3.69 Using the GLP study in accordance with 92/69/EC, HPLC method. Reported as 3.69 ± 0.36 at 20°C. (Measured)	Submitted confidential study (as cited in EU, 2008)	Adequate guideline study reported in a secondary source.
	3.75 Using shake-flask method (Measured)	Sasaki et al., 1981 (as cited in EU, 2008)	Consistent value reported in a secondary source.
	3.65 (Measured)	HSDB, 2003 (as cited in EU, 2008)	Sufficient details were not available to assess the quality of this study.
	3.8 (Measured)	WHO, 1998 (as cited in EU, 2008)	Sufficient details were not available to assess the quality of this study.
Flammability (Flash Point)	Auto ignition temperature: 512.77°C (Measured)	Akzo Nobel, 2003 (as cited in EU, 2008)	Sufficient details were not available to assess the quality of this study.
	>107.22°C Study performed using Seta closed cup method (Measured)	Akzo Nobel, 2003 (as cited in EU, 2008)	Adequate standardized method reported in a secondary source.
	252°C Study performed using Cleveland open cup method (Measured)	WHO, 1998; NAS, 2000; HSDB, 2003; EU, 2008	Adequate standardized method reported in a secondary source.

Tris (1,3-dichloro-2-propyl) phosphate CASRN 13674-87-8			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
Explosivity	Not expected to form explosive mixtures with air. (Estimated)	Professional judgment	No experimental data located; based on its use as a flame retardant.
Pyrolysis	When heated to decomposition, it emits toxic fumes of Cl^+ and P_{ox} (Measured)	Lewis, 2000	Limited study details provided.
	Thermal oxidative degradation in air at 370°C: Hydrogen halides, halogenated C2 and C3 species, acrolein (Measured)	HSDB, 2003	Limited study details provided.
	0.1 mole TDCPP heated at 250-260°C under reduced pressure, 3 mm Hg, results in an overall yield of 60 wt%. Pyrolysis products identified: trans-1,3-dichloropropene 26.7%; cis-1,3-dichloropropene 36.0%; 1,2,3-trichloropropane 34.4%; 1-chloro-2-propene 2.9% (Measured)	Choudhry and Hutzinger, 1982	Semi-quantitative description of the pyrolysis products. No oxygenated or phosphorus-containing compounds as pyrolysis products. This study does not provide a complete profile of the pyrolysis.
pH	Not applicable (Estimated)	Professional judgment	Does not contain functional groups that are expected to ionize under environmental conditions.
pK_a	Not applicable (Estimated)	Professional judgment	Does not contain functional groups that are expected to ionize under environmental conditions.

Tris (1,3-dichloro-2-propyl) phosphate CASRN 13674-87-8				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
HUMAN HEALTH EFFECTS				
Toxicokinetics		**TDCPP is readily absorbed (100% assumed) by the oral route of exposure. Absorption through human skin membranes *in vitro* was calculated to be 6.0 - 15.4% of the applied dose. TDCPP is distributed primarily to the liver, kidney and lung following oral, dermal, and intravenous exposure. Once in the tissues, the parent compound and metabolites are rapidly excreted. TDCPP is quickly and extensively metabolized by oxidation to its metabolite, bis (1,3-dichloro-2-propyl) phosphate (BDCP). Phase I metabolites included BDCPP, bis(1,3-dichloro-2-propyl) 1-chloro-2-propanol phosphate, 1,3-dichloro-2-propyl, 1-chloro-2-propanol phosphate, a product of two oxidative dechlorination reactions, and bis(1,3-dichloro-2-propyl),1-carboxy-3-cloro-2-propyl phosphate. A substitution of a chlorine atom by glutathione was the only phase II metabolite detected in this study. Excretion occurred primarily via the urine (50%), but also through feces and expired air. No accumulation in the body is expected due to rapid elimination of the compound.**		
Dermal Absorption *in vitro*		*In vitro* absorption of TDCPP in acetone through skin of adult hairless mice. Dermal loading rate: 0.013 - 0.067 - 0.13 µg/cm Absorption rate (SD%): 57-45-39 (7.3-11-13) % Absorption vs. dermal loading: Inverse, as dose increases percent absorbed decreases	Buist et al., 2009	Adequate study details reported in a secondary source.
Absorption, Distribution, Metabolism & Excretion	**Oral, Dermal or Inhaled**	Radiolabelled TDCPP was orally administered to male Sprague-Dawley rats at a single dose of 0.2, 2, and 20 µmol/kg (~ 86 µg/kg, 860 µg/kg, and 8.6 mg/kg); There was > 90% absorption from the GI tract within 24 hours; TDCPP was then distributed in the body to the kidney > liver > lung > blood > muscle.	Nomeir et al., 1981 (as cited in ECHA, 2012)	Study details reported in a secondary source; Test substance identified as Fyrol FR-2; test substance purity not reported;
		TDCPP is readily absorbed by the	EU, 2008	Summary of toxicokinetic studies

Tris (1,3-dichloro-2-propyl) phosphate CASRN 13674-87-8				
PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
		oral route of exposure with 100% absorption assumed based on animal studies. Absorption through human skin membrane *in vitro* was calculated to be 15.4, 10.69, and 6.0% for doses of 0.003, 0.01, and 0.12 mg/m^3, respectively. TDCPP is distributed preferentially to the liver, kidney and lung following oral, dermal, and intravenous exposure. Once in the tissues, the parent compound and metabolites were rapidly excreted resulting in low concentration levels in the tissues. TDCPP is quickly and extensively metabolized by oxidation to its metabolite bis (1,3-dichloro-2-propyl) phosphate (BDCP). Excretion occurred primarily through the urine (50%), but also through feces and expired air. No accumulation in the body is expected because of rapid elimination of the compound.		reviewed in secondary source.

Tris (1,3-dichloro-2-propyl) phosphate CASRN 13674-87-8				
PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
	Other	Male Sprague-Dawley rats were administered an unspecified dose of ^{14}C-TDCPP by intravenous jugular vein catheters; TDCPP was quickly distributed from plasma to tissues. Administered TDCPP was detected in all tissues after 5 and 30 minutes, but was only detected in fat after 8 hours. TDCPP could not be detected in any tissues 24 hours after administration; In the tissues, the highest concentration of TDCPP was in the kidney (6.75 nmoles/g), liver (2.75 nmoles/g), small intestine (1.98 nmoles/g), and blood (1.84 nmoles/g); In rats, BDCP is reported to be the major metabolite of TDCPP; Following intravenous administration of TDCPP, only 19% could be recovered in the body within a half hour; 82% of TDCPP remained in the body, while <0.1% was detected in the urine and feces after 30 minutes. The primary route of elimination of TDCPP is due to its metabolism to BDCP which is mainly excreted in the urine and feces.	Lynn et al., 1981 (as cited in ECHA, 2012)	Study details reported in a secondary source; Test substance purity not reported.
		Incubation experiments using 1.0 mg/mL HLM or S9 proteins, 50 µM TBOEP or TCEP, or TCPP, or 20 µM TPHP or TDCPP and NADPH regenerating solution in 1 mM total	Van den Eade et al., 2013	Study details reported in an abstract.

Tris (1,3-dichloro-2-propyl) phosphate CASRN 13674-87-8				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		volume were conducted for 1 hour. There was a 46% and 68% clearance of the compound in the HLM and S9 incubations, respectively. Phase I metabolites included the oxidative dechlorination products of TDCPP and the hydrolysis product BDCPP, (M1), bis(1,3-dichloro-2-propyl) 1-chloro-2-propanol phosphate (M2), 1,3-dichloro-2-propyl, 1-chloro-2-propanol phosphate (M3), a product of two oxidative dechlorination reactions (M4), and bis(1,3-dichloro-2-propyl),1-carboxy-3-cloro-2-propyl phosphate (M5). A substitution of a chlorine atom by glutathione (M6), was the only phase II metabolite detected; this adduct was the primary metabolite present.		
Acute Mammalian Toxicity		**LOW: TDCPP is not acutely toxic via the oral, dermal and inhalation routes of exposure.**		
Acute Lethality	**Oral**	Rat oral LD_{50} of >2,000 mg/kg; clinical signs observed during the first 5 days after dosing included hypokinesia, piloerection, soiled coats, ataxia, chromodacryorrhea, rhinorrhea, and salivation.	Cuthbert, 1989b; WHO, 1998	Test substance identified as Tolgard TDCP MK1; Other studies available only in secondary sources reported similar results.
		Mouse oral LD_{50} = 2,250 mg/kg (female): LD_{50} = 2,670 mg/kg (male); Treated animals exhibited ataxic gait, hyperactivity, convulsion and death. No mortality was observed in controls or in males at 2,210 mg/kg	Kamata et al., 1989	No body weight or gross necropsy examination.

Tris (1,3-dichloro-2-propyl) phosphate CASRN 13674-87-8				
PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
		or females at 1,890 mg/kg.		
		Rat oral LD_{50} = 2,830 mg/kg	Eldefrawi et al., 1977 (as cited in ATSDR, 2012)	Limited study details reported in a secondary source.
		Rat oral LD_{50} = 3,160 mg/kg: No effects at 1,000 mg/kg. Dose-related depression at or above 2,160 mg/kg; survivors appeared normal by day 5. No gross lesions in survivors; fatalities had congestion of heart, lung, and liver	Hall and Kamienski, 1981; Akzo Nobel, 2001	Test substance identified as Fyrol FR-2; purity: not specified.
		Rabbit oral LD_{50} = 6,800 mg/kg; Clinical signs shortly after dosing included ataxia, weakness, and diarrhea; survivors normal by day 9. Necropsy revealed no abnormalities.	Akzo Nobel, 2001	Test substance identified as Fyrol FR-2; purity: not specified.
	Dermal	Rat dermal LD_{50} > 2,000; No deaths and no clinical signs were noted 24 hours after treatment.	Cuthbert, 1989a; WHO, 1998	Reported in secondary source; test substance identified as Tolgard TDCP MK1; study predates the preferred study guidelines.
		Rabbit dermal LD_{50} >4,650 mg/kg; 24-hour method, occluded. Mortality after 14 days = 0/4. No overt signs of toxicity and no gross necropsy findings.	Bullock and Heil, 1981; Akzo Nobel, 2001	Test substance identified as Fyrol FR-2; purity not specified; The available studies predate the preferred study guidelines, and did not report purity, but together indicated no mortality at the guideline limit dose of 2,000 mg/kg. The report specifying a 14-day observation period is presented in more detail.
	Inhalation	Rat inhalation LC_{50} ≥9.8 mg/L; No mortality after 14 days; initial	Henderson and Jainer, 1981	The available study on TDCPP predates the preferred guidelines.

Tris (1,3-dichloro-2-propyl) phosphate CASRN 13674-87-8				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		signs of moderate depression		The duration was shorter than currently recommended and no deaths were observed. Analysis of aerosol particle size was not mentioned so it is not known whether the size was respirable. Necropsies were not performed. Purity not specified.
		Rat inhalation LC_{50} >5,220 mg/m^3 (>5.22 mg/L)	Anderson, 1990; WHO, 1998	Limited study details reported in secondary source; test substance identified as aerosol of TDCPP (Amgard TDCP); duration unspecified.
Carcinogenicity		**HIGH: Based on sufficient evidence of carcinogenicity in a two-year combined chronic toxicity and carcinogenicity assay in rats. This substance is also included as a substance known to cause cancer on the Proposition 65 list of chemicals.**		
	OncoLogic Results			No data located.
	Carcinogenicity (Rat and Mouse)			No data located.

Tris (1,3-dichloro-2-propyl) phosphate CASRN 13674-87-8				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Combined Chronic Toxicity/Carcinogenicity	Rat, oral, 2-year combined chronic toxicity and carcinogenicity assay; rats (60/sex/group) were administered 0, 5, 20, 80 mg/kg-day (in the diet) for 2 years. Ten rats/sex/dose were randomly chosen for termination at 12 months; the remainder at 24 months. Results: Dose-related increased incidences of renal cortical adenomas in both sexes and testicular interstitial tumors in males (≥ 20 mg/kg-day); increased incidence of hepatocellular adenomas, and carcinomas combined in both sexes and adrenal cortical adenomas in females (80 mg/kg-day)	Freudenthal and Henrich, 2000; ATSDR, 2012	The NRC (2000) concluded that this study provides sufficient evidence of carcinogenicity of TDCPP in rats following chronic oral exposure. Test substance purity: 95%; The mode of action for carcinogenicity could not be determined.
	Other	TDCPP is included on the Proposition 65 list of chemicals known to cause cancer, July 5, 2013	California EPA, 2013	TDCPP was originally listed on October 28, 2011.
Genotoxicity		**MODERATE: Based on a weight of evidence including positive results in *in vitro* gene mutation and chromosomal aberration tests. Negative results were obtained in *in vivo* chromosomal aberration and unscheduled DNA synthesis assays.**		
	Gene Mutation *in vitro*	Positive in strain TA98 by liquid preincubation assay (with metabolic activation)	Abe and Urano, 1994	Limited study details reported.
		Positive in strain TA100 by plate incorporation assay.	Gold et al., 1978; Soederlund et al., 1985	Limited study details reported.
		Negative: mammalian cell gene mutation test in V79 Chinese hamster lung cells (with or without metabolic activation). Doses: 0, 0.02 mM TDCPP	Soederlund et al., 1985	Test substance purity: not reported.

Tris (1,3-dichloro-2-propyl) phosphate CASRN 13674-87-8				
PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
		Positive: dose-related positive results for TDCPP and its metabolite 1,3-dichloro-2-propanol in TA100 with S9 (phenobarbital-induced) in standard plate assays at concentrations up to 500 µg/plate. In a liquid preincubation quantitative assay, results for TDCPP were essentially negative-only increasing mutation frequencies at cytotoxic concentrations (survival <3%). However, its metabolites increased mutant frequencies with less cytotoxicity: 1,3-dichloro-2-propanone positive at <80% survival and 1,3-dichloro-2-propanol positive at <30% survival.	Majeska and Matheson, 1983	Limited study details reported.
		Positive in *Salmonella typhimurium* strains TA97, TA100 (presence of S9 from Aroclor-induced hamster liver) and in strain TA1535 (in the presence of S9 from Aroclor-induced rat or hamster liver); negative in *S. typhimurium* strains TA98 andTA1537 with or without the presence of exogenous metabolic activation. Doses: 0, or 5 concentrations between 10 and 10,000 µg/plate	Mortelmans et al., 1986	Test substance purity reported as 94.4%; positive controls gave expected increases; solvent control and all other test combinations were negative.
		Negative in *S. typhimurium* strains TA98, TA100, TA1535, TA1537, TA1538 (without metabolic activation) and in strains TA98,	Nakamura et al., 1979	Test substance purity: Assayed as ~94% TDCPP, plus ~6% bis(1-chloromethyl-2-chloroethyl)(2,3-dichloropropyl) phosphate.

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PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
		TA1537, or TA1538 (with metabolic activation); weakly positive in TA100 and TA1535 at the highest concentrations (with metabolic activation) Doses: 0, 10, 30, 100,. 300 µg/plate		
		Negative: mammalian cell gene mutation test in mouse lymphoma L5178Y cells (with or without metabolic activation). Doses: 0, and five concentrations up to ~32 nL/mL without S9, and six concentrations up to 70 nL/mL with S9.	Brusick et al., 1979; Matheson and Brusick, 1981	Test substance purity: not reported; test conditions chosen based on preliminary assays so that 50% growth reduction occurred at highest concentration.
		Negative: TDCPP was not mutagenic in *S. typhimurium* strains TA100, TA1535, or TA1538 (without activation or when Aroclor-induction was used to prepare the S9 fraction).	Prival et al., 1977	The highest exposure level was 10 µL per plate.
	Gene Mutation *in vivo*	Negative: sex-linked recessive lethal test in *Drosophila melanogaster* (100 males/concentrations); TDCPP added to feed of males for 24 hours, subsequently mated with virgin unexposed females; no metabolic activation. Doses: 2.5 and 25% in feed (1% gum tragacanth in 3% sucrose)	Brusick and Jagannath, 1977; Jagannath and Brusick, 1981; WHO, 1998	Test substance: tragacanth in 3% sucrose.

Tris (1,3-dichloro-2-propyl) phosphate CASRN 13674-87-8				
PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
	Chromosomal Aberrations *in vitro*	Positive in chromosome aberration assay in mouse lymphoma L5178Y cells (with PCB- or phenobarbital-induction metabolic activation compared to noninduced S9 activation)	Brusick et al., 1979; Matheson and Brusick, 1981	Test substance purity: not reported.
		Positive in sister chromatid exchange assay in mouse lymphoma L5178Y cells; TDCPP increased the incidence of sister chromatid exchanges in mouse lymphocytes under all three test conditions.	Brusick et al., 1979; Matheson and Brusick, 1981	Test substance purity: not reported.
		Negative for chromosomal aberrations or polyploidy in CHO cells with or without metabolic activation	EU, 2008	Sufficient study details from unpublished study reported in a secondary source.

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PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
	Chromosomal Aberrations *in vivo*	Negative in an *in vivo* bone marrow chromosomal aberration assay in CD1 mice (4-8 males/group); Concentrations: 0, 0.05, 0.17, and 0.5 mL/kg; using the specific gravity of 1.52, the doses were 0, 76, 260, or 760 mg/kg. The highest dose was the maximum tolerated dose. Negative control was DMSO. Exposure duration, frequency: By oral gavage in once or daily on 5 consecutive days. Mice were sacrificed at 6, 24, and 48 hours after single dose or 6 hours after the last of 5 doses. Between 233 and 400 cells were scored. Triethylenemelamine was used as the positive control. No evidence of increased frequency of chromosomal aberrations with TDCPP. Positive control produced expected large increase in micronucleated polychromatic erythrocytes.	Brusick et al., 1979; Matheson and Brusick, 1981	Test substance: Technical grade; purity not reported
		TDCPP administered to mice (route unspecified) at a dose of 2,000 mg/kg did not induce micronuclei in bone marrow erythrocytes	Thomas and Collier, 1985; WHO, 1998	Limited study details reported in a secondary source.

Tris (1,3-dichloro-2-propyl) phosphate CASRN 13674-87-8				
PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
	DNA Damage and Repair	Negative in unscheduled DNA synthesis in mammalian cells (hepatocytes) in culture; TDCPP was not genotoxic at 0.05 mM; at 0.1 mM, a moderate response was observed in hepatocytes from untreated rats, but not phenobarbital-treated rats. TBPP was used as the positive control and yielded positive results in induced and non-induced hepatocytes.	Soederlund et al., 1985	Test substance purity: not reported.
		Negative for unscheduled DNA synthesis (UDS) in rat hepatocytes; male Hsd:SD rats were administered TDCPP by gavage at doses of 500, 1,000, and 2,000 mg/kg in 0.5% methylcellulose; Rats were sacrificed at 2-4 hours and at 14-16 hours following dosing; vehicle controls and positive controls (dimethylnitrosamine) were used; hepatocytes were cultured at the selected sacrifice time points and analyzed for UDS; All treated groups at both time points produced a negative response for UDS and the vehicle and positive control groups resulted in an appropriate response.	EU, 2008	Sufficient study details from unpublished study reported in a secondary source.
		Negative for unscheduled DNA synthesis (UDS) assay in primary rat hepatocyte cells.	EU, 2008	Conducted according to OECD guideline 486 and EC method B.39
	Other			No data located.

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Reproductive Effects		**HIGH: Based on a LOAEL of 5 mg/kg-day (NOAEL not established) for atrophy and decreased secretory product of the seminal vesicle in an oral two-year combined chronic toxicity and carcinogenicity assay in rats. Effects were also seen in the testes (eosinophilic material in lumen, periarteritis nodosa) at 20 mg/kg-day and the epididymis (oligospermia and degenerated seminal product) at 80 mg/kg-day.**		
	Reproduction/Developmental Toxicity Screen			No data located.
	Combined Repeated Dose with Reproduction/ Developmental Toxicity Screen			No data located.
	Reproduction and Fertility Effects	Rat, oral, 2-year combined chronic toxicity and carcinogenicity assay; Rats (60/sex/group) were administered 0, 5, 20, 80 mg/kg-day (in the diet) for 2 years. Ten rats/sex/dose were randomly chosen for termination at 12 months; the remainder at 24 months. Reproductive effects in males included effects on seminal vesicles (atrophy, decreased secretory product) at ≥ 5 mg/kg-day, testes (eosinophilic material in lumen, periarteritis nodosa) at ≥ 20 mg/kg-day, and epididymis (oligospermia and degenerated seminal product) at 80 mg/kg-day. NOAEL: Not established LOAEL: 5 mg/kg-day	Freudenthal and Henrich, 2000	The authors reported the lowest dose of 5 mg/kg-day as a NOAEL and the mid-dose of 20 mg/kg-day as a LOAEL. However, as evaluated in NRC (2000), the lowest dose of 5 mg/kg-day was a LOAEL for atrophy and decreased secretory product of the seminal vesicle; test substance purity: 95%; These effects for reproductive tissues are reported from a 2-year combined chronic toxicity and carcinogenicity assay, and not from a study designed to test reproductive effects specifically; other reproductive parameters were not examined.
		In a 12-week oral study, rabbits were gavaged with TDCPP and then mated with untreated females.	Wilczynski et al., 1983; ATSDR, 2012	Data not sufficient to satisfy the reproductive toxicity endpoint since it was described only in an

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		Increased absolute kidney weight and relative liver weight in high dose animals; No effects on male reproductive parameters was reported; there were no histopathological findings in testes, or epididymides. NOAEL: 20 mg/kg-day LOAEL: 200 mg/kg-day (highest dose tested) (Estimated by analogy)		abstract and females were not tested.
	Other			No data located.
Developmental Effects		**MODERATE: Based on NOAELs of 100 and 200 mg/kg bw-day in two prenatal developmental toxicity studies in rats. A LOAEL of 400 mg/kg-day was established for increased resorptions and fetal mortality that occurred in conjunction with maternal toxicity and lethality. In addition, abnormal development (short tail, reduced body weight) was evident in a study examining developmental phenotypes in zebrafish embryos/larvae. This study adds weight of evidence for developmental toxicity of TDCPP. There were no data located for the developmental neurotoxicity endpoint.**		
	Reproduction/ Developmental Toxicity Screen			No data located.
	Combined Repeated Dose with Reproduction/ Developmental Toxicity Screen			No data located.

Tris (1,3-dichloro-2-propyl) phosphate CASRN 13674-87-8				
PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
	Prenatal Development	Rat (Sprague-Dawley), oral (gavage), 0, 25, 100, or 400 mg/kg-day on GD 6-15. Maternal: Clinical signs of toxicity (urine stains, hunched appearance, and alopecia) at 400 mg/kg-day; decreased food consumption (100, 400 mg/kg/day); overall body weights reduced in high-dose dams Developmental: No effects on implantation efficiency or mean number of corpora lutea. Increased number of resorptions and decreased fetal viability (400 mg/kg-day); decreased skeletal development, related to growth retardation and decreased fetal size (400 mg/kg/day); incidences of malformations were not determined to be treatment related. Maternal toxicity: NOAEL: 25 mg/kg-day LOAEL: 100 mg/kg-day (based on clinical signs and transient decreased body weight gain) Developmental toxicity: NOAEL: 100 mg/kg-day LOAEL: 400 mg/kg-day (based on increased resorptions and fetal mortality)	Kapp et al., 1981; ATSDR, 2012	Adverse developmental effects occurred only at maternally lethal doses. Test substance: Fyrol-2; test substance purity not reported. Conducted by methods consistent with OECD Guideline 141
		Rat (Wistar), oral (gavage), exposed	Tanaka et al., 1981	Adverse developmental effects

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PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
		to 0, 25, 50, 100, 200, or 400 mg/kg-day on GD 7-19. Maternal: mortality (400 mg/kg-day); decreased food consumption (200, 400 mg/kg-day), reduced terminal body weight on GD20 (400 mg/kg-day); increased absolute and relative kidney weight (200, 400 mg/kg-day) Developmental: No effect on corpora lutea, mean number of implants, fetal body weight, fetal sex ratio, or number of dead or live fetuses. No effect on behavior and functional test. Increased number of dead fetuses and live fetuses (400 mg/kg-day, due to the loss of one whole litter); No malformations were reported in any of the treated groups. Maternal toxicity: NOAEL: 100 mg/kg-day LOAEL: 200 mg/kg-day (based on increased kidney weight) Developmental toxicity: NOAEL: 200 mg/kg-day LOAEL: 400 mg/kg-day (based on increased fetal death)		occurred only at maternally lethal doses; test substance purity not reported.
		Zebrafish embryos/larvae exposed to TDCPP (3 µM) from 0.75 h postfertilization (hpf). Inhibition of cell rearrangement (4 hpf), delay in	Fu et al., 2013	Data are from a non-standard study for assessing hazard for this endpoint.

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		epiboly (5.7 and 8.5 hpf), abnormal development (short tail, reduced body size) and death (14-45 hpf). Trunk curvature was observed to be the main phenotype (96 hpf) in larvae exposed to 1 or 3 μM TDCPP.		
	Postnatal Development			No data located.
	Prenatal and Postnatal Development			No data located.
	Developmental Neurotoxicity	Uncertain concern for developmental neurotoxicity based on the potential for Cholinesterase (ChE) inhibition in dams that may result in alterations of fetal neurodevelopment (Estimated)	Professional judgment	Estimated based on a structural alert for organophosphates for the neurotoxicity endpoint.
	Other			No data located.
Neurotoxicity		**LOW: Based on a weight of evidence. TDCPP did not produce neurotoxicity in acute, chronic or developmental studies in rats or in acute and subchronic studies in hens. TDCPP induced oxidative stress in undifferentiated PC12 cells, but did not impair cell growth or viability. However, there may be some potential for neurotoxicity based on a structural alert for organophosphates.**		
	Neurotoxicity Screening Battery (Adult)			No data located.
	Other	Rat (Wistar), oral (gavage), exposed to 0, 25, 50, 100, 200, or 400 mg/kg-day on GD 7-19; Seven dams from each of the control and 200 mg/kg-day groups were permitted to litter normally and evaluated for implantation sites, delivery index, number of live offspring at birth and survival on PND 4, at 4^{th} week, and at 10^{th} week. Litters were culled to 10 offspring on postnatal day 4 (PND 4) and	Tanaka et al., 1981	Full descriptions of these tests were not available in the English summary and therefore could not be compared to the guideline protocol; this study does not fully satisfy the developmental neurotoxicity endpoint because it omitted some parameters specified under the guideline: developmental landmarks for sexual maturity, auditory startle test, and neurohistopathological

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		subjected to behavioral tests (open field, water maze, rota rod, inclined screen, pain reflex and Preyer's reflex). Absolute organ weights of 10 organs plus testis, uterus and ovary were measured in offspring. In postnatal observations, there were no effects on behavior and functional tests (≤ 200 mg/kg-day) NOAEL: 200 mg/kg-day (highest tested non-lethal dose) LOAEL: Not established		examinations.
		In a 2-year combined chronic toxicity and carcinogenicity assay, rats (60/sex/group) were fed 0, 5, 20, 80 mg/kg-day. Ten rats/sex/dose were randomly chosen for termination at 12 months; the remainder at 24 months. There were no lesions of the brain or spinal cord in rats exposed to TDCPP at doses as high as 80 mg/kg-day reported. NOAEL: 80 mg/kg-day (highest dose tested) LOAEL: Not established	Freudenthal and Henrich, 2000	Test substance purity: 95%.; no functional tests of neurotoxicity were performed; this study was a combined chronic toxicity/carcinogenicity assay, and was not designed to specifically examine neurological endpoints.
		Oral, rat (10 rats/dose), 0, 2,000, or 3,980 mg/kg in corn oil was administered by gavage to male Sprague-Dawley rats; There were no effects on plasma or	Bullock et al., 1981	Test substance reported as Fyrol FR-2; purity not specified.

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PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
		erythrocyte cholinesterase levels measured at 4 or 14 hours after dosing. NOAEL: >3,980 LOAEL: Not established		
		Acute oral delayed neurotoxicity in White Leghorn Hens (4/dose); dosed (gavage) at 10,000 mg/kg once; Positive control: 500 mg/kg tri-ortho-tylol phosphate (TOCP), negative control: 15 mg/kg tetraethyl pyrophosphate (TEPP). Toxic signs were not reported specifically for TDCPP, but for all compounds tested at the maximum tolerated dose, signs included listlessness and ataxia. Inhibition of NTE activity was 7% for TDCPP and the negative control TEPP, but 85% for the positive control (TOCP). NOAEL: Not established LOAEL: 10,000 mg/kg	Morey et al., 1978	Test substance: Fyrol FR-2; conflicting reports of test substance purity (one part of the report stated that the purity was not reported, whereas another part of the report indicated purity >99%); the current guideline specifies that testing is not necessary at doses above 2,000 mg/kg; unpublished industrial acute study performed prior to the existence of the guidelines, do not entirely conform to current guidelines, and may lack detail such as the purity of the TDCPP sample; only one test substance dose administered.
		Acute oral delayed neurotoxicity in Hohite Leghorn Hens (4/dose); dosed (gavage) at 420 mg/kg-day; Positive control: 90 or 120 mg/kg-day tri-ortho-tylol phosphate (TOCP); No overt signs of neurotoxicity with TDCPP treatment. Positive control caused inability to walk, hypertension, ataxia, and prostration.	Bullock and Kamienski, 1972; Bullock and Kamienski, 1981b; WHO, 1998	Test substance: Fyrol FR-2, purity not reported; Navy MIL-H-19457B (SHIPS) protocol; Necropsy not performed; unpublished industrial acute study performed prior to the existence of the guidelines, do not entirely conform to current guidelines, and may lack detail such as the

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PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
		NOAEL: 420 mg/kg-day (only dose tested) LOAEL: Not established		purity of the TDCPP sample; only one test substance dose administered.
		Subchronic oral delayed neurotoxicity in Hohite Leghorn Hens (10/dose); dosed (gavage) at 0, 4, 20, 100 mg/kg-day for 90 days; TOCP was the positive control. Hens treated with TDCPP at the high dose exhibited mean reductions in body weight during the latter part of the study, but no overt signs of neurotoxicity and no histopathological effects in the nervous tissues. Positive control hens exhibited consistently lower body weight gain, clinical signs of toxicity (locomotor impairment and ataxia) that became more severe with time. Histopathology results were not reported for the positive control. NOAEL: Not established LOAEL: Not established	Akzo Nobel, 2001	Test substance purity not reported. Robust summary from Akzo-Nobel, 2001a; unpublished, unidentified study dated 1979; histopathology was not reported for the positive control; unpublished industrial acute study performed prior to the existence of the guidelines, do not entirely conform to current guidelines, and may lack detail such as the purity of the TDCPP sample.
		Undifferentiated PC12 cells exposed to TDCPP for 24 hours; rapid mitotic inhibition in undifferentiated cultures and significantly reduced cell numbers during neurodifferentiation. TDCPP induced oxidative stress, but did not impair cell growth or viability	Dishaw et al., 2011	Adequate study details reported in a primary source.
		There is potential for neurotoxicity	Professional judgment	Estimated based on a structural

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		based on a structural alert for organophosphates. (Estimated)		alert for organophosphates and professional judgment.
Repeated Dose Effects		**HIGH: Based on a LOAEL of 5 mg/kg-day for atrophy and decreased secretory product of the seminal vesicle in an oral 2-year combined chronic toxicity and carcinogenicity assay in rats (NOAEL not established). Effects were also seen in the testes (eosinophilic material in lumen, periarteritis nodosa) at 20 mg/kg-day and the epididymis (oligospermia and degenerated seminal product) at 80 mg/kg-day.**		
		Rat, oral, 2-year combined chronic toxicity and carcinogenicity assay; Rats (60/sex/group) were administered 0, 5, 20, 80 mg/kg-day (in the diet) for 2 years. Increased mortality in high-dose males; reduced body weights in high-dose males and females; signs of anemia (lower hemoglobin, hematocrit, erythrocyte counts) in high-dose rats. At the mid-dose, increased absolute and relative kidney weight males and females, absolute liver weight and relative thyroid weight in males, and relative liver weight in females; increased relative liver weight in males and absolute and relative thyroid weights in females at the high dose. Increased incidences of nonneoplastic lesions (not strictly dose-related in that incidences were depressed in high-dose groups): Kidney lesions (convoluted tubule hyperplasia) in males at ≥ 20 mg/kg-day and in females at 80 mg/kg-day. Other	Freudenthal and Henrich, 2000; NRC, 2000	Freudenthal and Henrich (2000) reported the lowest dose of 5 mg/kg-day as a NOAEL and the mid-dose of 20 mg/kg-day as a LOAEL. However, as evaluated in NRC (2000), the lowest dose of 5 mg/kg-day was a LOAEL for atrophy and decreased secretory product of the seminal vesicle; test substance purity: 95%.

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PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
		systemic lesions at 80 mg/kg/day involved the parathyroid (hyperplasia) in males and the liver (foci) and spleen (erythroid/myeloid hyperplasia) in females. Lesions in the vesicles (atrophy, decreased secretory product) at ≥ 5 mg/kg-day, testes (eosinophilic material in lumen, periarteritis nodosa) at ≥ 20 mg/kg-day, and epididymis (oligospermia and degenerated seminal product) at 80 mg/kg-day. NOAEL: Not established LOAEL: 5 mg/kg-day (based on atrophy and decreased secretory product of the seminal vesicle; hyperplasia of convoluted tubule epithelium in males at 24 months)		
		In a 90-day study, mice (Slc/ddY) were fed TDCPP at 0, 0.01, 0.04, 0.13, 0.42, and 1.33 % in the diet (average daily dose: males-0, 13.2, 47.3, 171.0, 576.0, 1,792.3 mg/kg-day; female - 0, 15.3, 62.5, 213.6, 598.0, 1,973.1 mg/kg-day) Slight anemia in males at 0.42% after 3 months; Anemia in females at 0.13 % after 1 month and 0.42% at 3 months; Elevated albumin/globulin rations in males in all groups at 3 months; Increased alkaline phosphatase in females at 0.42% at 1	Kamata et al., 1989	Study reported limited relevant information in English abstract and data tables; histopathology analysis appears limited to the liver.

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		month, but did not differ from controls at the 3 month evaluation; dose-related increase in organ relative liver weight (0.13%) and relative kidney weight (0.42%), in males at 3 months compared to controls; Increased relative liver weight (0.04%), absolute liver weight (0.42%), absolute and relative kidney weight (0.13%); slight focal necrosis of the liver was observe in 2/12 females at 0.42%. NOAEL: 0.01% (15.3 mg/kg-day) LOAEL: 0.04% (62.5 mg/kg-day) based on increased relative liver weight in females		
		Morbidity survey conducted on 124 male, full-time workers with occupational exposure at a TDCPP manufacturing plant to determine if there was an increased incidence of respiratory conditions among those exposed; The survey population had an occupational health program physical examination in 1981; survey group divided into groups according to age (20-29, 30-39, 40-49, >50); The control population consisted of non-exposed workers; The ratio of exposed to non-exposed workers was 93:31 people; Full-shift time	Murphy, 1981; EU, 2008	Cohort study details reported in a secondary source; the non-exposed (control) populations was about one third the size of the exposed population; it is also difficult to determine if non-exposed workers may have been previously exposed, or if exposed workers may have been exposed to other compounds outside of their occupational environment; actual exposure doses were not reported.

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		weighted averages (TWA) were determined for the breathing zone for December 1978 - May 1979. The exposure dose was calculated to be near the limit of detection at 8 ppb; the survey consisted of a 175-self-administered health questionnaire, physical examination, pulmonary function test, chest x-ray, and an electrocardiogram; clinical and biochemical analysis was also performed. After taking into account smoking status; exposed workers had a decreased incidence of respiratory conditions compared to non-exposed workers; in addition there were no abnormal clinical findings; There was an increase in benign neoplasms, dermatitis, and gynacomastia in exposed workers compared to non-exposed workers.		
	Immune System Effects	Mice were administered a subcutaneous injection of 0, 0.25, 2.5, or 25 mg/kg-day once daily for 4 days (total cumulative doses of 0, 1, 10, or 100 mg/kg) Twenty percent of high-dose mice exhibited lymphoid depletion of the thymus. Statistically significant decreases in lipopolysaccharide (B-cell antigen) at 2.5 mg/kg-day and	Tanaka et al., 1981	Study predates the guideline for immunotoxicity; There is some uncertainty as the test material, reported as Fyrol FR2, but miss-identified by the authors as tris(2,3-dichloropropyl) phosphate; test substance purity reported as >95%; The study methods differed from the guideline in the short exposure

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		concanavalin A (T-cell antigen) at 25 mg/kg-day. NOAEL: 0.25 mg/kg-day LOAEL: 2.5 mg/kg-day based on decreased concanavalin A, T-cell antigen		period (4 rather than 28 days), parenteral administration (rather than oral or inhalation route), measurement of serum immunoglobulin in non-immunized rather than immunized mice, and the omission of some tests (enumeration of immunological cell subpopulations, test for NK-cell activity).
Skin Sensitization		**LOW: Not a skin sensitizer in guinea pigs.**		
	Skin Sensitization	Not a skin sensitizer in guinea pigs; The sensitization score for Fyrol FR-2 was zero.	Akzo Nobel, 2001; EU, 2008	Study details reported in a robust summary for an unpublished and unidentified study dated 2001; test substance identified as Fyrol FR-2
Respiratory Sensitization		**No data were located**		
	Respiratory Sensitization			No data located.
Eye Irritation		**LOW: TDCPP produced slight conjunctival effects in rabbits that cleared within 24 to 48 hours.**		
	Eye Irritation	Slightly irritating, rabbits; slight conjunctival redness and slight discharge were noted; effects cleared by 24 hours.	Cuthbert and Jackson, 1990; WHO, 1998	Limited study details reported in a secondary source; Test substance identified as Tolgard TDCP MK1; purity not specified.
		Transient, mild conjunctival effects in 3/6 rabbits (reversible in 48 hours)	Bullock and Kamienski, 1981a; EU, 2008	Test substance identified as Fyrol FR-2; purity not specified.
		Not irritating, rabbits; average Draize score of zero.	Murphy, 1981; Akzo Nobel, 2001; EU, 2008	Test substance purity not specified.

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Dermal Irritation		**LOW: TDCPP produced mild skin irritation in rabbits that cleared within 72 hours.**		
	Dermal Irritation	Mild skin irritant, rabbits (24-hour); No edema on intact or abraded skin in any rabbit; mild erythema was visible at 24 hours, but cleared by 72 hours; score of 0.63.	Hicks et al., 1981; EU, 2008	Report cited EPA protocol. Back hair was shaved, each rabbit tested on intact and abraded skin, occlusive dressing removed after 24 hours, observations at 24 and 72 hours; test substance identified as Fyrol FR-2; purity unspecified.
		Irritating to skin, rabbits; well-defined (score 2) erythema in 2 New Zealand White rabbits and slight erythema in a third rabbit 1 hour after patch removal.	Cuthbert, 1989a; WHO, 1998; EU, 2008	Limited study details reported in a secondary source; test substance identified as Tolgard EDCPP MK1; purity not specified; duration of exposure not specified.
		Not a skin irritant, rabbits (4-hour); No erythema or edema on intact or abraded skin in any rabbit.	Bullock and Kamienski, 1981a; EU, 2008	Test substance identified as Fyrol FR-2; purity not specified; Back hair shaved, each rabbit tested on intact and abraded skin, occlusive dressing removed after 4 hours, observations at 4, 24 and 48 hours.

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PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
Endocrine Activity	**TDCPP in house dust has been correlated with altered levels of hormones related to fertility and thyroid function in men. TDCPP inhibited the luciferase expression induced by dihydrotestosterone in a reporter-gene assay using cultured cells and induced delays in remethylation of the zygotic genome (mechanism that may be associated with enhanced developmental toxicity) in zebrafish. In addition, TDCPP disrupted steroidogenic pathways and metabolism of estrogen in human cell lines (H2925R and WVLN) and in zebrafish. A 2-year combined chronic toxicity and carcinogenicity assay in rats resulted in changes of the parathyroid, testes, and epididymis; it is unclear if these observed changes may be an indication of endocrine activity.**		
	Hormone levels and semen quality were assessed in men living in homes with elevated TDCPP levels in house dust. Each interquartile range (IQR) increase in TDCPP in dust was associated with a 17% increase in prolactin and a 3% decline in free levels of the thyroid hormone thyroxine.	Betts, 2010; Meeker and Stapleton, 2010	Limited study details summarized in a secondary source.
	In a luciferase reporter-gene assay using cultured cells, TDCPP inhibited the luciferase expression induced by dihydrotestosterone. IC_{50} for antiandrogenic activity = 4.7×10^{-5} IC_{50} for antiestrogenic activity = 8.9×10^{-5}	Ohyama et al., 2006	Primary source in Japanese with English abstract
	TDCPP exposure during five stages of embryogenesis in zebrafish induced delays in remethylation of the zygotic genome (mechanism that may be associated with enhanced developmental toxicity). Significant increase in mortality and developmental abnormalities at exposure concentrations of 0.75-96	McGee et al., 2012	Sufficient study details reported.

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PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	hours post-fertilization.		
	Human cell lines (H2925R and WVLN cells) were tested for sex hormone synthesis and steroidogenic gene transcription (H295R) and estrogen receptor binding activity (MVLN); zebrafish (*Danio rerio*) were tested for sex hormone levels and gene transcriptions. Increased 17 beta-estradiol (E2) and testosterone (T) levels, transcription of steroidogenic genes were upregulated; two sulfotransferase genes downregulated (H295R cells); there was no estrogen receptor agonist activity, while there was antagonist inhibiting binding of E2 to estrogen receptor (MVLN cells); Increased plasma T and E2 concentrations in zebrafish exposed to TDCPP for 14 days; decreased testosterone and 11-ketotestosterone and increased E2 in male zebrafish; significant upregulation of CYP17 and CYP19 transcription (males and females); vitellogenin (VTG)1 gene was down-regulated in female fish and up-regulated in male fish.	Liu et al., 2012	Sufficient study details reported in a primary source.
	Morbidity survey conducted on 124 male, full-time workers with occupational exposure at a TDCPP manufacturing plant to determine if there was an increased incidence of	Murphy, 1981; EU, 2008	Cohort study details reported in a secondary source; the non-exposed (control) populations was about one third the size of the exposed population; it is also

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PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	respiratory conditions among those exposed; After taking into account smoking status; exposed workers had a decreased incidence of respiratory conditions compared to non-exposed workers; in addition there were no abnormal clinical findings; There was an increase in gynacomastia in exposed workers compared to non-exposed workers.		difficult to determine if non-exposed workers may have been previously exposed, or if exposed workers may have been exposed to other compounds outside of their occupational environment; actual exposure doses were not reported.
	Rat, oral, 2-year combined chronic toxicity and carcinogenicity assay; Rats (60/sex/group) were administered 0, 5, 20, 80 mg/kg-day (in the diet) for 2 years. Systemic lesions at 80 mg/kg/day involved the parathyroid (hyperplasia) in males and the liver (foci) and spleen (erythroid/myeloid hyperplasia) in females. Lesions in the vesicles (atrophy, decreased secretory product) at = 5 mg/kg-day, testes (eosinophilic material in lumen, periarteritis nodosa) at = 20 mg/kg-day, and epididymis (oligospermia and degenerated seminal product) at 80 mg/kg-day. It is unclear if the observed changes may be an indication of endocrine activity.	Freudenthal and Henrich, 2000; NRC, 2000	Freudenthal and Henrich (2000) reported the lowest dose of 5 mg/kg-day as a NOAEL and the mid-dose of 20 mg/kg-day as a LOAEL. However, as evaluated in NRC (2000), the lowest dose of 5 mg/kg-day was a LOAEL for atrophy and decreased secretory product of the seminal vesicle; test substance purity: 95%.

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Immunotoxicity		**TDCPP produced lymphoid depletion of the thymus and decreases in LPS (B-cell antigen) and Con A (T-cell antigen) in mice following subcutaneous injection for 4 days.**		
	Immune System Effects	Mice were administered a subcutaneous injection of 0, 0.25, 2.5, or 25 mg/kg-day once daily for 4 days (total cumulative doses of 0, 1, 10, or 100 mg/kg) Twenty percent of high-dose mice exhibited lymphoid depletion of the thymus. Statistically significant decreases in lipopolysaccharide (B-cell antigen) at 2.5 mg/kg-day and concanavalin A (T-cell antigen) at 25 mg/kg-day. NOAEL: 0.25 mg/kg-day LOAEL: 2.5 mg/kg-day based on decreased concanavalin A, T-cell antigen	Tanaka et al., 1981	Study predates the guideline for immunotoxicity; There is some uncertainty as to the test material which was reported as Fyrol FR2 but mis-identified by the authors as tris(2,3-dichloropropyl) phosphate; test substance purity reported as >95%; The study methods differed from the guideline in the short exposure period (4 rather than 28 days), parenteral administration (rather than oral or inhalation route), measurement of serum immunoglobulin in non-immunized rather than immunized mice, and the omission of some tests (enumeration of immunological cell subpopulations, test for NK-cell activity).

Tris (1,3-dichloro-2-propyl) phosphate CASRN 13674-87-8			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
ECOTOXICITY			
ECOSAR Class			
Acute Aquatic Toxicity	**HIGH: Based on a measured 96-hour LC_{50} of 1.1 mg/L in fish, a 48-hour LC_{50} of 3.8 mg/L in daphnia, and a 72-hour E_rC_{10} = 2.3 mg/L in green algae.**		
Fish LC_{50}	*Oncorhynchus mykiss* (rainbow trout) 96-hour LC_{50} = 1.1 mg/L (semi-static test conditions) 96-hour NOEC = 0.56 mg/L 24-hour LC_{50} = 1.8 mg/L 48-hour LC_{50} = 1.5 mg/L 72-hour LC_{50} = 1.3 mg/L (Experimental)	ECHA, 2012	Test substance identified as Amgard TDCP; study conducted according to OECD guidelines; the toxicity value is below the reported water solubility of TDCPP (18 mg/L).
	Salmo gairdneri (Rainbow trout) 96-hour LC_{50} = 1.4 mg/L Static conditions; exposed to 0, 0.63, 1.25, 2.5, 5, 10 mg/L All mortalities occurred within the first 24 hours. Mortality was dose related. One fish died in the lowest dose group (0.63 mg/L). All fish died in the 5 and 10 mg/L groups. (Experimental)	Akzo Nobel, 2001	A NOEC was not observed and is therefore less than 0.63 mg/L.
	Killifish (*Oryzias latipes*) 96-hour LC_{50} = 3.6 mg/L (static test conditions) Deformation of the spine was observed in 7/10 killifish exposed to 3.5 mg/L TDCPP for 24 hours. (Experimental)	Sasaki et al., 1981	The test concentrations used were not reported. A control group was not tested.
	Goldfish (*Carassius auratus*) 96-hour LC_{50} = 5.1 mg/L (static test conditions)	Sasaki et al., 1981	Goldfish are not a designated test species, as per OPPTS 850.1075 (Fish Acute Toxicity Test,

Tris (1,3-dichloro-2-propyl) phosphate CASRN 13674-87-8			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	(Experimental)		Freshwater and Marine); used were not reported. A control group was not tested.
	Goldfish (*Carassius auratus*); exposed to 1 and 5 mg/L (static test conditions) Fish were exposed to 1 or 5 mg/L TDCPP in water or acetone. None of the fish in the 1 mg/L treatment had died after 168 hours. All fish in the 5 mg/L treatment died within 24 hours. The most conspicuous signs of toxicity were sluggishness and disoriented swimming prior to death. (Experimental)	Eldefrawi et al., 1977	Goldfish are not a designated test species, as per OPPTS 850.1075 (Fish Acute Toxicity Test, Freshwater and Marine). The study cannot be used to establish an LC_{50} value.
	A laundered or unlaundered 38 cm x 64 cm section of garment (0.24 square meter area; 227 g/m^3), which had been treated with Fyrol FR-2, was placed in tanks with six goldfish. Fish in the tank became progressively more sluggish and all died within 3 hours. The measured concentration of Fyrol FR2 in the test water was 30 mg/L. Fish exposed for 96 hours to the same section of fabric after it had been laundered did not die. (Experimental)	Ahrens et al., 1979	Data for mortality in control fish were not presented in the study; goldfish are not a designated test species, as per OPPTS 850.1075 (Fish Acute Toxicity Test, Freshwater and Marine). This study in inadequate for determining a hazard designation.
	Freshwater Fish 96-hour LC_{50} = 6.26 mg/L (Estimated) (Estimated) ECOSAR: Esters	ECOSAR v1.11	Estimate for the Esters class was provided for comparative purposes. See Section 5.5.1.

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PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
Daphnid LC_{50}	*Daphnia magna* 48-hour LC_{50} = 3.8 mg/L (flow-through test conditions) Negative control, solvent control (dimethylformamide), 0.98, 1.6, 2.8, 3.8, 5.1 mg/L Daphnia in the negative and solvent control groups appeared normal, as did the organisms in the 0.98 and 1.6 mg/L groups. Mortality in the 2.8, 3.8, and 5.1 mg/L groups was 0, 70, and 80%, respectively. Daphnid (15%) in the 2.8 mg/L group were lethargic at study termination. (Experimental)	Akzo Nobel, 2001; EU, 2008	The amount of solvent used in the control group and the TDCPP treatments is estimated to be approximately 300 mg/L. This exceeds the recommended maximum solvent concentration of 100 mg/L. The estimate is based on a reported dimethylformamide volume of 0.1 ml, a test chamber volume of 300 ml and a specific gravity of 0.95.
	Daphnia magna 48-hour EC_{50} = 4.6 mg/L (Experimental)	EU, 2008	Study did not include analysis of exposure concentrations; values are consistent with other experimental value.
	Daphnia 48-hour LC_{50} = 10.91 mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	Estimate for the Esters class was provided for comparative purposes. See Section 5.5.1.
Green Algae EC_{50}	*P. subcapitata* 96-hour $EC_{50} \geq 2.8$ mg/L (biomass and growth rate) 72-hour ErC10 = 2.3 mg/L NOEC > 1.2 mg/L (Experimental)	EU, 2008	Study details reported in a secondary source; conducted according to OECD guideline 201 reported toxicity values are below the reported water solubility for TDCPP (18 mg/L).
	Selenastrum capricornutum 96-hour E_bC_{50} = 12 mg/L 96-hour E_rC_{50} = 39 mg/L 96-hour NOAEC = 6 mg/L static test conditions; 0, 2, 6, 18, 54,	Akzo Nobel, 2001	A number of problems are evident with this study, namely the pH changed markedly during the study, and the reported pH and water temperature were outside of

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	or 162 mg/L (Experimental)		the recommended values for this algal species.
	Green algae 96-hour EC_{50} = 3.58 mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	Estimate for the Esters class was provided for comparative purposes. See Section 5.5.1.
Chronic Aquatic Toxicity	**HIGH: Based on a measured 21-day NOEC of 0.5 mg/L (LOEC = 1.0 mg/L) in daphnid for reduced reproduction; the NOEC and LOEC for reduced growth was 1.0 mg/L and 2.0 mg/L, respectively. Experimental data for algae indicate a Moderate hazard concern. No experimental data were located for fish. ECOSAR estimates and an estimated ChV using an Acute-to-Chronic Ratio (ACR) derived for the phosphate ester class that was applied to experimental acute data for this chemical predicts a HIGH concern for fish.**		
Fish ChV	Freshwater fish ChV = 0.05 mg/L (Estimated)	Professional judgment	An ACR of 24 was derived for the phosphate ester class based on experimental data for Tris (p-t-butylphenyl) phosphate (TBPP). The acute-to-chronic ratio was applied to available experimental acute fish data for Tris (1,3-dichloro-2-propyl)phosphate (ChV = 1.1 mg/L /24 = 0.05 mg/L)
	Freshwater fish ChV = 0.33 mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	Estimate for the Esters class was provided for comparative purposes. See Section 5.5.1.

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PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
Daphnid ChV	Daphnia magna 21-day LOEC = 1.0 mg/L (reproduction) 21-day NOEC = 0.5 mg/L (reproduction) 21-day NOEC = 1.0 mg/L (growth) 21-day LOEC = 2.0 mg/L (growth) semi-static test conditions (Experimental)	EU, 2008	Study details reported in a secondary source; test substance identified as Fyrol FR-2; purity >99%.
	Daphnia magna ChV = 4.64 mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	Estimate for the Esters class was provided for comparative purposes. See Section 5.5.1.
Green Algae ChV	*P. subcapitata* 96-hour $EC_{50} \geq 2.8$ mg/L (biomass and growth rate) 72-hour ErC10 = 2.3 mg/L NOEC > 1.2 mg/L (Experimental)	EU, 2008	Study details reported in a secondary source; conducted according to OECD guideline 201 reported toxicity values are below the reported water solubility for TDCPP (18 mg/L).
	Selenastrum capricornutum 96-hour E_bC_{50} = 12 mg/L 96-hour E_rC_{50} = 39 mg/L 96-hour NOAEC = 6 mg/L static test conditions; 0, 2, 6, 18, 54, or 162 mg/L (Experimental)	Akzo Nobel, 2001	A number of problems are evident with this study, namely the pH changed markedly during the study, and the reported pH and water temperature were outside of the recommended values for this algal species.
	Green algae ChV = 1.57 mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	Estimate for the Esters class was provided for comparative purposes. See Section 5.5.1.

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
ENVIRONMENTAL FATE				
Transport		**Level III fugacity models incorporating available physical and chemical property data indicate that at steady state, TDCPP is expected to be found primarily in soil and to a lesser extent, sediment and water. It is not expected to dissociate at environmentally-relevant pH values. TDCPP is expected to have moderate mobility in soil, based on measured K_{oc} values obtained from studies performed in clay loam, loamy sand and clay samples. Leaching through soil to groundwater may occur, though it is not expected to be an important transport mechanism. Estimated volatilization half-lives indicate that it will be non-volatile from surface water. Based on the measured vapor pressure, TDCPP is expected to exist in both the vapor and particulate phases in the atmosphere. Particulates will be removed from air by wet or dry deposition.**		
	Henry's Law Constant (atm-m^3/mole)	$<10^{-8}$ (Estimated)	Professional judgment; EPI v4.11	Cutoff value for nonvolatile compounds.
	Sediment/Soil Adsorption/Desorption - K_{oc}	1,780 according to OECD 106 using GLP; 0.01 M calcium chloride was equilibrated with each of three soils, a clay loam, a loamy sand and a clay, one sediment and one activated sludge solid. Reported as a range of 1,540 – 2,010. (Measured)	Schaefer and Ponizovsky, 2006 (as cited in EU, 2008)	Adequate, OECD guideline study.
	Level III Fugacity Model	Air = 0% Water = 4% Soil = 90% Sediment = 5% (Estimated)	EPI v4.11	Estimation model was calculated using all applicable measured input value.

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Persistence		**HIGH: The persistence for TDCPP is based on experimental guideline biodegradation studies. There is evidence of TDCPP biodegradation resulting in a half-life greater than 60 days. A river die away test found 22% removal of TDCPP in 14 days and a non-guideline soil test reported 6% removal in 17 weeks with radiolabeled TDCPP. In ready biodegradability tests, OECD TG 301B, 301C and 301D, 0 to <1% biodegradation of TDCPP occurred after 28 days. Additionally, no evidence of TDCPP removal was found in 28 days in an OECD 302C guideline study. TDCPP will undergo hydrolysis under alkaline conditions, with half-lives of 15 days measured at pH 9 and 50°C. TDCPP is relatively stable to hydrolysis under neutral and acidic conditions, a half-life of >1 year was found under pH 4 and pH 7 conditions. TDCPP is not expected to be susceptible to direct photolysis by sunlight, since it does not absorb light at wavelengths >290 nm.**		
Water	**Aerobic Biodegradation**	Passes Ready Test: No Test method: OECD TG 301B: CO_2 Evolution Test Modified Sturm Test 0% by CO_2 evolution. DOC reduction not calculated due to solubility issues. 0% by CO_2 evolution. DOC red. Not calculated due to solubility issues. (Measured)	Hattori et al., 1981 (as cited in Jenkins, 1990; Akzo Nobel, 2001; EU, 2008)	OECD guideline study, however solubility issues were found.
		Passes Ready Test: No Test method: OECD TG 301D: Closed Bottle Test No inhibition of bacterial cultures in 10 days. (Measured)	Bisinger, 1990; Akzo Nobel, 2001	Adequate, OECD guideline study.
		Passes Ready Test: No Test method: OECD TG 301C: Modified MITI Test (I) Reported as average, 1% by BOD using activated sludge inoculum. Initial concentrations 100 mg/L (test	CERI, 1999 (as cited in EU, 2008)	OECD guideline study, reported in a secondary source.

Tris (1,3-dichloro-2-propyl) phosphate CASRN 13674-87-8				
PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
		substance), 30 mg/L (sludge). The sludge was from ten sites in Japan: four sewage plants and six surface waters. (Measured)		
		Study results: 0%/28 days Test method: 302C: Inherent - Modified MITI Test (II) 0% by O_2 uptake (Measured)	WHO, 1998	EURAR notes that this study can only be seen as a short screening test, from which no conclusions regarding inherent biodegradability of TDCPP can be draw since no acclimation period was used.
		Study results: 22%/14 days Test method: River Die-Away test Oh River: 12.5%/7 days; 18.5%/14 days Neya River: 0%/7 days; 5.4%/14 days Osaka Bay: 0%/7 days; 22%/14 days Initial concentrations: 20 mg/L in Oh River water and 1 mg/L in Neya River water. Concentration in seawater not reported. Analysis by Molybdenum Blue calorimetric assay for increase in phosphate ion. (Measured)	Hattori et al., 1981 (as cited in WHO, 1998; EU, 2008)	Adequate, guideline study.
		Study results: 100%/12 hours Test method: Other Using isolated bacterium strains, *Sphingobium sp.* strain TCM1 and	Takahashi et al., 2012	Measured biodegradation rates demonstrate removal by this pathway using isolated strains.

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		1,3-DCP-degrading bacterium Arthrobacter sp. Strain PY1, complete detoxification of TDCPP was achieved in 12 hours. The degradation products were 1 phosphate, 6 HCl and 3 glycerol. (Measured)		
	Volatilization Half-life for Model River	>1 year (Estimated)	EPI v4.11	Estimation model was calculated using all applicable measured input values.
	Volatilization Half-life for Model Lake	>1 year (Estimated)	EPI v4.11	Estimation model was calculated using all applicable measured input values.
Soil	**Aerobic Biodegradation**	Study results: 6%/17 weeks Test method: Other ^{14}C radiolabelled TDCPP was applied to the soil surface and the soils (sand, loam, clay loam and sandy loam) were incubated at 20 ± 2°C. Each soil type was analyzed at intervals of 0, 7, 14, 35, 63 and 122 days. (Measured)	Schaefer and Ponizovsky, 2006 (as cited in EU, 2008)	Reported in a secondary source. Study used ^{14}C-labeled test substance, analyzed by HPLC.
	Anaerobic Biodegradation			No data located; chlorinated alkyl phosphates are outside the domain of the available estimation methods.
	Soil Biodegradation with Product Identification			No data located.
	Sediment/Water Biodegradation			No data located.
Air	**Atmospheric Half-life**	1 day (Estimated)	EPI v4.11	
		Reaction of TDCPP with oxidative species such as ozone or hydroxyl radicals can proceed rapidly. Vacuum	Echigo et al., 1996 (as cited in EU, 2008)	Non guideline study reported in a secondary source provides data indicating a potential for removal

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PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
		UV light at 185 and 254 nm, the study conditions were not representative of typical environmental conditions. (Measured)		by photodegradation, although the rate of removal and applicability of this pathway under environmental conditions is unknown.
Reactivity	**Photolysis**	Not a significant fate process (Estimated)	Professional judgment; Mill, 2000	The substance does not contain functional groups that would be expected to absorb light at environmentally significant wavelengths.
	Hydrolysis	50%/>1 year at pH 4 and 7; 14.7 days at pH9 OECD 111; EPA Ser. 835 OPPTS No. 835.2110. GLP-compliant. Initial concentration, 10 mg/L. Study length, 5 days at 50°C. Preliminary study. (Measured)	Akzo Nobel, 2001 (as cited in EU, 2008)	GLP-compliant test run according to accepted guidelines.
		50%/28 days at pH 9 OECD 111; EPA Ser. 835 OPPTS No. 835.2110. GLP-compliant. Definitive 30-day study at 40°C. (Measured)	Akzo Nobel, 2001	GLP-compliant test run according to accepted guidelines.
		50%/128 days at pH 9 OECD 111; EPA Ser. 835 OPPTS No. 835.2110. GLP-compliant. Definitive 30-day study at 20°C. (Measured)	Akzo Nobel, 2001	GLP-compliant test run according to accepted guidelines.
Environmental Half-life		>1 year (Estimated)	PBT Profiler	Half-life estimated for the predominant compartment, as determined by EPI methodology.

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Bioaccumulation		**LOW: Based on multiple experimental BCF values below or near 100, the Low bioaccumulation designation criteria. Toxicokinetic studies indicate that TDCPP and metabolites are rapidly formed and eliminated. However, biomonitoring studies report detection of this compound in pine needles, human adipose tissue, human seminal plasma samples, fish and herring gull eggs.**		
	Fish BCF	*Cyprinus carpio* 0.3 - 22 at two concentrations over 6 weeks (Measured)	MITI Japan, 1993	Nonguideline study with results consistent with other reported values.
		<113 *Oryzias latipes* Reported as 113 at 24 hours, 110 at 55 hours and 77 at 96 hours; static study with killifish at 25°C (Measured)	Sasaki et al., 1981	Consistent information for killifish under both static and flow-through conditions, over a variety of observation times, and with varying initial concentrations of test substance.
		5 at 24 hours and 3 at 55 hours; static study with goldfish at 25°C (Measured)	Sasaki et al., 1981	Consistent information for goldfish under both static and flow-through conditions, over a variety of observation times, and with varying initial concentrations of test substance.
		59 *Oryzias latipes* BCF values of 31 ± 6 to 59 ± 16 reported. Samples from fish taken at 3, 4, 6, 30 and 32 days. TDCPP concentrations of 40, 80, 300 and 400 ppb used in the flow-through study with killifish at 25°C (Measured)	Sasaki et al., 1981	BCF is independent of concentration; continuous flow-through results correlate to static results
	Other BCF			No data located.
	BAF	100 (Estimated)	EPI v4.11	Estimation model was calculated using all applicable measured input values.

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PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
	Metabolism in Fish	Apparent metabolism is much faster in killifish than in goldfish. ~10% of applied TDCPP remains in the water in the presence of killifish after 96 hours (Measured)	Sasaki et al., 1981	Non guideline study.
		Depuration rate/elimination half-life of 1.65 hours in killifish when exposed fish are moved to clean water (Measured)	Sasaki et al., 1982	Non guideline study.

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PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
ENVIRONMENTAL MONITORING AND BIOMONITORING			
Environmental Monitoring	TDCPP has been detected in water samples from surface water samples from 139 streams obtained in 30 states across the continental United States from 1999-2000. It has also been detected in groundwater samples from 47 sites in 18 different states as part of a national reconnaissance program of water quality in the United States. TDCPP was found in several streams in Johnson County, Kansas from 2002-2003, public drinking water in the US and Puerto Rico, St. Vrain Creek, Colorado, the Netherlands Rhine delta, Freshwater Streams in Hessen/Germany, Ruhr river in Germany, German Bight (an area heavily influenced by the Elbe estuary plume) in the North Sea, ground water in UK, Arctic Ocean, Sea of Japan, Northern Pacific Ocean, East Indian Archipelago, Philippine Sea, Indian Ocean, Southern Ocean, German Bight, North Sea, Oslo, Norway, Birkenes, Southern Norway (remote), Ny Alesund, Norwegian Arctic (remote), Northern Finland (remote), three volcanic lakes located in Central Italy, the Tiber River, Yodo river basin, Yamato River in Japan; water in Galicia Spain. TDCPP has been detected in air and dust samples from ambient air of Kitakyushu, Japan, indoor air environments in Tokyo, Japan, house dust in Spain, indoor air or dust from Zurich, Sweden, New Zealand, Germany and the US. TDCPP has been detected in precipitation samples from snow and rain in middle Germany and snow from northern Sweden. TDCPP has been detected in sediment samples from Taihu Lake, China, the rivers Danube, Neckar and Rhine, the Elbe river and Ruhr river (Bacaloni et al., 2007, 2008; EU, 2008; Regnery and Puettmann, 2008; Kanazawa et al., 2010; Meeker and Stapleton, 2010; ATSDR, 2012; Bollmann et al., 2012; Rodil et al., 2012; Salamova et al., 2014).		
Ecological Biomonitoring	TDCPP has been detected in fish from the Yamato river, pine needles from nine sites in the Sierra Nevada foothills and herring gull eggs from the Channel-Shelter Island colony in Lake Huron (Okumura, 1994; Aston et al., 1996; EU, 2008; Chen et al., 2011; Chen et al., 2012).		
Human Biomonitoring	In Canada, TDCPP was detected in human adipose tissue and it has been identified in human seminal plasma. This chemical was not included in the NHANES biomonitoring report (Hudec et al., 1981; LeBel and Williams, 1986; EU, 2008; CDC, 2009; ATSDR, 2012).		

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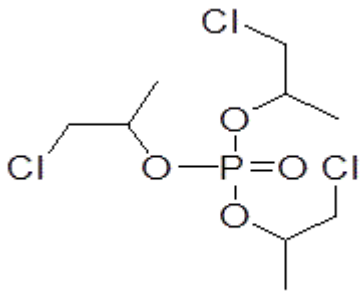
Tris (2-chloro-1-methylethyl) phosphate (TCPP)

Screening Level Toxicology Hazard Summary

This table contains hazard information for each chemical; evaluation of risk considers both hazard and exposure. Variations in end-of-life processes or degradation and combustion by-products are discussed in the report but not addressed directly in the hazard profiles. The caveats listed below must be taken into account when interpreting the information in the table.

VL = Very Low hazard L = Low hazard M = Moderate hazard H = High hazard VH = Very High hazard – Endpoints in colored text (VL, L, M, H, and VH) were assigned based on empirical data. Endpoints in black italics *(VL, L, M, H,* and *VH*) were assigned using values from estimation software and professional judgment [(Quantitative) Structure Activity Relationships "(Q)SAR"].

Chemical	CASRN	Human Health Effects										Aquatic Toxicity		Environmental Fate	
		Acute Toxicity	Carcinogenicity	Genotoxicity	Reproductive	Developmental	Neurological	Repeated Dose	Skin Sensitization	Respiratory Sensitization	Eye Irritation	Dermal Irritation	Acute	Chronic	Persistence	Bioaccumulation
Tris (2-chloro-1-methylethyl) phosphate (TCPP)	13674-84-5	L	*M*	L	H	H	*M*	M	L		L	L	M	*M*	H	L



	CASRN: 13674-84-5
	MW: 327.57
	MF: $C_9H_{18}Cl_3O_4P$
	Physical Forms: Liquid **Neat:**
	Use: Flame retardant

SMILES: O=P(OC(CCl)C)(OC(CCl)C)OC(CCl)C

Synonyms: 2-Propanol, 1-chloro-, 2,2`,2``-phosphate; TCPP; TCIPP; Tris(1-chloro-2-propyl)phosphate; Tris(2-chloroisopropyl)phosphate; 2-propanol, 1-chlorophosphate (3:1); 1-chloro-2-propyl phosphate (1:3); tris(1-chloromethylethyl) phosphate; phosphoric acid, tris(2-chloro-1-methyl ethyl) ester

Chemical Considerations: CASRN 13674-84-5 is a discrete organic chemical with a MW below 1,000. EPI v4.11 was used to estimate physical/chemical and environmental fate values in the absence of experimental data. Measured values from experimental studies were incorporated into the estimations. TCPP is produced by the reaction of phosphorus oxychloride and propylene oxide. The most abundant isomer in commercial products is the branched isomer, 2-Propanol, 1-chloro-, phosphate (3:1) (CASRN 13674-84-5) however other isomers are expected to be present and will be discussed in this report as appropriate when determining hazard designations. Chemical, fate, and toxicity data for the isomers represented by other CASRN were collected in the preparation of this AA and are listed below:

- 1-Propanol, 2-chloro-, 1,1`,1``-phosphate (3:1) (CASRN 6145-73-9);
- Phosphoric acid, bis(2-chloro-1-methylethyl) 2-chloropropyl ester (CASRN 76025-08-6) and
- Phosphoric acid, 2-chloro-1-methylethyl bis(2-chloropropyl) ester (CASRN 76649-15-5) (NAS, 2000).

Polymeric: No **Oligomeric:** Not applicable	
Metabolites, Degradates and Transformation Products: O,O-[bis(l-chloro-2-propyl)]-O-(2-Propionic acid) phosphate; bis(1-chloro-2-propyl) phosphate; bis(1-chloro-2-propyl) 1-hydroxy-2-propyl phosphate; bis(1-chloro-2-propyl) 1-carboxy -2-propyl phosphate; 1-chloro-2-propyl,1-hydroxy-2-propyl phosphate (OECD-SIDS, 2000; Van den Eade et al., 2013)	
Analog: Isomers anticipated to be present in the commercial product were considered in this evaluation, as indicated in the chemical considerations section **Endpoint(s) using analog values:** Not applicable	**Analog Structure:** Not applicable
Structural Alerts: Organophosphates; Neurotoxicity (EPA, 2012).	
Risk Phrases: This substance is not classified in the Annex I of Directive 67/548/EEC (ESIS, 2012).	
Hazard and Risk Assessments: Priority Existing Chemical Assessment report for Triphosphates by the National Industrial Chemicals Notification and Assessment Scheme (NICNAS) in 2001, Environmental Health Criteria for Flame Retardants by the World Health Organization in 1998, SIDS Initial Assessment Profile, EU Risk Assessment Report in 2008 and ATSDR Toxicological Profile for Phosphate Ester Flame Retardants in 2012 (WHO, 1998; OECD-SIDS, 2000; NICNAS, 2001; EU, 2008; ATSDR, 2012).	

Tris (2-chloro-1-methylethyl) phosphate CASRN 13674-84-5			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
PHYSICAL/CHEMICAL PROPERTIES			
Melting Point (°C)	-51 value expressed as pour point; Isoteniscopic ASTM D2897 Method (Measured)	OECD-SIDS, 2000; ECHA, 2013	Guideline study reported in a secondary source.
	-42 value expressed as pour point (Measured)	EC, 2000	Reported in a secondary source with limited study details.
	-65 (Measured)	NICNAS, 2001	Reported in a peer reviewed secondary source for the isomeric component CASRN 6145-73-9.
	72 (Measured)	van der Veen and de Boer, 2012	Cited in a peer reviewed source, this value is higher than the other studies which reported pour points.
Boiling Point (°C)	>288 GLP study (Measured)	ECHA, 2013	Reported in a secondary source.
	235 reported as 235-248°C. (Measured)	WHO, 1998; NAS, 2000	Reported in a peer reviewed source.
	220 Decomposes (Measured)	NICNAS, 2001	Reported in a peer reviewed secondary source for the isomeric component CASRN 6145-73-9.
	244 at 700 mmHg Decomposes (Measured)	OECD-SIDS, 2000	Test substance 75 +/- 10% pure with major impurities. Reported in a secondary source.
	359 (Measured)	van der Veen and de Boer, 2012	Cited in a peer reviewed source.
Vapor Pressure (mm Hg)	$1x10^{-5}$ at 25°C reported as 0.0014 Pa; GLP study (Measured)	ECHA, 2013	Reported in a secondary source.
	<2 at 25°C	OECD-SIDS, 2000	Adequate guideline study.

Tris (2-chloro-1-methylethyl) phosphate CASRN 13674-84-5			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	reported as 40 mm Hg at 110°C; according to Isoteniscopic, ASTM D2879 Method (Measured)		
	0.75 at 25°C (Measured)	van der Veen and de Boer, 2012	Reported in a peer reviewed source.
	<0.098 Reported as <13 Pa; temperature not specified (Measured)	NICNAS, 2001	Reported in a peer reviewed secondary source for the isomeric component CASRN 6145-73-9.
	$2.9x10^{-5}$ (Estimated)	EPI v4.11	According to the Modified Grain Method.
Water Solubility (mg/L)	1,080 (Measured) according to GLP flask method study	ECHA, 2013	Reported in a secondary source.
	1,200 (Measured)	NICNAS, 2001	Reported in a peer reviewed secondary source for isomeric component CASRN 6145-73-9.
	1,600 (Measured)	van der Veen and de Boer, 2012	Reported in a peer reviewed source.
	0.11% at 25°C (Measured)	OECD-SIDS, 2000; ECHA, 2013	Reported in secondary sources with limited details.
Log K_{ow}	2.68 HPLC method (Measured)	ECHA, 2013	Reported in a secondary source.
	2.59 (Measured)	van der Veen and de Boer, 2012	Reported in a peer reviewed source.
	3.33 Reported at 20°C according to EC Guideline 92/69 Annex V, Method A8; non-GLP (Measured)	OECD-SIDS, 2000	Guideline study reported in a secondary source; reproducibility concerns noted in results.
Flammability (Flash Point)	Flash point: 185°C according to Pensky-Martens Closed Cup ASTM D93 (Measured)	OECD-SIDS, 2000	Guideline study reported in s a secondary source.
	Flash point: 218°C (Measured)	van der Veen and de Boer, 2012	Guideline study reported in a

Tris (2-chloro-1-methylethyl) phosphate CASRN 13674-84-5			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
			secondary source.
	Flash point: 220°C Cleveland open cup (Measured)	NICNAS, 2001	Reported in a peer reviewed secondary source for isomeric component CASRN 6145-73-9.
Explosivity			No data located.
Pyrolysis			No data located.
pH	Not applicable (Estimated)	Professional judgment	Does not contain functional groups that are expected to ionize under environmental conditions.
pK_a	Not applicable (Estimated)	Professional judgment	Does not contain functional groups that are expected to ionize under environmental conditions.

Tris (2-chloro-1-methylethyl) phosphate CASRN 13674-84-5			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
HUMAN HEALTH EFFECTS			
Toxicokinetics	**TCPP is readily absorbed. Absorption through human skin membranes *in vitro* was calculated to be 2.3-32.8% of the applied dose. Twelve hours post- oral exposure, TCPP was detected in the brain, heart, muscle, and testes, more so in adipose tissue, spleen, and lungs, and in the highest amounts in the liver and kidney. TCPP is quickly and extensively metabolized with main metabolites being O,O-[bis(l-chloro-2-propyl)]-O-(2-propionic acid) phosphate, bis(1-chloro-2-propyl) monophosphoric acid and 1-chloro-2-propanol. TCPP was metabolized to a hydroxylated metabolite by chlorine substitution in liver S9 faction and liver slices followed by glucuronic acid conjugation. In incubation experiments, Phase I metabolites included the oxidative dechlorination products of TCPP and the hydrolysis product bis(1-chloro-2-propyl) phosphate (BCPP), bis(1-chloro-2-propyl) 1-hydroxy-2-propyl phosphate, bis(1-chloro-2-propyl) 1-carboxy -2-propyl phosphate and 1-chloro-2-propyl,1-hydroxy- 2-propyl phosphate; there were no phase II metabolites detected. BCPP was the most abundant metabolite. Once the tissues, the parent compound and metabolites are rapidly excreted. Excretion occurred primarily via the urine, but also in the feces and bile.**		
Dermal Absorption *in vitro*	Concentrations of TCPP tested over an 8 hour exposure period were 2.049, 99.96, or 997.33 µg/cm^2. The mean penetration of TCPP into the receptor fluid after 24 hours was 0.39, 9.64 and 17.75 µg/cm^2, for the low, mid and high dose, respectively. At 0.002 mg/cm^2, the total absorption ranged from 17 % to 32.8%, with a mean total absorption of 22.7 %. At the mid dose of 0.1 mg/cm^2, the total absorption ranged from 9.8% to 18.2%, with the mean total absorption of 13.6%. At 1 mg/cm^2, the total absorption ranged from 2.3% to 5.2%, with a mean total absorption of 3.7%.	TNO, 2006 (as cited in EU, 2008)	Adequate; guideline and GLP-compliant study. Data are from a secondary source.
	The actual concentrations of TCPP tested in an artificial sweat solution over an 8 hour exposure period were	TNO, 2005 (as cited in EU, 2008)	Guideline and GLP-compliant study. Study details reported in a secondary source.

Tris (2-chloro-1-methylethyl) phosphate CASRN 13674-84-5				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		76 µg/mL and 506 µg/L. At 24 hours after application, the total mean absorption of TCPP into the receptor fluid, the receptor compartment wash and the skin (excluding tape strips) was 33.3% and 38.1% for the low and high doses respectively. The mean recovery of TCPP in human skin was 93.1% and 92.2% for the low and high doses respectively. The permeability constant (Kp) for TCPP in artificial sweat under infinite conditions (24 hour exposure) was 7.65 x 10^{-3} cm/h.		
Absorption, Distribution, Metabolism & Excretion	**Oral, Dermal or Inhaled**	Male Wistar rats administered a single 50 µmol/kg (~14 mg/kg) gavage dose of ^{14}C-labeled TCPP Maximum concentration in tissues: 5.7 hours. Low tissue/blood ratios were recorded in the brain, heart, muscle, and testes. Moderate ratios were obtained in adipose tissue, the spleen, and lung; high ratios were recorded in the liver and kidneys. The highest amounts of radioactivity in the liver and kidney were detected during the first 12 hours after dosing. Seven days after dosing, the highest amount of radioactivity was found in the liver. The longest elimination half-lives from any tissue corresponded to adipose tissue (103 hours for TCPP).	Minegishi et al., 1988	Adequate
		^{14}C-labeled Fyrol PCF given to Sprague-Dawley rats at 20 or 200	Stauffer Chem Co, 1984 (as cited in OECD-SIDS, 2000; EU, 2008)	Data provided in a secondary source based on scientific review

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PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
		mg/kg via a single oral or i.v. administration. Urine was the major route of elimination. Test substance is rapidly metabolized with main metabolites being O,O-[bis(1-chloro-2-propyl)]-O-(2-propionic acid) phosphate, bis(1-chloro-2-propyl) monophosphoric acid and 1-chloro-2-propanol. The total body burden at the end of 8 days was less than 1% suggesting insignificant bioaccumulation.		of peer literature.
		Male Wistar rats administered a single 50 µmol/kg (~14 mg/kg) gavage dose of ^{14}C-labeled TCPP ~60% of TCPP was excreted in the urine; recovery within the 7 days approached 100%. Experiments in rats with cannulated bile ducts showed that peak biliary excretion occurred approximately 2 hours after dosing with TCPP. 45% of administered TCPP was excreted in the bile in 48 hours. Since the biliary/fecal excretion ratios for TCEP exceeded 1, it appeared that enterohepatic circulation occurred.	Minegishi et al., 1988	Adequate
		Male Wistar rats were administered 50 µmol/kg TCPP. 97.8% of the radioactive dose was recovered; of the recovered dose, 67 and 22% were recovered in the urine and feces (respectively), 7.7% in expired air, and <1% in the carcass.	Minegishi et al., 1988	Adequate

Tris (2-chloro-1-methylethyl) phosphate CASRN 13674-84-5				
PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
		Little radioactivity remained in the tissues 168 hours after dosing.		
	Other	^{14}C-labeled TCPP incubated with rat liver fractions for 4 or 24 hours. TCPP was metabolized to a hydroxylated metabolite by chlorine substitution in liver S9 fraction and liver slices, followed by glucuronic acid conjugation in liver slices. 11% and 39% of unmetabolized TCPP were detected in S9 fraction and liver slices, respectively.	BASF, 2007 (as cited in EU, 2008)	Study details reported in a secondary source. Documentation insufficient for assessment of data quality.
		Incubation experiments using 1.0 mg/mL HLM or S9 proteins, 50 µM TBOEP or TCEP, or TCPP, or 20 µM TPHP or TDCPP and NADPH regenerating solution in 1 mM total volume were conducted for 1 hour. There was a 33% and 28% clearance of the compound in the HLM and S9 incubations, respectively. Phase I metabolites included the oxidative dechlorination products of TCPP and the hydrolysis product bis(1-chloro-2-propyl) phosphate (BCPP, M1), bis(1-chloro-2-propyl) 1-hydroxy-2-propyl phosphate (M2), bis(1-chloro-2-propyl) 1-carboxy -2-propyl phosphate (M3) and 1-chloro-2-propyl,1-hydroxy- 2-propyl phosphate (M4); there were no phase II metabolites detected. BCPP was the most abundant metabolite.	Van den Eade et al., 2013	Study details reported in an abstract

Tris (2-chloro-1-methylethyl) phosphate CASRN 13674-84-5				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Acute Mammalian Toxicity		**LOW: Based on LD_{50} and LC_{50} values for the oral, dermal, and inhalation routes of exposure.**		
Acute Lethality	**Oral**	Rat LD_{50} (range) = 1,073 – 3,600 mg/kg	SafePharm Labs Ltd, 1979a, 1979b; Stauffer Chem Co, 1972 (as cited in EC, 2000; EU, 2008)	Adequate by weight of evidence; data obtained from multiple secondary sources.
		Rat LD_{50} = 1,546 – 1,824 mg/kg (males); 1,017 – 1,101 mg/kg (females)	Mobil, 1980a, 1981a (as cited in EC, 2000; OECD-SIDS, 2000; EU, 2008)	Adequate by weight of evidence; data from secondary sources.
		Rat LD_{50} = 2,800 mg/kg (females); 4,200 mg/kg (males)	Huntingdon, 1997a, 1997b (as cited in EC, 2000; OECD-SIDS, 2000; EU, 2008)	Adequate; performed according to current standards and GLP-compliant.
		Rats exposed at 200, 500, or 2,000 mg/kg. All rats (females) died at 2,000 mg/kg; no mortalities at other dose levels. LD_{50} > 500 mg/kg (males) and >632 mg/kg (females)	Stropp, 1996 (as cited in EU, 2008; ATSDR, 2012)	Study details reported in a secondary source.
		Rat LD_{50} = 931- 1,550 mg/kg	SafePharm Labs Ltd, 1994, 1996a, 1996b, 1997a, 1997b (as cited in EU, 2008)	Adequate; conducted according to OECD guidelines.
		Rat LD_{50} = 2,000 mg/kg (males) and 1,260 mg/kg (females)	Litton Bionetics, 1977 (as cited in ATSDR, 2012)	Study details from an anonymous source reported in a secondary source.
		Rat 96-h LD_{50} = 1,500 mg/kg (females)	Kawasaki et al., 1982 (as cited in ATSDR, 2012)	Study details reported in a secondary source.
	Dermal	Rabbit LD_{50} >2,000 mg/kg	Stauffer Chem Co, 1970, 1979; Mobil, 1980b, 1981b (as cited in EC, 2000; EU, 2008)	Study details reported in a secondary source. Test substance identified as TCPP in some studies; Antiblaze 80 or Fyrol PCF in others. Purity of the test substance reported in some studies.
		Rat LD_{50} >2,000 mg/kg	Inveresk Res Int, 1989b (as cited in	Study details from several studies

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
			OECD-SIDS, 2000; EU, 2008)	reported in secondary source. At least one study was performed according to OECD guidelines and GLP.
	Inhalation	Rat 4-h LC_{50} (whole-body): >5 mg/L (males); ~5 mg/L (females)	Env Affairs, 1981a (as cited in EC, 2000; OECD-SIDS, 2000; EU, 2008)	Study based on EPA guidelines; sufficient study details reported; analyses of test concentrations and cumulative mass of the particles were performed.
		Rat 4-h LC_{50} (nose-only) >7 mg/L	Inveresk Res Int, 1990a (as cited in EC, 2000; EU, 2008)	OECD guideline study performed according to GLP. Test concentrations and particle size distribution analyses were performed; sufficient study details reported. Purity (total of four isomers) >97.9%.
		Rat 1-h LC_{50} (whole-body) >17.8 mg/L	Env Affairs, 1981b (as cited in EC, 2000; EU, 2008)	Study based on EPA guidelines; sufficient study details reported.
Carcinogenicity		**MODERATE: There were no experimental data located for this endpoint; carcinogenic effects cannot be ruled out.**		
	OncoLogic Results			No data located.
	Carcinogenicity (Rat and Mouse)			No data located.
	Combined Chronic Toxicity/Carcinogenicity			No data located.
	Other			No data located.

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Genotoxicity		**LOW: Based on weight of evidence from multiple studies. TCPP did not cause gene mutations in bacteria *in vitro* or chromosome aberrations in rat bone marrow *in vivo*.**		
	Gene Mutation *in vitro*	In multiple studies: Negative for mutation in *Salmonella typhimurium* strains TA97a, TA98, TA100, TA102, TA104, TA1535, TA1537, and/or TA1538 in the presence or absence of metabolic activation at up to 1 mM.	Zeiger et al., 1992; Abe and Urano, 1994; Follmann and Wober, 2006 (as cited in EU, 2008; ATSDR, 2012)	Study details reported in a secondary source; similar to guideline studies. Exact purity of test substances was not reported, but a reagent grade chemical was used.
		Negative; gene mutation in *E. coli* strains W3110/po1A+ and p3478/polA- at doses up to 20 µl/plate in the presence or absence of metabolic activation.	Tenneco Chem Inc, 1977 (as cited in EU, 2008)	Adequate; data from a secondary source.
		Negative; gene mutation in *Saccharomyces cerevisiae* strain D4 in the presence or absence of activation.	Stauffer Chem Co, 1976, 1978d (as cited in EU, 2008)	Adequate; data reported in a secondary source.
		Positive in the presence of metabolic activation; gene mutation in L5178Y mouse lymphoma cells. Negative in the absence of metabolic activation.	Covance Labs, 2005; Env Affairs, 1981c (as cited in EU, 2008)	Adequate; data reported in a secondary source. Results considered equivocal in one assay because a dose-response relationship could not be ascertained. Results were positive with activation in a confirmatory mouse lymphoma assay.
		Positive; transformation of BALB/3T3 cells	Stauffer Chem Co, 1978e (as cited in EU, 2008)	Data reported in a secondary source. Positive at all doses (39-312 nl/ml 50-400 µg/ml); however, no dose-response relationship was observed.
		Negative; forward mutation in mouse lymphoma L5178Y cells at TK locus in the presence or absence of	Stauffer Chem Co, 1978c (as cited in EU, 2008)	Acceptable, well-documented publication report which meets basic scientific principles. Data

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PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
		metabolic activation.		reported in a secondary source.
		Negative; transformation of BALB/3T3 cells at up to 40 nL/mL (51.6 µg/mL).	Stauffer Chem Co, 1980b (as cited in EU, 2008)	Adequate; similar to guideline study. Data reported in a secondary source. Although tests were positive for one study, no dose-response was observed.
	Gene Mutation *in vivo*			No data located.
	Chromosomal Aberrations *in vitro*			No data located.
	Chromosomal Aberrations *in vivo*	Negative for induction of micronuclei in Sprague-Dawley rats administered TCPP in the feed at up to 20,000 ppm for 90 days.	NTP, 2013	Adequate; limited study details available from NTP website.
		Negative for chromosomal aberrations in bone marrow of Sprague-Dawley rats orally exposed.	Stauffer Chem Co, 1978b (as cited in EU, 2008)	Study conducted according to OECD guidelines; study details reported in secondary source.
		Positive in males and negative in female for induction of micronuclei in B6C3F1 mice administered TCPP in feed at 1, 1250, 2500, 5,000, 10,000, or 20,000 ppm for 90 days.	NTP, 2013	Adequate; limited study details available from NTP website.
	DNA Damage and Repair	Negative for DNA damage (comet assay) in the presence or absence of activation in Chinese hamster V79 cells. The test substance caused cytotoxicity (neutral red uptake assay) in the presence, but not absence of activation.	Follmann and Wober, 2006	Purity of test substance was not reported, but a reagent grade chemical was used.
		Negative; UDS in rat liver cells	Williams et al., 1989; Bayer, 1991b (as cited in EU, 2008)	Adequate; data reported in a secondary source. Guideline and GLP-compliant study.
		TCPP did not induce DNA damage in	Covance Labs, 2006 (as cited in	Study conducted similar to

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		the liver or rats treated up to 1,500 mg/kg.	EU, 2008; ECHA, 2013)	guidelines and GLP-compliant; study details reported in secondary source.
		TCPP did not induce DNA strand breaks in V79 cells in the presence or absence of activation (alkaline comet assay) at concentrations up to 1 mM.	Follmann and Wober, 2006	Purity of test substance was not reported, but a reagent grade chemical was used.
		Equivocal results UDS in human diploid WI-38 cells. The test material was weakly active at 0.01 µl/mL in activated and nonactivated systems without an associated dose response at higher concentrations.	Stauffer Chem Co, 1978a (as cited in EU, 2008)	Data were from a secondary source. Test results were deemed equivocal because no clear dose-response relationship could be ascertained, and performed using a non-standard cell line. Results in other cell types were negative.
	Other			No data located.
Reproductive Effects		**HIGH: Based on an unestablished NOAEL and a LOAEL of 99 mg/kg-day for decreased uterine weights in F0 female rats fed TCPP in a 2-generation reproduction study. Two other studies reported no significant effects on reproductive parameters in rats exposed to TCPP in the diet at doses greater than 893 mg/kg-day.**		
	Reproduction/Developmental Toxicity Screen			No data located.
	Combined Repeated Dose with Reproduction/ Developmental Toxicity Screen			No data located.
	Reproduction and Fertility Effects	Two-generation reproduction study in Wistar rats (28/sex/group) Doses: 0, 85, 293 and 925 mg TCPP/kg-day for males and 0, 99, 330 and 988 mg TCPP/kg-day for females (administered in the diet) Decreased body weight and food consumption was observed in mid and	TNO, 2007 (as cited in EU, 2008)	Adequate; guideline (OECD 416) and GLP-compliant study. Data obtained from a secondary source only; primary source not specified; uterine and seminal vesicle weight changes were not accompanied by histopathological changes.

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PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
		high dose parental animals and the effects on uterus weights seen in all dosed F0 animals. There were no treatment related effects in pre-coital time, mating index, female fecundity index, male and female fertility index, duration of gestation and post-implantation loss There was no effect on sperm parameters at necropsy In females, the length of the longest oestrus cycle and the mean number of cycles per animal were statistically significantly increased in high dose animals of both generations. A decrease in uterus weight was observed in all dosed females in F0 and in high dose females in F1. Decreased relative and absolute seminal vesicle weights were reported in the mid and high dose F0 and F1 males. NOAEL: Not established LOAEL: 99 mg/kg-day based on effects on uterus weights (lowest dose tested). F0 Males: NOAEL: 85 mg/kg-day LOAEL: 293 mg/kg-day based on decreased seminal vesicle weight		

Tris (2-chloro-1-methylethyl) phosphate CASRN 13674-84-5				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Other	Dietary study in rats; exposure: GD 0 - 20; doses: up to 893 mg/kg-day No significant effect on the numbers of implantations or resorptions. NOAEL: 893 mg/kg-day (highest dose tested) LOAEL: Not established	Kawasaki et al., 1982 (as cited in ATSDR, 2012)	Limited study details reported in a secondary source. Unknown purity of test substance. The 893 mg/kg-d dose level was the highest dose tested. The true NOAEL may be higher.
		In a 90 day study, 20 male and 20 female Sprague Dawley rats were fed diets containing 0, 800, 2,500, 7,500 and 20,000 ppm of TCPP, there were no effects observed in the testes or ovaries of treated animals when examined at necropsy NOAEL: 20,000 ppm (Highest concentration tested) LOAEL: Not established	Freudenthal and Henrich, 1999	Inadequate for complete assessment of reproductive toxicity; data are for the Fyrol PCF mixture (about tris (2-chloroisopropyl) phosphate (about 70%) and 2-chloropropanol phosphate (about 23%).
Developmental Effects		**HIGH: Based on an unestablished NOAEL and a LOAEL of 99 mg/kg-day for an increased number of runts in rats exposed to TCPP in the diet in a 2-generation reproduction study. Another study reported no significant developmental effects in offspring of rats gestationally exposed to TCPP in the diet at doses up to 893 mg/kg-day.** **There were no data located for the developmental neurotoxicity endpoint; there is uncertain concern for developmental neurotoxicity based on the potential for Cholinesterase (ChE) inhibition in dams that may result in alterations of fetal neurodevelopment.**		
	Reproduction/ Developmental Toxicity Screen			No data located.
	Combined Repeated Dose with Reproduction/ Developmental Toxicity Screen			No data located.

Tris (2-chloro-1-methylethyl) phosphate CASRN 13674-84-5				
PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
	Prenatal Development	Dietary study in Wistar rats Exposure: GD 0 - 20; doses: 0.01, 0.1, and 1% in the diet (up to 893 mg/kg-day) No significant effects on fetal weight or incidences of external malformations. Cervical ribs, missing ribs, and delayed ossification of sternebrae were more frequent in treated groups but not significantly different from controls. Neonatal growth and survival during the 4 weeks after weaning was comparable among groups. NOAEL: 893 mg/kg-day (highest dose tested) LOAEL: Not established	Kawasaki et al., 1982 (as cited in EU, 2008; ATSDR, 2012)	Data obtained from a secondary source; limited study details were available in the secondary source. Unknown purity of test substance. The 893 mg/kg-d dose level was the highest dose tested. The true NOAEL may be higher.
	Postnatal Development			No data located.
	Prenatal and Postnatal Development			No data located.
	Developmental Neurotoxicity	Uncertain concern for developmental neurotoxicity based on the potential for Cholinesterase (ChE) inhibition in dams that may result in alterations of fetal neurodevelopment (Estimated)	Professional judgment	Estimated based on a structural alert for organophosphates for the neurotoxicity endpoint.
	Other	Two-generation reproduction study in Wistar rats (28/sex/group) Doses: 0, 85, 293 and 925 mg TCPP/kg-day for males and 0, 99, 330 and 988 mg TCPP/kg-day for females (administered in the diet) Decreased mean number of pups	TNO, 2007 (as cited in EU, 2008)	Data reported in a secondary source. Adequate; guideline (OECD 416) and GLP-compliant study. Data obtained from a secondary source.

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PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
		delivered was observed in the mid dose group of the F1 generation and in the high dose groups of both generations. Pup mortality (PND1-4) was statistically significantly increased in the low and high dose F0 groups and in the high doseF1 group. This effect was only observed when the pup was used as the statistical unit. The effect observed in the F1 generation was mainly due to the loss of one litter (10 pups) of a single dam on PND4. There was no statistically significant difference in the mean number of pups on PND4. In the F0 generation, the mean number of runts was statistically significantly increased in all dose groups on PND1 and persisted to PND21 in the mid and high dose groups. In F1 generation, the number of runts was increased in the high dose group on PND14 and in all dose groups on PND21. In both generations, the number of runts in the high dose groups increased during the course of the lactation period. There was no effect on pup weight at PND1 in either generation. There was no effect on pup weight on PND1 in both generations. Mean pup weights of the high dose group were significantly decreased in F0 generation from PND14 onwards and in the F1		

Tris (2-chloro-1-methylethyl) phosphate CASRN 13674-84-5				
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		generation from PND 7 onwards. Mean pup weights were decreased in mid dose groups on PND21 No difference in anogenital distance of the male or female F2 pups was observed between the treated and control animals. Vaginal opening was delayed (not significantly) in the high dose group. Preputial separation was statistically significantly delayed in the high dose group. The body weight of the high dose male and females of the F2 generation was significantly decreased from PND28 until PND42 (91% and 89% of control at PND42 for females and males of this group, respectively). The effects observed in this dose group on vaginal opening and preputial separation is most likely secondary to toxicity. At necropsy of the pups there were no treatment related macroscopic findings. NOAEL: Not established LOAEL: 99 mg/kg-day based on treatment related effect on the number of runts in F0 generation (lowest dose tested).		

Tris (2-chloro-1-methylethyl) phosphate CASRN 13674-84-5				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Neurotoxicity		**MODERATE: Based on the weight of evidence from a structural alert for organophosphates and an *in vitro* study. In an *in vitro* study using undifferentiated and differentiating PC12 cells, TCPP promoted differentiation of the cholinergic phenotype of PC12 cells. There were no effects on cholinesterase activity in a dietary study in rats fed TDCPP and no evidence of delayed neurotoxicity in one study of hens orally treated with TCPP.**		
	Neurotoxicity Screening Battery (Adult)			No data located.
	Other	Potential for neurotoxicity based on structural alert for organophosphates (Estimated)	Professional judgment	Estimated based on a structural alert and professional judgment.
		In vitro neurotoxicity study using undifferentiated and differentiating PC12 cells. Changes in DNA synthesis, oxidative stress, differentiation into dopaminergic or cholinergic neurophenotypes, cell number, cell growth and neurite growth were assessed. TCPP promoted differentiation of the cholinergic phenotype only. There were no other adverse neurological effects.	Dishaw et al., 2011	Study details reported in a primary source
		14-day dietary study in CD-1 rats treated with 0, 4200, 6600, 10,600, and 16,600 ppm (approximately 0, 417, 648, 1,015, 1,636 mg/kg-day for males and 382, 575, 904, 1,517 mg/kg/day for females). There were no effects on cholinesterase activity. NOAEL: 16,600 ppm (1,636 mg/kg-day); highest dose tested	Stauffer Chem Co, 1980a	Test substance was identified as Fyrol PCF, a mixture containing TCPP (~70%) and 2-chloropropanol phosphate (~22%); limited study details reported in a robust summary.

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		LOAEL: Not established		
		Delayed oral neurotoxicity in White leghorn hens (18/treatment group and 10 controls); doses: 13,200 mg/kg (10 mL/kg) by gavage; exposure period: Two treatments, three weeks apart Treated hens showed loss of body weight and transient reductions in food consumption immediately following treatment. There was no evidence of delayed motor impairment; no histological changes to nervous tissues were found. NOAEL: 13,200 mg/kg; highest dose tested LOAEL: Not established	Sprague et al., 1981; OECD-SIDS, 2000	Study details reported in a primary source; not a guideline study.
Repeated Dose Effects		**MODERATE: Based on reported morphological changes in the kidney and thyroid reported in rats fed the Fyrol PCF mixture (tris (2-chloroisopropyl) phosphate [~70%] and 2-chloropropanol phosphate [~ 23%]) in the diet for 90 days at doses of 481 mg/kg-day and 570 mg/kg-day in males and females, respectively. Decreased body weight gain and food consumption was reported in rats fed Fyrol PCF for 14 days. Also, rats exposed to TCPP in the diet for 28 days reported increased mortality in females at a dose of 1,000 mg/kg-day; the NOAEL for this study was identified as 100 mg/kg-day which falls within the Moderate hazard criteria range. Criteria values are tripled for chemicals evaluated in 28-day studies. There is uncertainty about where effects may occur given that the identified NOAEL (100 mg/kg-day) and LOAEL (1,000 mg/kg-day) bridges the Moderate (30 - 300 mg/kg-day) and Low (> 300 mg/kg-day) hazard designation range; effects occurring within the Moderate range cannot be ruled out.**		
		90-day dietary study in CD Sprague-Dawley rats (20/sex/group) administered 0, 800, 2,500, 7,500, or 20,000 ppm Fyrol PCF (average doses	Freudenthal and Henrich, 1999; OECD-SIDS, 2000	Data are for the Fyrol PCF mixture (about tris (2-chloroisopropyl) phosphate (about 70%) and 2-chloropropanol

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PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
		of 0, 52, 160, 481, and 1,349 mg/kg-day for males and 0, 62, 171, 570, and 1,352 mg/kg-day for females estimated by the study authors) At the high-dose, body weights were significantly decreased relative to controls. Significantly increased absolute and relative liver weights were observed in all treated males and in females in the two highest dose groups. Mild periportal hepatocellular swelling was noted in some animals at 20,000 ppm; no changes in liver histopathology were seen at other doses. Males showed significantly increased relative kidney weights at ≥ 7,500 ppm; microscopic kidney changes (very mild cortical tubular degenerative effects) were observed in males at 7,500 ppm and at 20,000 ppm males and females. Increased incidence of very mild thyroid follicular changes was noted in the two highest dose groups. Histopathological changes occurred in the absence of significant effects on hematology or clinical chemistry endpoints (including those associated with liver and kidney function). NOAEL: 2,500 ppm (160 and 171 mg/kg-day for males and females, respectively) LOAEL: 7,500 ppm (481 and 570		phosphate (about 23%).

Tris (2-chloro-1-methylethyl) phosphate CASRN 13674-84-5				
PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
		mg/kg-day for males and females, respectively) based on minimal morphological changes (kidney, thyroid)		
		14-day dietary study in CD-1 rats treated with 0, 4,200, 6,600, 10,600, and 16,600 ppm (approximately 0, 417, 648, 1,015, 1,636 mg/kg/day for males and 382, 575, 904, 1,517 mg/kg/day for females) A significant reduction in body weight gain and decreased food consumption was observed in male rats at 10,600 ppm in week 1. There were no effects on hematology, clinical chemistry, or cholinesterase activity. Increased liver weights occurred in the absence of histopathological changes. NOAEL: 6,600 ppm (648 mg/kg-day) LOAEL: 10,600 ppm (1,015 mg/kg-day) based on decreased body weight gain and food consumption in males.	Stauffer Chem Co, 1980a (as cited in EC, 2000; EU, 2008)	Test substance was identified as Fyrol PCF, a mixture containing TCPP (~70%) and 2-chloropropanol phosphate (~22%); limited study details reported in a robust summary.
		28-day gavage study in Wistar rats (6/sex/group) dosed daily with 0, 10, 100, or 1,000 mg/kg-day test substance (97.85% pure). Increased mortality in high-dose females. No effect on body weight or food consumption. Increased water intake in high-dose groups. No effect on hematology, clinical chemistry or urinalysis. Necropsy did not show	Bayer, 1991c (as cited in EC, 2000; EU, 2008)	Only qualitative data reported in a secondary source. Study appears to have examined a comprehensive number of endpoints; criteria values are tripled for chemicals evaluated in 28-day studies; there is uncertainty about where effects may occur given that the identified NOAEL (100 mg/kg-

Tris (2-chloro-1-methylethyl) phosphate CASRN 13674-84-5				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		gross alterations. Histopathology showed adaptive effects in the liver from high-dose rats. NOAEL: 100 mg/kg-day; LOAEL: 1,000 mg/kg-day (increased mortality in females).		day) and LOAEL (1,000 mg/kg-day) bridges the Moderate (30 - 300 mg/kg-day) and Low (>300 mg/kg-day) hazard designation range; effects occurring within the Moderate range cannot be ruled out.
		7-day repeated-dose gavage study in rats exposed to 1,000 mg/kg-day (other doses, if any, were not reported). No effects on body weight gain or relative organ weights (brain, heart, lungs, liver, spleen, kidneys, or adrenals) at doses up to 1,000 mg/kg-day NOAEL: 1,000 mg/kg-day LOAEL: Not established	Kawasaki et al., 1982 (as cited in ATSDR, 2012)	Limited study details reported in a secondary source.
Skin Sensitization		**LOW: TCPP is not a skin sensitizer.**		
	Skin Sensitization	Human; not sensitizing	BASF, 1979 (as cited in EC, 2000)	Limited data available from a secondary source.
		Mouse (local lymph node assay); not sensitizing	SafePharm Labs Ltd, 2005 (as cited in EU, 2008)	Adequate; guideline and GLP-compliant. Study details reported in a secondary source.
		Guinea pig; not sensitizing	SafePharm Labs Ltd, 1979e (as cited in EC, 2000; EU, 2008)	Limited data available from a secondary source. Not performed according to GLP.
Respiratory Sensitization		**No data located.**		
	Respiratory Sensitization			No data located.

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Eye Irritation		**LOW: TCPP was not irritating to slightly irritating in rabbits.**		
	Eye Irritation	Rabbit; not irritating	Stauffer Chem Co, 1972, 1979; SafePharm Labs Ltd, 1979c; Bayer, 1991a (as cited in EC, 2000; EU, 2008)	Adequate by weight of evidence. Data from secondary sources.
		Rabbit; slightly irritating. Transient; effects typically resolved 24 to 72 hours post-administration.	Mobil, 1981d, 1980d; Inveresk Res Int, 1990b (as cited in EC, 2000; OECD-SIDS, 2000; EU, 2008)	Study details reported in a secondary source.
		Extensive experimental data indicate that TCPP is non-irritant to the rabbit eye.	EU, 2008	Data are from a secondary source; primary data sources not specified.
Dermal Irritation		**LOW: Based on weight of evidence from multiple studies. TCPP is not irritating to skin in humans and rabbits.**		
	Dermal Irritation	Human; not irritating	BASF, 1979 (as cited in EC, 2000)	Study details reported in a secondary source.
		Rabbit; not irritating	Mobil, 1981c, 1980c; Stauffer Chem Co, 1972 (as cited in EC, 2000; EU, 2008)	Study details reported in a secondary source.
		Rabbit; slightly irritating. Transient; effects typically resolved within 72 hours.	Stauffer Chem Co, 1979; SafePharm Labs Ltd, 1979d; Inveresk Res Int, 1989a (as cited in EC, 2000; OECD-SIDS, 2000; EU, 2008)	Study details reported in a secondary source.
		Extensive experimental data indicate that TCPP in non-irritant to rabbit skin.	EU, 2008	Study details reported in a secondary source; primary data sources not specified.

Tris (2-chloro-1-methylethyl) phosphate CASRN 13674-84-5			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
Endocrine Activity	**TCPP increased 17B estradiol and testosterone production in H295R cells, up-regulated steroidogenic genes and down-regulated sulfotransferases. TCPP also inhibited dihydrotestosterone and 17B estradiol induced expression indicating antiandrogenic or antiestrogenic activity, while TCPP was found to not induce estrogenic or anti-estrogenic effects in a yeast reporter gene assay and a human endometrial cancer cell assay.**		
	Two-generation reproduction study in Wistar rats (28/sex/group) Doses: 0, 85, 293 and 925 mg TCPP/kg-day for males and 0, 99, 330 and 988 mg TCPP/kg-day for females (administered in the diet) Decreased body weight and food consumption was observed in mid and high dose parental animals and the effects on uterus weights seen in all dosed F0 animals. In females, the length of the longest oestrus cycle and the mean number of cycles per animal were statistically significantly increased in high dose animals of both generations. A decrease in uterus weight was observed in all dosed females in F0 and in high dose females in F1.	TNO, 2007 (as cited in EU, 2008)	Adequate; guideline (OECD 416) and GLP-compliant study. Data obtained from a secondary source only; primary source not specified; the observed changes may be an indication of endocrine activity.
	TCPP significantly increased 17B-estradiol (at 100 mg/L) and testosterone production (at ≥1 mg/L) in H295R cells. The transcription of other steroidogenic genes (CYP11A1, CYP112B, HSD3B2) were up-regulated and sulfotransferases (SULT1E1, SULT2A1) were down-	Liu et al., 2012	Test substance purity was not reported.

Tris (2-chloro-1-methylethyl) phosphate CASRN 13674-84-5			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	regulated in response to treatment with TCPP.		
	TCPP inhibited expression induced by dihydrotestosterone (IC_{50} = 1.8 x 10^{-4}M) and 17B-estradiol (IC_{50} = 2.3 x 10^{-4}M); indicating that TCPP may have antiandrogenic and/or antiestrogenic activities.	Ohyama et al., 2006	Study details from the primary report are available; however, only the study summary and figure legends are reported in English.
	TCPP did not induce estrogenic or anti-estrogenic effects at up to 10 µM as based on results of the recombinant yeast reporter gene assay and Ishikawa (human endometrial cancer) cell assay.	Follmann and Wober, 2006	Adequate.
	7-day repeated-dose gavage study in rats exposed to 1,000 mg/kg-day (other doses, if any, were not reported). No effects on adrenals weights at doses up to 1,000 mg/kg-day	Kawasaki et al., 1982 (as cited in ATSDR, 2012)	Limited study details reported in a secondary source.
	90-day dietary study in CD Sprague-Dawley rats (20/sex/group) administered 0, 800, 2,500, 7,500, or 20,000 ppm Fyrol PCF (average doses of 0, 52, 160, 481, and 1,349 mg/kg-day for males and 0, 62, 171, 570, and 1,352 mg/kg-day for females estimated by the study authors) Increased incidence of very mild thyroid follicular changes was noted in the two highest dose groups. Histopathological changes occurred in the absence of significant effects on hematology or clinical chemistry endpoints (including those associated	Freudenthal and Henrich, 1999 (as cited in OECD-SIDS, 2000)	Data are for the Fyrol PCF mixture (about tris (2-chloroisopropyl) phosphate (about 70%) and 2-chloropropanol phosphate (about 23%); the observed changes may be an indication of endocrine activity.

Tris (2-chloro-1-methylethyl) phosphate CASRN 13674-84-5			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	with liver and kidney function).		
	Two-generation reproduction study in Wistar rats (28/sex/group) Doses: 0, 85, 293 and 925 mg TCPP/kg-day for males and 0, 99, 330 and 988 mg TCPP/kg-day for females (administered in the diet) No difference in anogenital distance of the male or female F2 pups was observed between the treated and control animals. Vaginal opening was delayed (not significantly) in the high dose group. Preputial separation was statistically significantly delayed in the high dose group. The body weight of the high dose male and females of the F2 generation was significantly decreased from PND28 until PND42 (91% and 89% of control at PND42 for females and males of this group, respectively). The effects observed in this dose group on vaginal opening and preputial separation is most likely secondary to toxicity. At necropsy of the pups there were no treatment related macroscopic findings. NOAEL: Not established LOAEL: 99 mg/kg-day based on treatment related effect on the number of runts in F0 generation (lowest dose tested).	TNO, 2007 (as cited in EU, 2008)	Data reported in a secondary source. Adequate; guideline (OECD 416) and GLP-compliant study. Data obtained from a secondary source.

Tris (2-chloro-1-methylethyl) phosphate CASRN 13674-84-5			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
Immunotoxicity	**No data located.**		
Immune System Effects			No data located.
ECOTOXICITY			
ECOSAR Class			
Acute Aquatic Toxicity	**MODERATE: Based on experimental LC_{50} and EC_{50} values for fish, daphnia, and algae.**		
Fish LC_{50}	*Poecilia reticulata* 96 hour LC_{50} = 30 mg/L (static test conditions) (Experimental)	Griebenow, 1998 (as cited in EC, 2000; EU, 2008)	The test substance was identified as technical grade TCPP; specific purity was not reported. Guideline-like study (OECD 203); however analytical monitoring was reportedly not performed.
	Pimephales promelas 96 hour LC_{50} = 51 mg/L (static test conditions) (Experimental)	Meeks, 1985c (as cited in EC, 2000; OECD-SIDS, 2000; EU, 2008)	LC_{50} based on linear regression from 168 hours exposure and actual test concentrations. Differences in nominal and actual test concentrations were attributed to limited water solubility of the test substance. Analytical monitoring was performed and study was conducted according to guideline (OECD 203) and GLP.
	Killifish (*Oryzias latipes*) 48-hour LC_{50} = 54 mg/L (Experimental)	MITI, 1992 (as cited in EC, 2000; EU, 2008)	Not standard duration for acute toxicity to fish; no additional details were available. Reported method: Japanese Industrial Standard (JIS K0102-1986-71) Testing Methods for Industrial Waste Water.
	Brachydanio rerio 96 hour LC_{50} = 56.2 mg/L LC_0 = 31.6 mg/L;	Kanne, 1991 (as cited in EC, 2000; EU, 2008)	Analytical monitoring was performed; study was conducted according to GLP. The test

Tris (2-chloro-1-methylethyl) phosphate CASRN 13674-84-5			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	LC_{100} = 100 mg/L (static test conditions) (Experimental)		substance was 97.9% pure including all isomers.
	Lepomis macrochirus 96 hour LC_{50} = 84 mg/L; NOEC = 9.8 mg/L (static test conditions) (Experimental)	Meeks, 1985b (as cited in EC, 2000; OECD-SIDS, 2000; EU, 2008)	LC_{50} based on linear regression from 120 hours exposure and actual test concentrations. Differences in nominal and actual test concentrations were attributed to limited water solubility of the test substance. Analytical monitoring was performed and study was conducted according guideline (OECD 203) and GLP.
	Wild-type Zebrafish embryos (20 per replicate) exposed to TCPP under static conditions at 0.05 to 50 µM until 96 hours post-fertilization (24 hours post-hatch). No effects on mortality, gross developmental malformations, delayed hatching, or obvious signs of impaired locomotion NOEC = 50 µM (Experimental)	McGee et al., 2012	Adequate details were provided; purity of the test substance was only 96%.
	Freshwater Fish 96-hour LC_{50} = 13.3 mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	Estimate for the Esters class was provided for comparative purposes. See Section 5.5.1.

Tris (2-chloro-1-methylethyl) phosphate CASRN 13674-84-5			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
Daphnid LC_{50}	*Daphnia magna* EC_{50} = 131 (65-335) mg/L 48-hour NOEC = 33.5 mg/L (Experimental)	Meeks, 1985a (as cited in EC, 2000; OECD-SIDS, 2000; EU, 2008)	Study was conducted according to guideline (OECD 202) and GLP; analytical monitoring was performed. The 48 hour EC_{50} is based on actual test concentrations. Differences in nominal and actual concentrations were attributed to limited water solubility of the test substance.
	Daphnia magna 48-hour EC_{50} = 63 mg/L (Experimental)	Griebenow, 1998 (as cited in EC, 2000; EU, 2008)	Not a guideline study; study not conducted according to GLP.
	Daphnia 48-hour LC_{50} = 25.1mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	Estimate for the Esters class was provided for comparative purposes. See Section 5.5.1.
Green Algae EC_{50}	*Selenastrum capricornutum* 96 hour EC_{50} (biomass) = 47 (95% CI: 41-50) mg/L EC_{50} (growth rate) = 73 (95% CI: 57-97) mg/L NOEC = 6 mg/L LOEC = 18 mg/L (Experimental)	Kroon and van Ginkel, 1992 (as cited in EC, 2000; OECD-SIDS, 2000; EU, 2008)	Guideline (OECD 201) and GLP-compliant. Value appears to be based on nominal test concentrations.
	Scenedesmus subspicatus 72 hour EC_{50} (biomass) = 45 mg/L (Experimental)	Griebenow, 1998 (as cited in EC, 2000; EU, 2008)	Study details reported in a secondary source; not a guideline study and not conducted according to GLP. No additional data were available.
	Pseudokirchneriella subcapitata 72-hour EC_{50} (growth rate) = 82 mg/L;	Dejardins, 2004 (as cited in EC, 2000; EU, 2008)	Guideline study (OECD 201) and GLP-compliant. Study details

Tris (2-chloro-1-methylethyl) phosphate CASRN 13674-84-5			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	NOEC = 13 mg/L (Experimental)		reported in a secondary source; primary source not specified (identified as a review article).
	Green algae 96-hour EC_{50} = 9.3 mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	Estimate for the Esters class was provided for comparative purposes. See Section 5.5.1.
Chronic Aquatic Toxicity	**MODERATE: Based on experimental aquatic toxicity values for algae and estimated ChV values in fish, daphnia, and algae. An estimated chronic aquatic toxicity value derived using an acute-to-chronic ratio (ACR) for the phosphate esters class and was applied to the available experimental acute data for this chemical and indicated a Moderate hazard. An experimental NOEC for *Daphnia magna* indicated a Low hazard designation for mortality and reproduction, while estimated ChV values (Esters class) range from Low to High hazard range. There were no experimental chronic aquatic toxicity data located for fish. There is potential concern based on estimates and the uncertainty due to the lack of experimental data; therefore a Moderate hazard designation was assigned.**		
Fish ChV	Freshwater fish ChV = 1.25 mg/L (Estimated)	Professional judgment	An ACR of 24 was derived for the phosphate ester class based on experimental data for Tris (p-t-butylphenyl) phosphate (TBPP). The acute-to-chronic ratio was applied to available experimental acute fish data for Tris (2-chloro-1-methylethyl) phosphate (ChV = 30 mg/L (96-hr fish LC_{50}) /24= 1.25 mg/L)
	Freshwater fish ChV = 0.83 mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	Estimate for the Esters class was provided for comparative purposes. See Section 5.5.1.

Tris (2-chloro-1-methylethyl) phosphate CASRN 13674-84-5			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
Daphnid ChV	*Daphnia magna* (4 replicates of 10 daphnia per concentration) were exposed to 10, 18, 32, 56 and 100 mg/L of the test material for a period of 21 days. All animals at 56 mg/L died within 12 days. 21-day NOEC (mortality and reproduction) = 32 mg/L (Experimental)	Sewell et al., 1995 (as cited in OECD-SIDS, 2000; EU, 2008)	Adequate; guideline (OECD 211) and GLP study. Data are from a secondary source; primary source was not specified (from a review article).
	Daphnia magna ChV > 10 mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	Estimate for the Esters class was provided for comparative purposes. See Section 5.5.1.
Green Algae ChV	*Selenastrum capricornutum* 96 hour NOEC = 6 mg/L LOEC = 18 mg/L (Experimental)	Kroon and van Ginkel, 1992 (as cited in EC, 2000; OECD-SIDS, 2000; EU, 2008)	Guideline (OECD 201) and GLP-compliant. Value appears to be based on nominal test concentrations.
	Pseudokirchneriella subcapitata 72-hour NOEC = 13 mg/L (Experimental)	Dejardins, 2004 (as cited in EC, 2000; EU, 2008)	Guideline study (OECD 201) and GLP-compliant. Study details reported in a secondary source; primary source not specified (identified as a review article).
	Green algae ChV = 3.18 mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	Estimate for the Esters class was provided for comparative purposes. See Section 5.5.1.

Tris (2-chloro-1-methylethyl) phosphate CASRN 13674-84-5				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
ENVIRONMENTAL FATE				
Transport		**Level III fugacity models incorporating available physical and chemical property data indicate that at steady state, TCPP is expected to be found primarily in soil and to a lesser extent, water. TCPP is expected to have moderate mobility in the soil, based on its measured Koc. TCPP will not volatilize from moist soil and water surfaces based on its Henry`s Law constant. Volatilization from dry surfaces is not expected based on its vapor pressure. TCPP will exist almost entirely in the vapor phase in the atmosphere.**		
	Henry's Law Constant (atm-m^3/mole)	$6x10^{-8}$ (Measured)	van der Veen and de Boer, 2012	Reported in a peer reviewed source.
	Sediment/Soil Adsorption/Desorption - K_{oc}	162 (Measured)	van der Veen and de Boer, 2012	Reported in a peer reviewed source.
	Level III Fugacity Model	Air = 0.1% Water = 12.4% Soil = 86.1% Sediment = 1.4% (Estimated)	EPI v4.11	
Persistence		**HIGH: Based on measured persistence data. TCPP had 14% biodegradation after 28 days according to OECD 301E, although in the modified MITI test, OECD 301C, 0% biodegradation was found after 28 days using an activated sludge inoculum. TCPP achieved 21% degradation after 28 days in an inherent modified MITI test, OECD 302C. These data suggest a half-life greater than 60 days. TCPP is not expected to be susceptible to direct photolysis by sunlight. The atmospheric half-life of vapor-phase TCPP is estimated to be 2.9 hours, however it is not expected to partition greatly to the atmosphere.**		
Water	**Aerobic Biodegradation**	Passes Ready Test: No Test method: OECD TG 301E: Modified OECD Screening Test Reported as 14% after 28 days. 97.9% pure (Measured)	OECD-SIDS, 2000	OECD Guideline study.
		Passes Ready Test: No Test method: OECD TG 301C: Modified MITI Test (I) Reported as 0% after 28 days.	OECD-SIDS, 2000	OECD Guideline study.

Tris (2-chloro-1-methylethyl) phosphate CASRN 13674-84-5				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		(Measured)		
		Study results: 21%/28d Test method: 302C: Inherent - Modified MITI Test (II) (Measured)	WHO, 1998	Reported in a peer reviewed source.
	Volatilization Half-life for Model River	>1 year (Estimated)	EPI v4.11	
	Volatilization Half-life for Model Lake	>1 year (Estimated)	EPI v4.11	
Soil	**Aerobic Biodegradation**	Study results: 0%/80d Test method: Field Test No decrease in concentration after 80 days using a landfill leachate inoculum under aerobic conditions. (Measured)	ATSDR, 2012	Reported in peer reviewed secondary source.
	Anaerobic Biodegradation			No data located; chlorinated alkyl phosphates are outside the domain of the available estimation methods.
	Soil Biodegradation with Product Identification			No data located.
	Sediment/Water Biodegradation			No data located.
Air	**Atmospheric Half-life**	0.239 days Based on a 12 hour day (Estimated)	EPI v4.11	
Reactivity	**Photolysis**	Not a significant fate process. (Estimated)	Professional judgment	The substance does not contain functional groups that would be expected to absorb light at environmentally significant wavelengths.
	Hydrolysis	Hydrolyzes slowly under alkaline or	WHO, 1998	Reported in peer reviewed

Tris (2-chloro-1-methylethyl) phosphate CASRN 13674-84-5				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		acidic conditions. (Measured)		secondary source.
		50%/11y at pH 7 Additional half-life estimates: 11 years at pH 5; 11 years at pH 6; 11 years at pH 8; 10 years at pH 9; 5 years at pH 10 (Estimated)	EPI v4.11	
Environmental Half-life		120 days (Estimated)	PBT Profiler	Half-life estimated for the predominant compartment (soil), as determined by EPI methodology.
Bioaccumulation		**LOW: Multiple experimental BCF values are below 100, the Low bioaccumulation designation criteria. Toxicokinetic studies indicate that TCPP and metabolites are rapidly formed and eliminated, consistent with the estimated BAF. Biomonitoring studies report detection of this compound in human milk samples and herring gull eggs, demonstrating that these materials are likely bioavailable and could be observed in a biological matrix. However, the rate of metabolism and elimination may be successfully competing with that of uptake, which is also consistent with the experimental BCF results. The biomonitoring studies are not inconsistent with a Low designation**		
	Fish BCF	4.6 Reported as < 1.9-4.6 in carp (Measured)	EC, 2000	Consistent with other reported measured values.
		2.8 Reported as ~0.8-2.8 in carp (Measured)	EC, 2000	Consistent with other reported measured values.
		8.51 (Measured)	van der Veen and de Boer, 2012	Reported in a peer reviewed source.
	Other BCF	Root concentration factors: <1 for barley, carrots Leaf concentration factors: 26 for barley; 3.9 for meadow fescue and 42 for carrot napoli	Eggen et al., 2012, 2013; Trapp and Eggen, 2013	Nonguideline study indicating that plant uptake and translocation is possible for this compound.

Tris (2-chloro-1-methylethyl) phosphate CASRN 13674-84-5				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		Seed concentration factors: <0.01 for barley and rape (Measured)		
	BAF	12.8 (Estimated)	EPI v4.11	
	Metabolism in Fish			No data located.
ENVIRONMENTAL MONITORING AND BIOMONITORING				
Environmental Monitoring		TCPP has been detected in drinking water, groundwater, surface water (coastal and marine); rain and snow samples; sediment, household dust, indoor air, ambient air and airborne particles over the oceans near the polar region (Staaf and Ostman, 2005; Regnery and Puttmann, 2009; Saito et al., 2009; Takigami et al., 2009; Regnery et al., 2011; Bollmann et al., 2012; Cao et al., 2012; Moller et al., 2012; Rodil et al., 2012; Salamova et al., 2014).		
Ecological Biomonitoring		TCPP was also detected in herring gull eggs collected at Lake Huron (Chen et al., 2012).		
Human Biomonitoring		TCPP has been detected in human pooled milk collected from Swedish women after delivery of their first babies in 1997-2006 at 22-82 ng/g lipid. TCPP was not included in the NHANES biomonitoring report (CDC, 2009; HSDB, 2013).		

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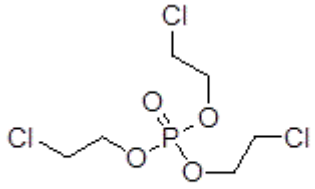
Tris (2-chloroethyl) phosphate (TCEP)

Screening Level Toxicology Hazard Summary

This table contains hazard information for each chemical; evaluation of risk considers both hazard and exposure. Variations in end-of-life processes or degradation and combustion by-products are discussed in the report but not addressed directly in the hazard profiles. The caveats listed below must be taken into account when interpreting the information in the table.

VL = Very Low hazard L = Low hazard M = Moderate hazard H = High hazard VH = Very High hazard – Endpoints in colored text (VL, L, M, H, and VH) were assigned based on empirical data. Endpoints in black italics *(VL, L, M, H,* and *VH*) were assigned using values from estimation software and professional judgment [(Quantitative) Structure Activity Relationships "(Q)SAR"].

Chemical	CASRN	Human Health Effects											Aquatic Toxicity		Environmental Fate	
		Acute Toxicity	Carcinogenicity	Genotoxicity	Reproductive	Developmental	Neurological	Repeated Dose	Skin Sensitization	Respiratory Sensitization	Eye Irritation	Dermal Irritation	Acute	Chronic	Persistence	Bioaccumulation
Tris (2-chloroethyl) phosphate (TCEP)	115-96-8	H	H	M	M	H	M	M	L		L	L	H	*H*	M	L



CASRN: 115-96-8

MW: 285.49

MF: $C_6H_{12}Cl_3O_4P$

Physical Forms: Liquid
Neat: Liquid

Use: Flame retardant

SMILES: O=P(OCCCl)(OCCCl)OCCCl

Synonyms: Ethanol, 2-chloro-, phosphate (3:1); 2-chloroethanol phosphate; Phosphoric acid, tris(2-chloroethyl)ester; Tri(2-chloroethyl) phosphate Tri(2-chloroethyl) phosphoric acid ethyl ester; Tri-beta-chloroethyl phosphate; Trichloroethyl phosphate; Tri(2-chloroethyl) orthophosphate; Tri(2-chloroethyl)ester phosphoric acid; Tris-beta-chloroethyl phosphate; Tris(2-chloroethyl) phosphate; Tris(chloroethyl) phosphate; Tris(monochloroethyl) phosphate; TCEP

Trade names: 3CF; Celanese Celluflex CEF; Celluflex CEF; CLP; Disflamoll TCA; AI3-15023; Amgard TCEP; Antiblaze TCEP; Celanese Celluflex CEF; Disflamoll TCA; Fyrol CEF; Fyrol CF; Genomoll P; Hostaflam UP810; Levagard EP; Niax 3CF; Niax Flame retardant 3CF; Nuogard TCEP; Tolgard TCEP; Triclofos

Chemical Considerations: This phosphate ester is a discrete organic chemical with a MW below 1,000. EPI v4.11 was used to estimate some environmental fate values due to an absence of experimental data. Measured values from experimental studies were incorporated into the EPI estimations. This compound may be manufactured by epoxide opening with either ethylene oxide or ethylene chlorohydrin in the presence of phosphorus oxychloride. 1,2 dichloroethane is an impurity in some commercial products (IARC, 1990; CELLTECH, 2009; ATSDR, 2012).

Polymeric: No **Oligomeric:** Not applicable	
Metabolites, Degradates and Transformation Products: Thermal degradation: Carbon monoxide, hydrogen chloride, 2-chloroethane and dichloroethane, carbon dioxide, benzene, toluene, chloromethane, chloroethane, 1,2-dichloroethane, chloropropenes, 1,2,3-trichloropropane, 2-chloroethanol, acetaldehyde, chloroacetaldehyde, chloroacetone, bis(2-chloroethyl) ether, bis(2-chloroethoxy)methane; methyl formate, methyl acetate, 2-chloroethyl acetate, phosphate and vinyl chloride. Metabolites: 2-chloroethanol and bis(2-chloroethyl)hydrogen phosphate and other unidentified metabolites by human and rat liver microsomes, liver, blood and plasma samples. Other metabolites reported include bis(2-chloroethyl) carboxymethyl phosphate, bis(2-chloroethyl) hydrogen phosphate and bis(2-chloroethyl 2-hydroxyethyl) phosphate glucuronide. Chloride ion and 2-chloroethanol degradation products from bacteria (Chapman et al., 1991; IPCS, 1998; NICNAS, 2001; Takahashi et al., 2008; EU, 2009; Van den Eade et al., 2013).	
Analog: None **Endpoint(s) using analog values:** Not applicable	**Analog Structure:** Not applicable
Structural Alerts: Organophosphates, neurotoxicity; aliphatic substituted alkyl halides, genetic toxicity; chlorinated hydrocarbons, liver toxicity; chlorinated hydrocarbons, reproductive toxicity. This chemical appears on the List of Chemicals Known to the State to Cause Cancer for the State of California: California Proposition 65 cancer, List of Chemicals of High Concern to Children for Washington State, List of Substances of Very High Concern for Authorisation published in accordance with Article 59(10) of the REACH Regulation (ECHA, 2009; State of Washington, 2011; EPA, 2012; California EPA, 2013).	
Risk Phrases: R60: May impair fertility; R22: Harmful if swallowed; R40: Limited evidence of a carcinogenic effect; R51/53: Toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment (ESIS, 2012).	
Hazard and Risk Assessments: Priority Existing Chemical Assessment report for Triphosphates by NICNAS in 2001; EU Risk Assessment Report in 2009; IARC Summaries & Evaluations report in 1990; part of the Toxicological profile for Phosphate Ester Flame Retardants by ATSDR (IARC, 1990; NICNAS, 2001; EU, 2009; ATSDR, 2012).	

Tris (2-chloroethyl) phosphate CASRN 115-96-8			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
PHYSICAL/CHEMICAL PROPERTIES			
Melting Point (°C)	-58 Measured by method DIN 51583, ASTM D 97-66 (Measured)	OECD-SIDS, 2006	Similar values are consistently reported in secondary sources.
	-55 (Measured)	IARC, 1990; EC, 2000; ATSDR, 2012	Similar values are consistently reported in secondary sources.
	-60 Reported as about -60°C (Measured)	EC, 2000	Similar values are consistently reported in secondary sources.
	<-70 pour point (Measured)	NICNAS, 2001; OECD-SIDS, 2006; EU, 2009	Value reported in a secondary source. Assumed to be measured.
Boiling Point (°C)	202 at 10 mmHg Measured by ASTM D1160 method at a reduced pressure (Measured)	EC, 2000	Adequate value measured by a standard test method.
	320 Decomposes 99.5% purity (Measured)	EU, 2009	Limited details available from secondary source.
	145 at 0 mmHg Value reported as 145°C at 0.66 hPa (Measured)	EC, 2000; NICNAS, 2001	Similar values are consistently reported in secondary sources.
	330 (Measured)	IARC, 1990; Lide, 2008; ATSDR, 2012	Value reported in a secondary source.
	Decomposes Rapid decomposition occurs above 220°C. Thermal decomposition products are carbon monoxide, hydrogen chloride, 2-chloroethane and dichloroethane. (Measured)	IPCS, 1998	Supporting information reported in a secondary source with limited details.

Tris (2-chloroethyl) phosphate CASRN 115-96-8			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
Vapor Pressure (mm Hg)	$1.6x10^{-5}$ at 25°C Values at higher temperatures measured by dynamic method; measured values reported as: 0.43 hPa at 136.9°C; 0.99 hPa at 143.5°C; 2.03 hPa at 158.6°C; 5.00 hPa at 174.1°C; 15.03 hPa at 196.2°C. (Extrapolated)	EU, 2009	The Clausius-Clapeyron equation was used to calculate the VP at 20°C (reported as such in source). Extrapolation to 25°C yields the value of $1.6x10^{-5}$ mmHg.
	0.062 at 25°C Measured with a conventional isoteniscope using a nitrogen atmosphere (Measured)	ATSDR, 2012	Value calculated from reported equation coefficients determined by experimental measurements and equation fitting. The calculated value is inconsistent with other available vapor pressure data. It is possible that the units of the calculation apply to meters Hg rather than mm Hg which would change the value to 0.000062 mm Hg at 25°C.
	$8.55x10^{-6}$ at 20°C Reported as 0.00114 Pa at 20°C (Extrapolated)	OECD-SIDS, 2006; EU, 2009	Value was extrapolated from a measured value of 43 Pa at 137°C.
	<0.075 at 20°C Reported as <0.1 hPa at 20°C. ASTM D232 method (Extrapolated)	EC, 2000	Value was approximated from data at higher temperatures
Water Solubility (mg/L)	7,000 (Measured)	Muir, 1984 (as cited in ATSDR, 2012)	Value reported in a secondary source.
	7,943 (Measured)	EC, 2000	Value reported in a secondary source with limited study details.

Tris (2-chloroethyl) phosphate CASRN 115-96-8			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	temperature not reported		
	7,820 (Measured) Reported as 7820 mg/L at 20°C, pH 4.7 - 6.1 according to Directive 84/449/EEC, A.6, Water Solubility method, 1984 using GLP	EC, 2000; EU, 2009	Adequate guideline study.
	5,000 (Measured) Reported as ca. 5 g/L at 20°C, 5.5 -7 pH at 10 vol% and 20°C by Society of Automotive Engineers (SAE) method	EC, 2000	Adequate study
Log K_{ow}	1.78 Reported as 1.78 at 20°C; Directive 84/449/EEC., A.8, Partition coefficient, 1984 Method, GLP (Measured)	EC, 2000; EU, 2009	Similar to the log Kow of 1.47 reported for a shake-flask method, but this is a more recent measurement and both were measured by the same source (Akzo Nobel Chemicals). Also similar to the KOWWIN program estimate of 1.63.
	1.47 OECD Guide-line 107, Partition Coefficient (n-octanol/water), Flask-shaking Method, 1981 (Measured)	EC, 2000	Adequate guideline study.
	1.7 (Measured)	IPCS, 1998; NICNAS, 2001	Reported in a secondary source with limited study details.
	1.6 (Estimated)	EPI v4.11	Estimated by the EPI Suite KOWWIN program (v1.68)
	1.44 (Measured)	MITI, 1992a (as cited in ATSDR, 2012)	Reported as measured in their laboratory, but measurement methods, temperatures and pH

Tris (2-chloroethyl) phosphate CASRN 115-96-8			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
			values are not reported.
Flammability (Flash Point)	Flash point: 216°C (Measured)	ATSDR, 2012	Limited study details reported in a secondary source.
	Flash point: 252°C Open cup (Measured)	EC, 2000	Non-GLP, standardized study.
	Flash point: 225°C Closed cup; DIN 51758 method (Measured)	EC, 2000	Adequate standardized method.
	Flash Point: 200°C ASTM D93 method using GLP; sample appears to catch fire at approx. 200°C, but does not show a distinct flash point as defined by the test method (Measured)	EC, 2000; EU, 2009	Adequate standardized method reported in a secondary source.
Explosivity			No data located.
Pyrolysis	Decomposition products: 1,2 dichloroethane and vinyl chloride 0.1 mol TCEP was decomposed in 20-mL flask at 250-260°C at 3 mmHg, the decomposition products were separated by gas-liquid chromatography, and analyzed with NMR and MS (Measured)	Okamoto et al., 1974	Supporting information provided.
pH	Not applicable (Estimated)	Professional judgment	Does not contain functional groups that are expected to ionize under environmental conditions.
pK_a	Not applicable (Estimated)	Professional judgment	Does not contain functional groups that are expected to ionize under environmental conditions.

Tris (2-chloroethyl) phosphate CASRN 115-96-8				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
HUMAN HEALTH EFFECTS				
Toxicokinetics		**TCEP is well absorbed and distributed following oral administration in rats and mice. TCEP and metabolites are rapidly eliminated principally in the urine. Urinary metabolites include bis(2-chloroethyl) carboxymethylphosphate, bis(2-chloroethyl)hydrogen phosphate and bis(2-chloroethyl)-2-hydroxyethyl-phosphate glucuronide. TCEP is metabolized by hepatic microsomal fraction in male rats and in humans, but is not metabolized by plasma or whole blood. In an incubation experiment, bis(2-chloroethyl) phosphate (BCEP) and hydroxyethyl 2-chloroethyl hydrogen phosphate were the only detected metabolites. No phase II metabolites were detected.**		
Dermal Absorption *in vitro*				No data located.
Absorption, Distribution, Metabolism & Excretion	**Oral, Dermal or Inhaled**	TCEP is metabolized by hepatic microsomal fraction in male rats but not in females. Liver slices and blood plasma indicated metabolism in both sexes. Liver slices and microsomes in humans metabolized TCEP, but plasma and whole blood did not.	Chapman et al., 1991 (as cited in WHO, 1998)	Limited study details reported in a secondary source.
		Wistar rats orally dosed with 50 µmol/kg ^{14}C-labeled TCEP. During the first 6 hours following administration, TCEP was distributed and concentrated by several tissues; primarily the liver and kidney. Most of the material was excreted within 24 hours and by 168 hours, <1% remained in tissues. Excretion was 96% in urine, 6% in feces and 2% in expired air. Urinary metabolites included: bis(2-chloroethyl) carboxymethyl phosphate, bis(2-chloroethyl) hydrogen phosphate and bis(2-chloroethyl) 2-hydroxyethyl phosphate glucuronide	Minegishi et al., 1988 (as cited in WHO, 1998)	Sufficient study details reported.
		Male and female Fischer-344 rats gavaged with 0, 175, 350 or 700	Herr et al., 1991 (as cited in WHO, 1998)	Sufficient study details reported.

Tris (2-chloroethyl) phosphate CASRN 115-96-8				
PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
		mg/kg ^{14}C-labeled TCEP; plasma concentrations and metabolites peaked by 30 minutes in rats given 175 mg/kw. No concentration differences of TCEP in hippocampus and other brain tissues.		
		Male B6C3F1 mice orally dosed with 175 mg ^{14}C-labeled TCEP/kg; >70% excretion in urine within 8 hours. Urinary metabolites: bis(2-chloroethyl) carboxymethyl phosphate, bis(2-chloroethyl) hydrogen phosphate and bis(2-chloroethyl) 2-hydroxyethyl phosphate glucuronide	Burka et al., 1991 (as cited in WHO, 1998)	Sufficient study details reported.
		TCEP is readily absorbed from the gastrointestinal tract and excreted within 72 hours following oral administration	EC, 2000	Limited study details reported in a secondary source.
		Absorption study in rats dosed with ^{14}C TCEP at 100-140 mg/kg via oral gavage or in the diet. 80% of the administered dose (gavage and diet) was excreted in urine within 5 days	EC, 2000	Limited study details reported in a secondary source.

Tris (2-chloroethyl) phosphate CASRN 115-96-8				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Other	Incubation experiments using 1.0 mg/mL HLM or S9 proteins, 50 µM TBOEP or TCEP, or TCPP, or 20 µM TPHP or TDCPP and NADPH regenerating solution in 1 mM total volume were conducted for 1 hour. There was a 7% and 13% clearance of the compound in the HLM and S9 incubations, respectively. Bis(2-chloroethyl) phosphate (BCEP) and hydroxyethyl 2-chloroethyl hydrogen phosphate were the only detected metabolites. No phase II metabolites were detected. BCEP was the major metabolite detected.	Van den Eade et al., 2013	
Acute Mammalian Toxicity		**HIGH: Based on an oral LD_{50} of 46.4 mg/kg in rats. TCEP exhibits low toxicity via the inhalation and dermal routes of exposure in rats and rabbits, respectively.**		
Acute Lethality	**Oral**	Rat oral LD_{50} = 46.4 – 1,000 mg/kg	ATSDR, 2012	Limited study details reported in a secondary source.
		Rat oral LD_{50} = 430 - 794 mg/kg	EC, 2000	Limited study details reported in a secondary source.
		Rat oral LD_{50} = 1150 mg/kg	Kynoch and Denton, 1990 (as cited in WHO, 1998; EC, 2000)	Limited study details reported in a secondary source; study conducted in accordance to GLP and Directive 84/449/EEC, B.1.
		Rat oral LD_{50} = 1,230 – 1,410 mg/kg	Smyth et al., 1951; Ulsamer et al., 1980 (as cited in WHO, 1998; EC, 2000; ATSDR, 2012)	Limited study details reported in a secondary source.
		Mouse oral LD_{50} = 1,500 mg/kg	EC, 2000	Limited study details reported in a secondary source.
		Rat oral LD_{50} = 3,600 mg/kg (3.6 g/kg)	Gardner, 1987 (as cited in WHO, 1998)	Limited study details reported in a secondary source.

Tris (2-chloroethyl) phosphate CASRN 115-96-8				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Dermal	Rabbit dermal LD_{50} = 2150 - ≥ 5,000 mg/kg	EC, 2000; OECD-SIDS, 2006; ATSDR, 2012	Limited study details reported in a secondary source.
	Inhalation	Rat 4-hour inhalation LC_{50} > 5 mg/L (5,000 mg/m^3)	EC, 2000; ATSDR, 2012	Limited study details reported in a secondary source.
		Rat 1-hour inhalation LC_{50} > 25.7 mg/L (nominal)	OECD-SIDS, 2006	Limited study details reported in a secondary source.
Carcinogenicity		**HIGH: TCEP was carcinogenic in rats and mice. Renal adenomas/carcinomas were present in rats and mice following 103 weeks of oral exposure. In addition, renal adenomas/carcinomas and forestomach and hemapoietic tumors were evident in mice following 18 months of dietary exposure. IARC has classified TCEP as a Category 3 carcinogen: "Not classifiable as to its carcinogenicity" based on inadequate evidence in experimental animals and no available human studies". However, NTP concludes that the renal adenomas observed in rats are clear evidence of carcinogenic activity. In addition, this chemical appears on the List of Chemicals Known to the State to Cause Cancer for the State of California.**		
	OncoLogic Results			No data located.
	Carcinogenicity (Rat and Mouse)	In a 103-week oral study, rats were gavaged with TCEP at 0, 44 or 88 mg/kg-day, 5 days/week. Reduced survival at the high dose. Renal tubular adenomas (occurring in ~50% of high-dose males, 10% of high-dose females and 10% of low-dose males); marked increase in the incidence of renal tubule cell hyperplasia in high dose males and females. Although adenomas are benign tumors, NTP concludes that renal adenomas represent an early stage in the development of carcinoma and is clear evidence of carcinogenic activity.	NTP, 1991 (as cited in EC, 2000; ATSDR, 2012)	Adequate study details reported in a primary source.
		In a 103-week oral study, mice were gavaged with TCEP at 0, 175, or 350 mg/kg-day 5 days/week. No significant differences in survival or body weight	NTP, 1991 (as cited in ATSDR, 2012)	Adequate study details reported in a primary source.

Tris (2-chloroethyl) phosphate CASRN 115-96-8				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		gain in comparison with controls. Renal tubular karyomegaly in 80% of high animals (a marker of nephropathy); Marginal increase in harderian gland neoplasms (primary adenomas, high dose females). NTP concludes that there is equivocal evidence of carcinogenic activity based on renal tubule cell neoplasms in male mice and marginally increased harderian gland adenomas in female mice.		
		In an 18-month dietary study, mice (Slc:ddY) were fed TCEP at 0, 0.012, 0.06, 0.3, and 1.5% daily (~0, 11, 53, 267, and 1333 mg/kg-day) Increased mortality and reduced weight gain in comparison with controls at the high dose. Significantly increased incidence of renal cell adenomas and carcinomas (high dose males); increased incidence of benign liver adenomas (males, 0.3% and 1.5%); increased incidence of forestomach and hematopoietic tumors (females).	Takada et al., 1989 (as cited in EC, 2000; ATSDR, 2012)	Limited study details reported in a secondary source (primary source is in Japanese with English abstract); doses are estimated assuming a mean body weight of 0.045 kg and daily food consumption of 0.004 kg/day (ATSDR 2012).
		Female (Sl/ddy) mice were treated dermally with ethanol solutions containing 5% or 50% TCEP for 79 weeks. No significant increase in tumors	Takada et al., 1991 (as cited in WHO, 1998)	Limited details reported in a secondary source.
	Combined Chronic Toxicity/Carcinogenicity			No data located.

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	Other	This chemical appears on the List of Chemicals Known to the State to Cause Cancer for the State of California: California Proposition 65	California EPA, 2013	Added to the California Proposition 65 list for cancer on April 1, 1992.
		IARC has classified TCEP as a Category 3 carcinogen: "not classifiable as to its carcinogenicity" based on inadequate evidence in experimental animals and no available human studies.	IARC, 1990 (as cited in NICNAS, 2001)	The NTP (1991) oral bioassay in rats and mice was not available to IARC when this agency classified TCEP.
Genotoxicity		**MODERATE: Based on weight of evidence from multiple studies. Results were positive in *in vitro* gene mutation and chromosomal aberrations tests. TCEP was cytotoxic in a neutral read uptake assay in Chinese hamster V79 cells, produced sister chromatid exchanges in Chinese hamster V79 cells and mouse lymphoma cells, and was positive in a cellular transformation study in mouse BALB/3t3 cells. TCEP was not mutagenic in bacteria or yeast, and did not produce chromosomal aberrations in any available *in vivo* studies. In addition, TCEP was negative in an Unscheduled DNA synthesis study in human WI-38 cells. There is potential for genetic toxicity based on a structural alert for aliphatic substituted alkyl halides.**		
	Gene Mutation *in vitro*	Positive, cytotoxicity in a neutral red uptake assay in Chinese hamster V79 cells. Negative in the absence of metabolic activation	Follmann and Wober, 2006 (as cited in ATSDR, 2012)	Sufficient study details reported in a primary source.
		Negative, *Salmonella typhimurium* strains TA98, TA100, TA1535 and TA1537, TA1538 with and without metabolic activation.	EC, 2000	Limited study details reported in a secondary source.
		Negative, *Saccharomyces cerevisiae* with and without metabolic activation	EC, 2000	Limited study details reported in a secondary source.
		Negative, mammalian cell HGPRT gene mutation assay in Chinese hamster V79 lung cells with and without metabolic activation	EC, 2000	Limited study details reported in a secondary source.
		Negative, mammalian cell gene mutation assay in L5178Y mouse	EC, 2000	Limited study details reported in a secondary source; Study was

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		lymphoma cells with and without metabolic activation		conducted in accordance with GLP and OECD Guideline 476.
		Negative, *Salmonella typhimurium* strains TA98, TA100, TA1535, TA1537 or TA1538 with and without metabolic activation	EC, 2000	Limited study details reported in a secondary source; Study was conducted in accordance with OECD Guideline 471
		Negative, *Salmonella typhimurium* strains TA98, TA100 with and without metabolic activation	Kubo et al., 2002	Sufficient study details reported in a primary source.
		Negative, *Salmonella typhimurium* strains TA97,TA98, TA100, TA104, TA1535, TA1537, and TA1538 with and without metabolic activation	Follmann and Wober, 2006 (as cited in ATSDR, 2012)	Sufficient study details reported in a primary source.
		Negative, *Salmonella typhimurium* strains TA100, TA1535, TA1537 or TA98 with and without metabolic activation	NTP, 1991	Sufficient study details reported.
	Gene Mutation *in vivo*			No data located.
	Chromosomal Aberrations *in vitro*	Positive, sister chromatid exchange assay in hamster V79 lung cells with and without metabolic activation. TCEP induced SCE's but no clear dose response was noted.	EC, 2000	Limited study details reported in a secondary source.
		Positive, sister chromatid exchange assay in L5178Y mouse lymphoma cells with metabolic activation. No increase in SCE's without metabolic activation.	EC, 2000	Study was conducted in accordance with GLP and OECD Guideline 479.
		Negative, chromosomal aberrations in CHO cells with and without metabolic activation.	Galloway et al., 1987 (as cited in NTP, 1991; EC, 2000)	Study was conducted in accordance with OECD Guideline 473.
		Equivocal, sister chromatid exchange assay in Chinese hamster (CHO) cells	Galloway et al., 1987 (as cited in NTP, 1991; EC, 2000)	Sufficient study details reported in a primary source.

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		with metabolic activation		
	Chromosomal Aberrations *in vivo*	Negative, mammalian erythrocyte micronucleus assay in mice orally gavaged with 1,000 mg/kg TCEP; cell collection for 24, 48 or 72 hours after dosing.	EC, 2000	Limited study details reported in a secondary source; study conducted according to OECD Guideline 474.
		Negative, chromosomal aberrations in rats orally gavaged with TCEP at doses of 0.062, 0.021, or 0.0062 ml/kg.	EC, 2000	Limited study details reported in a secondary source; study conducted according to GLP and OECD Guideline 475.
		Negative, mammalian erythrocyte micronucleus assay in mice administered 175, 350 or 700 mg/kg TCEP via intraperitoneal injection; cell collection for 24, 48 or 72 hours after dosing.	EC, 2000	Limited study details reported in a secondary source; study conducted according to GLP and OECD Guideline 474.
		Equivocal, chromosomal aberrations, micronucleus assay in male and female Chinese hamsters administered 62.5, 125, or 250 mg/kg TCEP via intraperitoneal injection; cell collection 24 hours later.	Sala et al., 1982 (as cited in ATSDR, 2012)	Sufficient study details reported in a primary source.
	DNA Damage and Repair	Negative, *Drosophila melanogaster*, somatic cell damage	Vogel and Nivard, 1993 (as cited in WHO, 1998)	Sufficient study details reported in a primary source.
		Negative, DNA damage in a comet analysis in Chinese hamster V79 cells with and without metabolic activation	Follmann and Wober, 2006 (as cited in ATSDR, 2012)	Sufficient study details reported in a primary source.
		Negative, DNA-binding *in vitro* (cell type not reported)	EC, 2000	Limited study details reported in a secondary source.
	Other	Positive, Cellular transformation in mouse BALB/3T3 cells. No further details provided.	EC, 2000	Limited study details reported in a secondary source.
		Negative, unscheduled DNA synthesis	EC, 2000	Limited study details reported in a

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		in human WI-38 cells with and without metabolic activation.		secondary source; study was conducted in accordance with GLP and OECD Guideline 482.
		Equivocal, Cellular transformation assay in C3H10T1/2 mouse embryo cells without metabolic activation. No data reported with presence of metabolic activation.	EC, 2000	Limited study details reported in a secondary source.
		There is potential for genotoxicity based on the structural alert for aliphatic substituted alkyl halides. (Estimated)	Professional judgment	Estimated based on a structural alert for aliphatic substituted alkyl halides and professional judgment.

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Reproductive Effects		**MODERATE: Based on the weight of evidence from multiple studies. Although a whole body inhalation study resulted in a NOAEL of 0.5 mg/m^3 and a LOAEL of 1.5 mg/m^3 (0.0012 mg/L) in male rats; this study is generally classified as having low reliability. TCEP was observed to have Moderate concern for reproductive toxicity when administered orally in rats and mice. In addition, there is potential for reproductive toxicity based on a structural alert for chlorinated hydrocarbons.**		
	Reproduction/Developmental Toxicity Screen	Male rats (strain not specified) were exposed to 0, 0.5 or 1.5 mg/m^3 TCEP via whole body inhalation continuously for 4 months. Testicular toxicity (0.5 and 1.5 mg/m^3), decreased sperm counts, decreased sperm motility and abnormal sperm morphology; increased number of spermatogonia with decreased numbers of sperm in the later stages of development was reported; When mated with untreated females: decreased fertility (1.5 mg/m^3); increased pre-and post-implantation loss; decreased litter size NOAEL: 0.5 mg/m^3 LOAEL: 1.5 mg/m^3	Shepelskaya and Dyshinevich, 1981 (as cited in WHO, 1998)	Limited study details reported in a secondary source. Original study in Russian. Study received a reliability score of 4 in the IUCLID data set.
	Combined Repeated Dose with Reproduction/ Developmental Toxicity Screen			No data located.

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Reproduction and Fertility Effects	In a continuous breeding study, Swiss CD-1 mice were orally gavaged with 175, 350 or 700 mg/kg-day TCEP; significant impairment of reproductive capacity and fertility at the mid- and high-dose groups NOAEL: 175 mg/kg-day LOAEL: 350 mg/kg-day (based on impaired reproductive capacity and fertility)	Chapin et al., 1997 (as cited in WHO, 1998; NICNAS, 2001; OECD-SIDS, 2006; ATSDR, 2012)	Sufficient study details reported.
		In a 13-week study, F-344 rats were orally gavaged with TCEP at 0, 22, 88 and 175 mg/kg-day. No adverse effect on cauda weights, absolute and relative epididymal weights, absolute and relative testes weights, sperm concentration, and number of abnormal sperm; reduced sperm motility; no increase in estrous cycle. NOAEL/LOAEL: Not determined	Morrissey et al., 1988 (as cited in WHO, 1998)	WHO 1998; Morrissey et al., 1988 (primary source). NOAEL/LOAEL cannot be determined because primary source provided only qualitative description of results.
		In a 13-week study, B6C3F1 mice were orally gavaged with TCEP at 0, 44, 175 and 700 mg/kg-day. No adverse effect on cauda weights, relative epididymis weight, motility or sperm concentration; decreased absolute epididymis weight and absolute and relative testes weights; increase in the number of sperm with abnormal morphology. No increase in estrous cycle length	Morrissey et al., 1988 (as cited in WHO, 1998)	WHO 1998: Morrissey et al., 1988 (primary source). NOAEL/LOAEL cannot be determined because primary source provided only qualitative description of results.

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		NOAEL/LOAEL: Not determined		
		There is potential for reproductive toxicity based on a structural alert for chlorinated hydrocarbons. (Estimated)	Professional judgment	Estimated based on a structural alert for chlorinated hydrocarbons and professional judgment.
	Other			No data located.
Developmental Effects		**HIGH: Based on the weight of evidence from multiple studies. Although a LOAEL of 175 mg/kg-day was identified based on decreased live male F2 pups in an 18-week continuous breeding study, no NOAEL was established. Effects < 50 mg/kg-day cannot be ruled out. Furthermore, since TCEP decreased cholinesterase activity, and decreased cholinesterase activity in dams can influence fetal neurodevelopment, there is also a concern for potential developmental neurotoxicity.**		
	Reproduction/ Developmental Toxicity Screen	In a continuous breeding study, mice were orally gavaged with 175, 300 or 700 mg/kg-day TCEP. NOAEL: Not established LOAEL: 175 mg/kg-day (based on decreased number of live male F2 pups per litter)	Chapin et al., 1997 (as cited in WHO, 1998; NICNAS, 2001; OECD-SIDS, 2006; ATSDR, 2012)	Adequate study details reported.
	Combined Repeated Dose with Reproduction/ Developmental Toxicity Screen			No data located.

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Prenatal Development	Pregnant rats were orally gavaged with 0, 50, 100 or 200 mg/kg-day TCEP on GDs 7-15. Reduced food consumption at the high dose; clinical signs of toxicity in dams (high dose) included piloerection and general weakness. Seven out of 30 females died during the study. No morphological or behavioral effects were observed in offspring. Development of offspring was normal and there were no abnormalities in functional behavior tests (open field, water maze, rota rod, inclined plane test, pain reflex or Preyer's reflex). Maternal: NOAEL: 100 mg/kg-day LOAEL: 200 mg/kg-day (based on clinical signs of toxicity in dams) Developmental: NOAEL: 200 mg/kg-day (highest dose tested) LOAEL: Not established	Kawashima et al., 1983 (as cited in WHO, 1998; EC, 2000; ATSDR, 2012)	Limited study details reported in a secondary source. Primary source is in Japanese with an English abstract.
		Pregnant mice were orally gavaged with 940 mg/kg-day TCEP (only dose tested) on GDs 6-13. Decreased maternal body weight gain. No adverse effects on viable litters, live born pups per litter, percent survival, birth weight, or pup weight gain. Maternal:	Hardin et al., 1987 (as cited in WHO, 1998; EC, 2000; ATSDR, 2012)	Limited study details reported in a secondary source.

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		NOAEL: not established; LOAEL: 940 mg/kg-day (based on decreased maternal body weight gain); only dose tested Developmental: NOAEL: 940 mg/kg-day (only dose tested); LOAEL: Not established		
	Postnatal Development			No data located.
	Prenatal and Postnatal Development			No data located.
	Developmental Neurotoxicity	There were no data located for the developmental neurotoxicity endpoint. Decreased cholinesterase activity in pregnant lab animals has been shown to have a negative impact on fetal brain development. As a result, there is uncertain potential for developmental neurotoxicity for this substance	Professional judgment	No data located.
	Other			No data located.

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Neurotoxicity		**MODERATE: Based on the weight of evidence from a number of studies. TCEP produced degenerative lesions in the cerebral cortex in female rats gavaged with 88 mg/kg-day (NOAEL = 44 mg/kg-day) in a 103-week study. In addition, necrotic lesions in the hippocampus were observed in female rats following oral administration of 175 mg/kg-day TCEP (NOAEL = 88 mg/kg-day) for 16 weeks. Ataxia and convulsive movements were observed in mice administered TCEP at doses of ≥ 350 mg/kg-day (NOAEL = 175 mg/kg-day) for 16 days. Convulsions were observed in female rats within 60 minutes following single oral gavage of 275 mg TCEP/kg-day. TCEP was attributed to death in dogs following ingestion of car seat cushions found to contain large amounts of the chemical. TCEP produced no evidence of neurotoxicity in white leghorn hens. TCEP promoted differentiation of the cholinergic phenotype only in an *in vitro* neurotoxicity study using undifferentiated and differentiating PC12 cells. There is potential for neurotoxicity based on a structural alert for organophosphates.**		
	Neurotoxicity Screening Battery (Adult)			No data located.
	Other	In a 103-week oral study, rats were gavaged with TCEP at 0, 44 or 88 mg/kg-day, 5 days/week. Degenerative lesions in the cerebral cortex (high dose, females). NOAEL: 44 mg/kg-day; LOAEL: 88 mg/kg-day (based on cerebrum gliosis in female rat)	NTP, 1991; Matthews et al., 1993 (as cited in ATSDR, 2012)	Sufficient study details reported.
		In 16-18 week oral studies, rats were gavaged with TCEP at 0, 22, 44, 88, 175 or 350 mg/kg-day, 5 days/week. In the 14-day study, serum cholinesterase (ChE) was decreased by 82 and 80% in female rats at 175 and 350 mg/kg-day, respectively. Inhibition was minimal in male rats. In the 16-18 week study, ChE decreased by 25 and 41% in female rats at 175 and 350 mg/kg-day, respectively and there was no change in male rats.	Matthews et al., 1990; NTP, 1991 (as cited in EC, 2000; ATSDR, 2012; NICNAS, 2001)	Sufficient study details reported in a primary source.

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PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
		Necrotic lesions in the hippocampus and thalamus (females, 175 mg/kg-day; male and females, 350 mg/kg-day). NOAEL: 88 mg/kg-day LOAEL: 175 mg/kg-day (based on necrotic lesions in hippocampus and thalamus)		
		In a 16-day oral study, mice were gavaged with 0, 175, 350 or 700 mg TCEP kg-day. Ataxia and convulsive movements were observed at ≥ 350 mg/kg-day during the first 3 days of dosing. NOAEL: 175 mg/kg-day LOAEL: 350 mg/kg-day (ataxia and conclusive movements)	NTP, 1991; ATSDR, 2012	Sufficient study details reported.
		Female Fischer-344 rats were gavaged once with 275 mg TCEP/kg. Convulsions within 60-90 minutes; extensive loss of CAI hippocampal pyramidal cells 7 days post-dosing. Impaired acquisition of a reference memory task in a water maze when trained and tested 3 weeks following treatment. NOAEL: Not established LOAEL: 275 mg/kg (based on impaired acquisition of a memory task 3 weeks post exposure); only dose tested	Tilson et al., 1990 (as cited in WHO, 1998; ATSDR, 2012)	Limited study details reported in a secondary source. True NOAEL/LOAEL cannot be determined because only one dose level was tested; it is uncertain if effects occurred at a lower dose.
		Two case reports in dogs:	Lehner et al., 2010	Adequate case studies reported in a

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		In one case, two American pit bulls presented with acute signs of central nervous system excitation (including seizures) in an emergency clinic; one dog died within 15 minutes and necropsy revealed frothy brown fluid in the stomach and edematous lungs. The other dog recovered fully following treatment. In a second case, a German Shepherd and a Rottweiler were found dead after having been left in a car overnight. Necropsy revealed signs of possible kidney damage and congested, dark lungs. Toxicological analysis in all deceased dogs revealed TCEP (> 2 ppm) in stomach contents and was attributed to ingestion of car seat cushions.		primary source; actual ingested doses were not determined.
		White leghorn hens were orally administered TCEP at 420 mg/kg-day for 5 days and were observed for 30 days following treatment. No neurotoxic reactions were evident.	Bullock and Kamienski, 1972 (as cited in WHO, 1998; EC, 2000)	Limited study details reported in a secondary source.
		Single intraperitoneal application of 1.0 mg/kg TCEP to white Leghorn hens. No evidence of delayed neurotoxicity.	EC, 2000	Limited study details reported in a secondary source.
		Single oral administration of 2.5 or 14.2 g/kg (2500 or 14,200 mg/kg) TCEP to white Leghorn hens. No microscopic changes in brain, spinal cord or sciatic nerve were found after the treatment. Plasma cholinesterase activity was inhibited by 87% and brain neuropathy target esterase by 30% (14.2 g/kg). No	Sprague et al., 1981 (as cited in WHO, 1998; EC, 2000)	Sufficient study details reported.

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		evidence of delayed neurotoxicity.		
		In vitro neurotoxicity study using undifferentiated and differentiating PC12 cells. Changes in DNA synthesis, oxidative stress, differentiation into dopaminergic or cholinergic neurophenotypes, cell number, cell growth and neurite growth were assessed. TCEP promoted differentiation of the cholinergic phenotype only. There were no other adverse neurological effects.	Dishaw et al., 2011	Sufficient study details reported in a primary source.
		There is potential for neurotoxicity based on a structural alert for organophosphates. (Estimated)	Professional judgment	Estimated based on a structural alert for organophosphates and professional judgment.

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Repeated Dose Effects		**MODERATE: Based on a LOAEL of 88 mg/kg-day in a 103-week oral study in rats. Effects included renal tubule epithelial hyperplasia and cerebral gliosis. Additional effects in rats following oral exposure to higher doses included slightly reduced serum cholinesterase activity and increased kidney and liver weights (175 and 270 mg/kg-day). Effects in mice following oral exposure included renal tubular karyomegaly and/or cytomegaly (350 and 700 mg/kg-day). No studies were available to assess effects of repeated exposures to TCEP via the inhalation or dermal routes of exposure. In addition, there is potential for liver toxicity based on a structural alert for chlorinated hydrocarbons.**		
		In a 103-week oral study, rats were gavaged with TCEP at 0, 44 or 88 mg/kg-day, 5 days/week. Reduced survival at the high dose. Renal tubule epithelial hyperplasia (high dose, both sexes), degenerative lesions in the cerebral cortex (high dose, females). There were no adverse effects on lymphoreticular tissues. NOAEL: 44 mg/kg-day LOAEL: 88 mg/kg-day (based on renal tubule epithelial hyperplasia in male and female rats and cerebrum gliosis in female rat)	NTP, 1991; Matthews et al., 1993 (as cited in ATSDR, 2012)	Sufficient study details reported.
		In a 103-week oral study, mice were gavaged with TCEP at 0, 175, or 350 mg/kg-day, 5 days/week. No significant differences in survival or body weight gain in comparison with controls. Renal tubular karyomegaly in 80% of high animals (a marker of nephropathy); Marginal increase in harderian gland neoplasms (primary adenomas, high dose females). There were no adverse effects on	NTP, 1991; EC, 2000; ATSDR, 2012	Sufficient study details reported.

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PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
		lymphoreticular tissues. NOAEL: 175 mg/kg-day LOAEL: 350 mg/kg-day (renal tubular karyomegaly)		
		In a 16-day oral study, rats were orally gavaged with 0, 44, 88, 175 or 350 mg/kg-day TCEP in corn oil 5 days/week for a total of 12 doses. No treatment-related deaths, differences in final mean body weight or histopathological lesions. Slightly reduced serum cholinesterase activity (females, 175 and 350 mg/kg-day); Increased absolute and relative kidney weights (males, 175 and 350 mg/kg-day); increased absolute and relative liver weights (females, 350 mg/kg-day) NOAEL: 88 mg/kg-day; LOAEL: 175 mg/kg-day (decreased serum cholinesterase activity, increased absolute and relative kidney weights)	Matthews et al., 1990 (as cited in NTP, 1991)	Sufficient study details reported.
		In a 16-day oral study, mice were orally gavaged with 0, 22, 44, 88, 175, 350 or 700 mg/kg-day TCEP in corn oil 5 days/week for a total of 12 doses. No treatment-related deaths, differences in final mean body weight or histopathological lesions. NOAEL: 700 mg/kg-day (highest dose tested)	Matthews et al., 1990 (as cited in NTP, 1991)	Sufficient study details reported.

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		LOAEL: Not established		
		In a 16-18 week oral study, rats were gavaged with TCEP at 0, 22, 44, 88, 175 or 350 mg/kg-day, 5 days/week. Mortality occurred at the high dose (4/10 males and 3/10 females); Significantly increased liver and kidney to body weight ratios (≥ 44 mg/kg-day in females; 350 mg/kg-day for males); Necrotic lesions in the hippocampus and thalamus (females, 175 mg/kg-day; both sexes, 350 mg/kg-day). NOAEL: 88 mg/kg-day LOAEL: 175 mg/kg-day (necrotic lesions in hippocampus and thalamus-females)	Matthews et al., 1990; NTP, 1991 (as cited in EC, 2000; NICNAS, 2001; ATSDR, 2012)	Sufficient study details reported.
		In a 16-week oral study, mice were gavaged with TCEP (in corn oil) at 0, 44, 88, 175, 350 and 700 mg/kg-day, 5 days/week. No treatment-related deaths, differences in final mean body weight or differences in cholinesterase activity. Kidney effects: tubule epithelial cells with enlarged nuclei (cytomegaly and karyomegaly) at the highest dose. NOAEL: 350 mg/kg-day LOAEL: 700 mg/kg-day (kidney effects)	Matthews et al., 1990; NTP, 1991 (as cited in EC, 2000; ATSDR, 2012)	Sufficient study details reported.
		In a 28-day dietary study, rats were fed TCEP at 0, 400, 1,000, 3,000 or 8,000 ppm daily (0, 37, 91, 270 and 730	EC, 2000; EU, 2009	Limited study details reported in a secondary source; doses were reported as ppm in the diet but

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		mg/kg-day) No mortalities. Significant reductions in body weight and food consumption (8,000 ppm); No treatment-related changes in clinical chemistry, hematology or urinalysis parameters; no adverse gross or microscopic effects. Significant increase in relative liver and kidney weights (3,000 and 8,000 ppm) NOAEL: 1,000 ppm (91 mg/kg-day) LOAEL: 3,000 ppm (270 mg/kg-day)		were converted to mg/kg-day using EPA 1988 reference values for body weight and food consumption.
		In a 28-day dietary study, rats were fed TCEP at 0, 500, 850, 1,500 and 2,000 ppm daily (~46, 78, 140, and 180 mg/kg-day). Decreased food consumption (8,000 ppm). No further clinical effects were observed and necropsy revealed no abnormalities. NOAEL: > 2,000 ppm (180 mg/kg-day; highest dose tested) LOAEL: Not established	EC, 2000; EU, 2009	Limited study details reported in a secondary source; doses were reported as ppm in the diet but were converted to mg/kg-day using EPA 1988 reference values for body weight and food consumption.
		In a 30-day dietary study, rats were fed TCEP up to a maximum dose of 400 mg/kg-day (other doses not reported). No deaths; no adverse effects were observed. NOAEL: 400 mg/kg-day (highest dose tested) LOAEL: Not established	Ulsamer et al., 1980 (as cited in EC, 2000)	Limited study details reported in a secondary source; Study received reliability score of 4 in the IUCLID data set.

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		There is potential for liver toxicity based on a structural alert for chlorinated hydrocarbons. (Estimated)	Professional judgment	Estimated based on a structural alert for chlorinated hydrocarbons and professional judgment.
Skin Sensitization		**LOW: TCEP is not a skin sensitizer in guinea pigs.**		
	Skin Sensitization	Not sensitizing to guinea pigs	EC, 2000; OECD-SIDS, 2006	Limited study details reported in a secondary source.
Respiratory Sensitization		**No data located.**		
	Respiratory Sensitization			No data located.
Eye Irritation		**LOW: TCEP produced mild conjunctival irritation in rabbits.**		
	Eye Irritation	Mild conjunctival irritation, rabbits	OECD-SIDS, 2006	Limited study details reported in a secondary source; Study conducted in accordance with OECD Guideline 404.
		Not irritating to rabbit eyes	EC, 2000	Limited study details reported in a secondary source; Study conducted in accordance with GLP and Directive 84/449/EEC, B.5 or OECD Guideline 405.
		Not irritating to rabbit eyes	EC, 2000	Limited study details reported in a secondary source.
Dermal Irritation		**LOW: TCEP was slightly irritating to rabbit skin.**		
	Dermal Irritation	Mild skin irritation, rabbits	OECD-SIDS, 2006	Limited study details reported in a secondary source; Study was conducted in accordance with OECD Guideline 404.
		Slightly irritating to rabbit skin	EC, 2000	Limited study details reported in a secondary source.
		Not irritating to rabbit skin	EC, 2000	Limited study details reported in a secondary source; Study was conducted in accordance with GLP

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PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
			and Directive 84/449/EEC, B.4 or OECD Guideline 404.
Endocrine Activity	**TCEP increased 17-estradiol (E2) and testosterone (T) concentrations following exposure for 48 hours in human H295R cells and inhibited luciferase expression induced by dihydrotestosterone in a reporter gene assay. TCEP was negative for estrogenic activity in a yeast two-hybrid assay and was not an estrogen receptor antagonist in human MVLN cells following a 72-hour incubation period. There were no adverse effects on endocrine glands of rats and mice administered TCEP via oral gavage for up to 103 weeks.**		
	In 103-week oral studies, rats were gavaged with TCEP at 0, 44 or 88 mg/kg-day and mice were gavaged with TCEP at 0, 175, or 350 mg/kg-day, 5 days/week. There were no adverse effects on endocrine glands in either species reported.	NTP, 1991; Matthews et al., 1993 (as cited in ATSDR, 2012)	Sufficient study details reported.
	No estrogenic or anti-estrogenic activity of TCEP in human endometrial cancer cells in a recombinant yeast reporter gene assay	Follmann and Wober, 2006	Sufficient study details reported in primary source.
	TCEP inhibited luciferase expression induced by dihydrotestosterone in a reporter gene assay	HSDB, 2013	Limited details reported in secondary source; study is in Chinese with an English abstract.
	No estrogen receptor antagonism in human MVLN cells following 72-hour incubation up to 10 mg/L TCEP	Liu et al., 2012	Sufficient study details reported in primary source.
	Increased 17ß-estradiol (E2) and testosterone (T) concentrations following exposure to ≥0.1 mg/TCEP for 48 hours in human H295R cells.	Liu et al., 2012	Sufficient study details reported in primary source.
	Negative for estrogenic activity in a yeast two-hybrid assay	Nishihara et al., 2000	Sufficient study details reported in primary source.

Tris (2-chloroethyl) phosphate CASRN 115-96-8				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Immunotoxicity		**TCEP produced a dose-dependent growth inhibition in B cells but not T cells in a mouse lymphocyte mitogenesis test. The IC_{50} was $1.0x10^{-5}$ mol/L.**		
	Immune System Effects	Lymphocyte mitogenesis test, mouse splenic lymphocyte cells; dose-dependent growth inhibition in B cell test but no inhibition in T cell test. IC_{50} (50% inhibition concentration): $1.0x10^{-5}$ mol/L	Sakazaki et al., 2001	Sufficient study details reported in a primary source.
		In 103 week oral studies, rats were gavaged with TCEP at 0, 44 or 88 mg/kg-day and mice were gavaged with TCEP at 0, 175, or 350 mg/kg-day 5 days/week. There were no adverse effects on lymphoreticular tissues in either species.	NTP, 1991; Matthews et al., 1993 (as cited in ATSDR, 2012)	Sufficient study details reported.
ECOTOXICITY				
ECOSAR Class				
Acute Aquatic Toxicity		**HIGH: Based on experimental LC_{50} values of 6.3 and 4.9 mg/L for fish and daphnia, respectively and an acute EC_{50} of 1.1 mg/L for algae.**		
Fish LC_{50}		Freshwater fish (*Oryzias latipes*) 96-hour LC_{50} = 6.3 mg/L (static test conditions) (Experimental)	EC, 2000	Limited study details reported in a secondary source; Study was conducted in accordance with OECD Guideline 203. No data on analytical monitoring.
		Freshwater fish (*Carassius auratus*) 96-hour LC_{50} = 90 mg/L (Experimental)	Sasaki et al., 1981 (as cited in WHO, 1998; EU, 2009)	Limited study details reported in a secondary source.
		Freshwater fish (*Oryzias latipes*) 96-hour LC_{50} = 210 mg/L (static test conditions) (Experimental)	Sasaki et al., 1981 (as cited in WHO, 1998; EC, 2000; EU, 2009)	Limited study details reported in a secondary source. No data on analytical monitoring.
		Freshwater fish (*Salmo gairdneri*) 96-	WHO, 1998; EC, 2000; EU, 2009	Limited study details reported in a

Tris (2-chloroethyl) phosphate CASRN 115-96-8			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	hour LC_{50} = 249 mg/L NOEC = 50 mg/L (static test conditions; test dilution was clear and colorless with colorless droplets of material on the surface) (Experimental)		secondary source; Study was conducted in accordance with GLP and OECD Guideline 203. No analytical monitoring was conducted.
	Freshwater fish (*Oryzias latipes*) LC_{50} = 251 mg/L (Experimental)	Yoshioka et al., 1986 (as cited in WHO, 1998)	Limited study details reported in a secondary source.
	Freshwater fish (*Leuciscus idus*) 48-hour LC_{50} = ca. 200 mg/L (static test conditions) (Experimental)	EC, 2000; EU, 2009	Limited study details reported in a secondary source. No data on analytical monitoring.
	Freshwater fish (*Oryzias latipes*) 48-hour LC_{50} = 300 mg/L (static test conditions) (Experimental)	MITI, 1992b (as cited in EC, 2000; WHO, 1998; EU, 2009)	Limited study details reported in a secondary source. No data on analytical monitoring.
	Freshwater fish (*Carassius auratus*) 168-hour/7 day LC_0/EC_0 = 5 mg/L; (static test conditions) (Experimental)	EC, 2000; EU, 2009	Limited study details reported in a secondary source. No data on analytical monitoring.
	Freshwater fish (*Cyprinus carpio*) 6-day LC_0 (dietary exposure) = 35 - 156 mg/kg food (Experimental)	EC, 2000	Limited study details reported in a secondary source. No data on analytical monitoring.
	Freshwater fish (*Cyprinus carpio*) 6-day LC_0 = 156 mg/kg food (Experimental)	EU, 2009	Limited study details provided in a secondary source.
	Freshwater fish 96-hour L C_{50} = 51 mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	Estimate for the Esters class was provided for comparative purposes. See Section 5.5.1.

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PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
Daphnid LC_{50}	*Daphnia magna* 24-hour EC_{50} = 4.9 mg/L (Experimental)	EC, 2000	Limited study details reported in a secondary source; Study conducted in accordance with OECD Guideline 202. No data on analytical monitoring.
	Daphnia magna 24-hour EC_{50} = 235 mg/L (Experimental)	EC, 2000; EU, 2009	Limited study details reported in a secondary source. No data on analytical monitoring.
	Daphnia magna 24-hour EC_{50} = 340 mg/L; EC_0 = 100 mg/L; EC_{100} = 1,000 mg/L (Experimental)	EC, 2000; EU, 2009	Limited study details reported in a secondary source; Study conducted in accordance with Directive 84/449/EEC, C.2.
	Daphnia magna 24-hour EC_{50} = 451 mg/L (Experimental)	EC, 2000; EU, 2009	Limited study details reported in a secondary source. Non-GLP; no data on analytical monitoring.
	Daphnia LC_{50} = 1,000 mg/L (Experimental)	Yoshioka et al., 1986 (as cited in WHO, 1998)	Limited study details provided in a secondary source; study duration not reported.
	Daphnid 48-hour LC_{50} > 100 mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	Estimate for the Esters class was provided for comparative purposes. See Section 5.5.1.
Green Algae EC_{50}	Green algae (*Scenedesmus subspicatus*) 72-hour EC_{50} = 1.1 mg/L (biomass) Green algae (*Scenedesmus subspicatus*) 72-hour EC_{50} = 3.6 mg/L (growth rate) (Experimental)	EC, 2000; EU, 2009	Limited study details reported in a secondary source. Non-GLP; no data on analytical monitoring.
	Green algae (*Scenedesmus subspicatus*) 96-hour EC_{50} = 1.2 mg/L (biomass) (Experimental)	EC, 2000; EU, 2009	Limited study details reported in a secondary source; no data on analytical monitoring.
	Green algae (*Scenedesmus subspicatus*) 48-hour EC_{50} = 2 mg/L (biomass)	EC, 2000; EU, 2009	Limited study details reported in a secondary source; no data on

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PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	Green algae (*Scenedesmus subspicatus*) 48-hour EC_{50} = 5 mg/L (growth rate) (Experimental)		analytical monitoring.
	Green algae (*Scenedesmus subspicatus*) 72-hour EC_{50} = 271-278 mg/L (growth rate) NOEC = 100 mg/L (Experimental)	EC, 2000; EU, 2009	Limited study details reported in a secondary source. Study conducted in accordance with GLP and OECD Guideline 201. Analytical monitoring was performed.
	Green algae (*Scenedesmus subspicatus*) 72-hour EC_{50} = 3.6 mg/L (growth rate) (Experimental)	EC, 2000; EU, 2009	Limited study details reported in a secondary source; no data on analytical monitoring.
	Green algae (*Scenedesmus subspicatus*) 48-hour EC_{50} = 5 mg/L (growth rate) (Experimental)	EC, 2000; EU, 2009	Limited study details reported in a secondary source; no data on analytical monitoring.
	Green algae (*Pseudokirchneriella subcapitata*) 96-hour EC_{50} = 117 mg/L (growth rate) NOEC = 5 mg/L (Experimental)	EC, 2000; EU, 2009	Limited study details reported in a secondary source. Study conducted in accordance with GLP and OECD Guideline 201. No analytical monitoring.
	Green algae 96-hour EC_{50} = 48 mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	Estimate for the Esters class was provided for comparative purposes. See Section 5.5.1.

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PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
Chronic Aquatic Toxicity	**HIGH: Two experimental studies were located for daphnia and two for algae, while there were no experimental chronic aquatic toxicity data for fish. The experimental 14 and 21-day NOECs of 1.9 and 13 mg/L in *Daphnia magna* and NOECs of 5 and 100 mg/L in *Pseudokirchneriella subcapitata* are within the Moderate - Low hazard designation range; however, chronic aquatic toxicity in fish cannot be ruled out due to the lack of experimental data . An estimated chronic aquatic toxicity value derived using an acute-to-chronic ratio (ACR) for the phosphate esters class and was applied to the available experimental acute data for this chemical and indicated a High hazard. ECOSAR estimates (Esters class) indicate a Moderate to Low hazard in fish, daphnia, and algae. In addition, this substance has been assigned the risk phrase R51/53: Toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment (ESIS, 2012). There is potential concern based on estimates and the uncertainty due to the lack of experimental data; therefore a High hazard designation was assigned.**		
Fish ChV	Freshwater fish ChV = 0.26 mg/L (Estimated)	Professional judgment	An ACR of 24 was derived for the phosphate ester class based on experimental data for Tris (p-t-butylphenyl) phosphate (TBPP). The acute-to-chronic ratio was applied to available experimental acute fish data for Tris (2-chloroethyl) phosphate (ChV = 6.3 mg/L /24 = 0.26 mg/L)
	Fish ChV = 4.04 mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	Estimate for the Esters class was provided for comparative purposes. See Section 5.5.1.
Daphnid ChV	*Daphnia magna* 14-day NOEC = 1.9 mg/L (Experimental)	EC, 2000	Limited study details reported in a secondary source; Study conducted in accordance with OECD Guideline 202. No data on analytical monitoring.
	Daphnia magna 21-day NOEC = 13 mg/L (reproduction rate) (Experimental)	EC, 2000	Limited study details reported in a secondary source; no data on analytical monitoring.

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		Daphnia ChV > 10 mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	Estimate for the Esters class was provided for comparative purposes. See Section 5.5.1.
Green Algae ChV		Green algae (*Scenedesmus subspicatus*) 72-hour (growth rate) NOEC = 100 mg/L (Experimental)	EC, 2000; EU, 2009	Limited study details reported in a secondary source. Study conducted in accordance with GLP and OECD Guideline 201. Analytical monitoring was performed.
		Green algae (*Pseudokirchneriella subcapitata*) 96-hour (growth rate) NOEC = 5 mg/L (Experimental)	EC, 2000; EU, 2009	Limited study details reported in a secondary source. Study conducted in accordance with GLP and OECD Guideline 201. No analytical monitoring.
		Green algae ChV > 10 mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	Estimate for the Esters class was provided for comparative purposes. See Section 5.5.1.
ENVIRONMENTAL FATE				
Transport		**Level III fugacity models incorporating available physical and chemical property data indicate that at steady state, TCEP is expected to be found primarily in soil and to a lesser extent, water. TCEP is expected to have high mobility in soil, based on estimated K_{OC} values. Leaching through soil to groundwater may occur, though it is not expected to be an important transport mechanism. Estimated volatilization half-lives indicate that it will be non-volatile from surface water. Volatilization from dry surface is also not expected based on its vapor pressure. In the atmosphere, TCEP is expected to exist in the vapor phase based on its vapor pressure.**		
	Henry's Law Constant (atm-m^3/mole)	$2.6x10^{-8}$ (Estimated)	EPI v4.11	Estimated by the HENRYWIN program Bond estimation method.
		$<10^{-8}$ (Estimated)	EPI v4.11	Estimated from the measured Water Solubility and extrapolated Vapor Pressure.

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Sediment/Soil Adsorption/Desorption - K_{oc}	100 (Estimated)	EPI v4.11	Estimated by the KOCWIN Log K_{ow} method using the measured Log K_{ow} value, 1.78.
		390 (Estimated)	EPI v4.11	Estimated by the KOCWIN MCI method.
	Level III Fugacity Model	Air = 0.004% Water = 10.9% Soil = 88.8% Sediment = 0.26% (Estimated)	EPI v4.11	Values were obtained from the measured log K_{ow}, water solubility and extrapolated vapor pressure.
Persistence		**MODERATE: Based on guideline experimental biodegradation data that taken together indicate that the resultant half-life is expected to be greater than 16 days but less than 60 days and therefore is consistent with the moderate hazard designation. After 48 days 70-90% degradation of TCEP occurred in activated sludge inoculum using OECD 301B, 50-90% degradation with adapted activated sludge using OECD 302A and 45% degradation after 4 weeks with OECD 301C. No degradation was found in an anaerobic biodegradation study after 58 days using ISO DIS 11734. TCEP is expected to hydrolyze slowly; although hydrolysis rates will be dependent on temperature and pH conditions according to experimental studies. TCEP is not expected to be susceptible to direct photolysis by sunlight, since it does not absorb light at wavelengths >290 nm. TCEP is not susceptible to significant degradation by ozone or hydroxyl radicals in experimental studies of water samples. The atmospheric half-live of vapor-phase TCEP is estimated to be less than one day.**		
Water	**Aerobic Biodegradation**	Passes Ready Test: No Test method: OECD TG 301C: Modified MITI Test (I) 4% degradation (by BOD) after a 4-week incubation period using an activated sludge inoculum (30 mg/L, predominantly domestic sludge, non-adapted) and 100 mg/L test substance (Measured)	MITI, 1992a; EC, 2000	Guideline study performed according to Japanese MITI and OECD guidelines.
		Passes Ready Test: No Test method: OECD TG 301B: CO_2 Evolution Test	EC, 2000	Adequate, guideline study.

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PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
		Activated sludge inoculum, 20 mg/L concentration of test substance, 70-90% degradation after 48 days; Result: Inherently biodegradable (Measured)		
		Study results: 100% Test method: Other Isolated bacterial cultures containing *Sphingobium sp.* strain TCM1 and *Xanthobacter autotrophicus* strain GJ10 degraded TCEP and the metabolite 2-chloroethanol (Measured)	Takahashi et al., 2012	Nonguideline pure culture study indicating the potential for complete bacterial biodegradation.
		Study results: 50-90%/24 hour Test method: 302A: Inherent - Modified SCAS Test Degradation reported as 50-90% after 24 hours; domestic, adapted activated sludge inoculum; 13 mg/L concentration of test substance; the 50-90% degradation was found within 24 hours after test periods ranging from 4 to 13 weeks. (Measured)	EC, 2000	Adequate, guideline study.
		Study results: 15%/21 days Test method: 302B: Inherent - Zahn-Wellens/EMPA Test Degradation reported as 15% after 21 days; industrial non-adapted activated sludge inoculum (Measured)	EC, 2000	Adequate, guideline study.
		Study results: 13%/28 days Test method: Other	EC, 2000	Nonguideline test conducted by a manufacturer.

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		Method: domestic activated sludge inoculum; 20 mg/L concentration of test substance (Measured)		
		Study results: <10%/27 days Test method: 302B: Inherent - Zahn-Wellens/EMPA Test Degradation reported as <10% after 27 days; Industrial, non-adapted activated sludge inoculum (Measured)	EC, 2000	Adequate, guideline study.
		Study results: 4%/28 days Test method: Other Method: domestic activated sludge inoculum; 20 mg/L concentration of test substance (Measured)	EC, 2000	Nonguideline test conducted by a manufacturer.
		Isolated bacterial cultures containing *Acidovorax* sp. BSB421 and *Sphingomonas agrestis* completely degraded 20 µM TCEP within 6 hours when they are the sole phosphorus sources. (Measured)	Takahashi et al., 2008, 2010	Nonguideline pure culture study indicating the potential for complete bacterial biodegradation.
	Volatilization Half-life for Model River	>1 year (Estimated)	EPI v4.11	Estimation model was calculated using all applicable measured input values and the Henry`s Law Constant obtained from the measured water solubility and extrapolated vapor pressure.

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Volatilization Half-life for Model Lake	>1 year (Estimated)	EPI v4.11	Estimation model was calculated using all applicable measured input values and the Henry`s Law Constant obtained from the measured water solubility and extrapolated vapor pressure.
Soil	**Aerobic Biodegradation**	Study results: DT_{50} = 167 Test method: Other DT90 >>100 days based on 5 mg/kg soil in a laboratory test for 100 days; kinetic curve fitted to a 2nd order square root function (Measured)	EU, 2009	Nonguideline study reported in a secondary source.
	Anaerobic Biodegradation	Study results: 0%/58 days Test method: Other Method = ISO DIS 11734; 80 mg/L concentration test substance related to DOC (Dissolved Organic Carbon); Test condition of 35°C +/- 2°C (Measured)	EC, 2000	Adequate guideline study.
	Soil Biodegradation with Product Identification			No data located.
	Sediment/Water Biodegradation			No data located.
Air	**Atmospheric Half-life**	0.5 days (Estimated)	EPI v4.11	
Reactivity	**Photolysis**	0% Not a significant fate process (Estimated)	Professional judgment; Mill, 2000	This compound does not contain functional groups that would be expected to absorb light of wavelengths >290 nm.
		Direct photolysis was insignificant; second-order rates of reaction determined by ultraviolet and ozone generated ·OH in water. (Measured)	Watts and Linden, 2009	Nonguideline study.
		<10% removal of TCEP in tertiary-	Wert et al., 2009	Nonguideline study indicating

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PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
		treated effluent samples collected from three wastewater treatment facilities when exposed to O_3 (Measured)		limited susceptibility to hydroxyl radical degradation.
	Hydrolysis	0%/1 day Hydrolysis measured in buffered water at 20°C; pH 2 to pH 12 with a chlorine concentration (100 mg/L) from calcium hypochlorate and hydrochloric acid. 100% of the chemical remained after one day at pH 2 to pH 8. (Measured)	Ishikawa and Baba, 1988	Adequate hydrolysis study examining hydrolysis in a water treatment facility.
		5%/1 day Hydrolysis measured in buffered water at 20°C and pH 2 to pH 12 with a chlorine concentration (100 mg/L) from calcium hypochlorate and hydrochloric acid. 95% of the chemical remained after one day at pH 10. 40% remained after one day at pH 12. (Measured)	Ishikawa and Baba, 1988	Adequate hydrolysis study examining hydrolysis in a water treatment facility.
		50%/20 days at pH 5 to pH 9 50%/17 days at pH 10 (Estimated)	EPI v4.11	Estimate generated by the HYDROWIN program. For phosphate esters, HYDROWIN estimates hydrolysis half-lives that consider both base-catalyzed and neutral hydrolysis rate constants at 25°C. Based on measured hydrolysis data that indicates little hydrolysis at acidic or neutral pH over a one-day period (Ishikawa and Baba, 1988), the estimates at pH 5 to pH 7 may be too fast.
		Slow hydrolysis in water; hydrolysis increases with temperature and at the extremes of the pH range. (Estimated)	IPCS, 1998	Supporting information provided in a secondary source.

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Environmental Half-life		120 days (Estimated)	PBT Profiler	Half-life estimated for the predominant compartment (soil), as determined by EPI and the PBT Profiler methodology.
Bioaccumulation		**LOW: Based on multiple experimental BCF values in four different species that are below 100, the cutoff for the Low bioaccumulation designation criteria. Biomonitoring studies have reported the detection of this compound in aquatic species, mammalian species, herring gull eggs and pine needles; DfE criteria specifically require these data to be considered in the hazard designation on a case by case basis. Available toxicokinetic studies indicate that in some species, metabolites of TCEP are rapidly formed and eliminated. This demonstrates that these materials are likely bioavailable and could be observed in a biological matrix. However, the rate of metabolism and elimination may be successfully competing with that of uptake, which is also consistent with the experimental BCF results. The biomonitoring studies are not inconsistent with a Low designation.**		
	Fish BCF	0.8 *Cyprinus carpio* Mean water concentration of 1 mg/L; 42 days exposure (Measured)	EC, 2000	Nonguideline study conducted for a manufacturer.
		2.2 *Oryzias latipes* Static test system; 96-hour exposure period; 4 mg/L concentration test substance (Measured)	EC, 2000	Nonguideline study conducted for a manufacturer.
		1.3 *Oryzias latipes* Flow-through test system; 96-hour exposure period; 4 mg/L concentration test substance (Measured)	EC, 2000	Nonguideline flow-through study conducted for a manufacturer.
		0.9 *Carassius auratus* Static test with a 96-hour exposure period to 4 mg/L test substance (Measured)	EC, 2000	Nonguideline study conducted for a manufacturer.
		5.1 *Cyprinus carpio* Whole body tissue analysis, a mean water concentration of 100 µg/L; 42 days exposure in flow-through system (Measured)	MITI, 1992a	Japanese MITI guideline study.
	Other BCF			No data located.

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	BAF	6.3 (Estimated)	EPI v4.11	Estimated by the BCFBAF program using the measured log K_{ow} (1.78) and the Arnot-Gobas method (upper trophic).
	Metabolism in Fish			No data located.
ENVIRONMENTAL MONITORING AND BIOMONITORING				
Environmental Monitoring		Detected in house dust, indoor air, urban and suburban air, river and sea sediments, surface waters, drinking water, wastewater effluents, ground waters, rainwater samples and food samples (IARC, 1990; Suzuki et al., 1994; Andresen et al., 2007; Bacaloni et al., 2008; Takigami et al., 2008, 2009; EU, 2009; Dougherty et al., 2010; Regnery and Puttmann, 2010a, 2010b; Ali et al., 2012a, 2012b; Alvarez et al., 2012; ATSDR, 2012; Bergh et al., 2012; Bollmann et al., 2012; Cao et al., 2012; Dodson et al., 2012; Matamoros and Salvado, 2012; Matamoros et al., 2012; Moller et al., 2012; Rodil et al., 2012; Eggen et al., 2013; HSDB, 2013; Kim et al., 2013; Kolpin et al., 2013; Salamova et al., 2014).		
Ecological Biomonitoring		Detected in pine needle samples collected in the Sierra Nevada foothills in California; herring gull eggs; mussel, fish and shellfish samples (Yasuhara and Morita, 1987; IARC, 1990; IPCS, 1998; EU, 2009; Chen et al., 2012).		
Human Biomonitoring		This chemical was not included in the NHANES biomonitoring report (CDC, 2009).		

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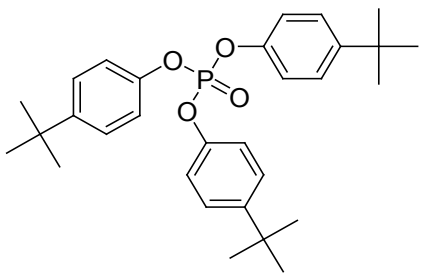
Tris (p-t-butylphenyl) phosphate (TBPP)

Screening Level Toxicology Hazard Summary

This table contains hazard information for each chemical; evaluation of risk considers both hazard and exposure. Variations in end-of-life processes or degradation and combustion by-products are discussed in the report but not addressed directly in the hazard profiles. The caveats listed below must be taken into account when interpreting the information in the table.

VL = Very Low hazard L = Low hazard M = Moderate hazard H = High hazard VH = Very High hazard – Endpoints in colored text (VL, L, M, H, and VH) were assigned based on empirical data. Endpoints in black italics *(VL, L, M, H,* and *VH*) were assigned using values from estimation software and professional judgment [(Quantitative) Structure Activity Relationships "(Q)SAR"].

Chemical	CASRN	Human Health Effects										Aquatic Toxicity		Environmental Fate	
		Acute Toxicity	Carcinogenicity	Genotoxicity	Reproductive	Developmental	Neurological	Repeated Dose	Skin Sensitization	Respiratory Sensitization	Eye Irritation	Dermal Irritation	Acute	Chronic	Persistence	Bioaccumulation
Tris (p-t-butylphenyl) phosphate (TBPP)	78-33-1	L	*M*	L	M	L	M	H	*M*		L	M	VH	VH	M	H



CASRN: 78-33-1
MW: 494.6
MF: $C_{30}H_{39}O_4P$
Physical Forms: Solid **Neat:**
Use: Flame Retardant

SMILES:
O=P(Oc(ccc(c1)C(C)(C)C)c1)(Oc(ccc(c2)C(C)(C)C)c2)Oc(ccc(c3)C(C)(C)C)c3 (CASRN 78-33-1; tris (t-butylphenyl) phosphate);
C(C)(C)(C)c1ccc(OP(=O)(Oc2ccc(C(C)(C)C)cc2)Oc2ccccc2)cc1 (CASRN 65652-41-7; di-t-butylphenyl phenyl phosphate);
C(C)(C)(C)c1ccc(OP(=O)(Oc2ccccc2)Oc2ccccc2)cc1 (CASRN 56803-37-3; p-(t-butylphenyl) diphenyl phosphate)

Synonyms: Phenol, 4-(1,1-dimethylethyl)-, 1,1`,1``-phosphate; Phenol, 4-(1,1-dimethylethyl)-, phosphate (3:1); Phosphate, tris(tert-butylphenyl); Tris(p-t-butylphenyl) phosphate; Tris(p-tert-butylphenyl) phosphate; Tris(tert-butylphenyl) phosphate; 1-(5,6-dimethyl-1h-benzimidazol-2-yl)ethanol; 4-(1,1-dimethylethyl)phenol, phosphate (3:1); p-tert-Butylphenol, phosphate (3:1); Phenol, 4-(1,1-dimethylethyl)-, 1,1`,1``-phosphate; Phenol, 4-(1,1-dimethylethyl)-, phosphate (3:1); Phenol, p-tert-butyl-, phosphate (3:1); Phenol, p-tert-butyl-, phosphate (3:1) (8CI); Phenol,4-(1,1-dimethylethyl)-,phosphate(3:1); Phosphate, tris(tert-butylphenyl); Tris(4-tert-butylphenyl) phosphate; Tris(p-t-butylphenyl) phosphate; Tris(p-tert-butylphenyl) phosphate

Chemical Considerations: The alternative, TBPP, may contain a mixture of t-butyl isomers and t-butyl substituted phenyl phosphate esters depending on the manufacturing, purification and processing of the compound. Isomers expected to be present will be discussed in this report as appropriate when determining hazard designations. A description of the sample tested, mixture components or isomer content is included in the report when available. However this information was not consistently reported in the literature. Chemical, fate, and toxicity data for components of the mixture represented by other CASRN were collected in the preparation of this AA and are listed below:

- Phenol, 4-(1,1-dimethylethyl)-, 1,1`,1``-phosphate (CASRN 78-33-1)
- Triphenyl phosphate (CASRN 115-86-6)
- t-Butylphenyl diphenyl phosphate (CASRN 56803-37-3)
- P-(t-butylphenyl) diphenyl phosphate (CASRN 981-40-8)
- Diphenyl-2-(tert-butyl)phenylphosphate (CASRN 83242-23-3)
- Bis(p-tert-butylphenyl) phenyl phosphate (CASRN 115-87-7)
- Di-(t-butyl) phenyl phenyl phosphate (CASRN 65652-41-7)
- Butylated triphenyl phosphate (CASRN 220352-35-2)
- Phenol, (1,1-dimethylethyl)-, phosphate (3:1) (CASRN 28777-70-0)
- 4-(1,1-Dimethylethyl)phenyl diphenyl ester phosphoric acid mixt. With triphenyl phosphate (CASRN 96300-96-8)

Estimated values using representative structures as indicated in the SMILES section of this assessment will be used to fill assessment data gaps. EPI v4.11 was used to estimate physical/chemical and environmental fate values in the absence of experimental data (Weil, 2001).

Polymeric: No **Oligomeric:** Not applicable	
Metabolites, Degradates and Transformation Products: Phenol; tert-butylphenol; diphenyl phosphate; triphenyl phosphate (Heitkamp and Cerniglia, 1986; Heitkamp et al., 1986)	
Analog: TBPP isomers and t-butyl substituted phenyl phosphate esters anticipated to be present in the commercial product were considered in this evaluation, as indicated in the chemical considerations section; Phosflex 71B for skin sensitization. **Endpoint(s) using analog values:** Not applicable	**Analog Structure:** Not applicable
Structural Alerts: Organophosphates; Neurotoxicity (EPA, 2012).	
Risk Phrases: Not classified by Annex VI Regulation (EC) No 1272/2008 (ESIS, 2012).	
Hazard and Risk Assessments: Hazard and risk assessments were not identified specifically for tris (t-butylphenyl) phosphate (CASRN 78-33-1), although the following hazard and risk assessments for related substances were found: Hydraulic Fluids Assessment by the Agency for Toxic Substances and Disease Registry; an Environmental risk evaluation report for Tertbutylphenyl diphenyl phosphate (CASRN 56803-37-3); and an Initial risk-based prioritization of HPV chemicals for Butylated triphenyl phosphate (ATSDR, 1997; EPA, 2008; Environment Agency, 2009).	

Tris (p-t-butylphenyl) phosphate (TBPP) CASRN 78-33-1			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
PHYSICAL/CHEMICAL PROPERTIES			
Melting Point (°C)			No data located.
Boiling Point (°C)	>300 (Estimated)	EPI v4.11; EPA, 1999	The estimated value for tris(p-t-butylphenyl) phosphate is greater than the cutoff value of >300°C, according to HPV assessment guidance.
	393 Decomposes Thermal decomposition temperature (Measured)	Dobry and Keller, 1957	Reported for CASRN 65652-41-7 and CASRN 115-87-7.
	405 Decomposes Thermal decomposition temperature (Measured)	Dobry and Keller, 1957	Reported for CASRN 56803-37-3 and CASRN 981-40-8.
Vapor Pressure (mm Hg)	$<1x10^{-6}$ at 25°C (Estimated)	EPI v4.11	Estimated using representative structures indicated in the SMILES section for tris (p-t-butylphenyl) phosphate and di-t-butylphenyl phenyl phosphate.
	$6.5x10^{-6}$ at 50°C from high temperature data (Extrapolated)	Carre and Bertrand, 1999	Reported for CASRN 78-33-1. The vapor pressure was extrapolated from high temperature data using linear log vapor pressure versus molecular weight approximation.
	$5x10^{-5}$ at 50°C from high temperature data (Extrapolated)	Carre and Bertrand, 1999	Reported for CASRN 65652-41-7. The vapor pressure was extrapolated from high temperature data using linear log vapor pressure versus molecular weight approximation.
	$1.4x10^{-6}$ at 25°C (Measured)	ChemID, 2013c	Reported for CASRN 56803-37-3.

Tris (p-t-butylphenyl) phosphate (TBPP) CASRN 78-33-1			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
Water Solubility (mg/L)	$9.6x10^{-7}$ for tris (p-t-butylphenyl) phosphate; $9.3x10^{-5}$ for di-t-butylphenyl phenyl phosphate (Estimated)	EPI v4.11	Estimated using representative structures indicated in the SMILES section. Values are less than the cutoff value, <0.001 mg/L, for nonsoluble compounds according to HPV assessment guidance.
	0.008 (Estimated) for t-butylphenyl diphenyl phosphate	EPI v4.11	Estimated using the representative structure for t-butylphenyl diphenyl phosphate indicated in the SMILES section.
	3.2 (Measured)	Saeger et al., 1979; ChemID, 2013c	A nonguideline study reported for a commercial mixture of CASRN 56803-37-3. This value is higher than would be expected for the pure substance.
Log K_{ow}	8.5 for di-t-butylphenyl phenyl phosphate; 6.6 for t-butylphenyl diphenyl phosphate (Estimated)	EPI v4.11	Estimated using representative structures indicated in the SMILES section.
	10 (Estimated)	EPI v4.11; EPA, 1999	Estimated for tris (p-t-butylphenyl) phosphate. The estimated value is greater than the cutoff value, >10, for non-soluble compounds according to HPV assessment guidance.
	5.12 (Measured)	EPA, 1999; ChemID, 2013c	Reported for CASRN 56803-37-3 in a nonguideline study for a commercial mixture.

Tris (p-t-butylphenyl) phosphate (TBPP) CASRN 78-33-1				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Flammability (Flash Point)		Nonflammable (Estimated)	Professional judgment	No data located; based on its use as a flame retardant.
Explosivity		Not expected to form explosive mixtures with air (Estimated)	Professional judgment	No experimental data located; based on its use as a flame retardant.
Pyrolysis				No data located.
pH		Not applicable (Estimated)	Professional judgment	Does not contain functional groups that are expected to ionize under environmental conditions.
pK_a		Not applicable (Estimated)	Professional judgment	Does not contain functional groups that are expected to ionize under environmental conditions.
HUMAN HEALTH EFFECTS				
Toxicokinetics		**Based on analogy to closely related compounds, TBPP is expected to have poor absorption through the skin, lungs and GI tract. There is evidence of dermal uptake in mixtures; however, it is uncertain if TBPP or other components of the mixture are promoting absorption.**		
Dermal Absorption *in vitro*				No data located.
Absorption, Distribution, Metabolism & Excretion	**Oral, Dermal or Inhaled**	CASRN 56803-37-5 is not readily absorbed when applied dermally to guinea pig skin.	Fabian, 1982	Data are for CASRN 56803-37-5.
		MIL-H-19457C hydraulic fluid (CASRN 28777-70-0) is rapidly absorbed following dermal administration	Dodd and Smith, 1994	Data are for MIL-H-19457C hydraulic fluid (CASRN 28777-70-0). Limited study details reported in a secondary source. Species not specified.
	Other	Absorption is nil through skin as neat solid, poor through skin when in solution, and poor through lungs and GI tract; based on analogy to closely related compounds	Professional judgment	Data are for CASRN 56803-37-3, 65652-41-7 and 78-33-1.

Tris (p-t-butylphenyl) phosphate (TBPP) CASRN 78-33-1				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Acute Mammalian Toxicity		**LOW: Based on experimental data for individual isomers and mixture components of TBPP via the oral, inhalation and dermal routes of exposure in rats and rabbits.**		
Acute Lethality	**Oral**	Rat oral LD_{50} > 4,640 mg/kg	Murphy, 1979	Data are for CASRN 56803-37-3.
		Rat oral LD_{50} > 5,000 mg/kg	Submitted confidential study	Data are for Phosflex 51B; 75-80 percent w/w tertbutylphenyl diphenyl phosphate (CASRN 56803-37-3), 20-25 percent w/w triphenyl phosphate (CASRN 115-86-6); conducted in accordance with OECD Guideline 401.
		Rat oral LD_{50} > 5 mL/kg (5,400 mg/kg)	ChemID, 2013b	Study details reported in a secondary source; data are for CASRN 28777-70-0.
		Rat oral LD_{50} > 10 g/kg (10,000 mg/kg)	Hagerman, 1984	Data are for CASRN 78-33-1; phosphen plasticiser P-7.
		Rat oral LD_{50} > 15,800 mg/kg	ChemID, 2013a	Study details reported in a secondary source; data are for CASRN 981-40-8.
		Rat oral LD_{50} > 15,800 mg/kg	Submitted confidential study	Data are for CASRN 56803-37-3.
		Rat oral LD_{50} = 20 g/kg (20,000 mg/kg)	Latourette, 1981	Data are for CASRN 56803-37-3. Mixed tert-butylphenyl phosphates with a MW of 335.
	Dermal	Rabbit dermal LD_{50} > 2,000 or > 4,640 mg/kg	Murphy, 1979	Data are for CASRN 56803-37-3.
		Rat dermal LD_{50} > 2,000 mg/kg	Submitted confidential study	Data are for Phosflex 51B; 75-80 percent w/w tertbutylphenyl diphenyl phosphate (CASRN 56803-37-3), 20-25 percent w/w triphenyl phosphate (CASRN 115-86-6); study equivalent to a limit test under OPPTS 870.1200 except that the group size was

Tris (p-t-butylphenyl) phosphate (TBPP) CASRN 78-33-1				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
				3/sex rather than 5/sex.
		Rabbit dermal LD_{50} > 7,900 mg/kg	Submitted confidential study	Data are for CASRN 56803-37-3.
		Rabbit dermal LD_{50} > 7,900 mg/kg	ChemID, 2013a	Study details reported in a secondary source; data are for CASRN 981-40-8.
		Rabbit dermal LD_{50} > 10 g/kg (10,000 mg/kg)	Latourette, 1981	Data are for CASRN 56803-37-3. Mixed tert-butylphenyl phosphates with a MW of 335.
	Inhalation	Rat 4-hour inhalation LC_{50} > 3.1 - 18.9 mg/L	Murphy, 1979	Data are for Phosflex 51B; 75-80 percent w/w tertbutylphenyl diphenyl phosphate (CASRN 56803-37-3), 20-25 percent w/w triphenyl phosphate (CASRN 115-86-6).
		Rat inhalation LC_{50} > 200 mg/L	Latourette, 1981	Data are for CASRN 56803-37-3. Mixed tert-butylphenyl phosphates with a MW of 335.
Carcinogenicity		**MODERATE: TBPP is estimated to have marginal risk for carcinogenicity based on the OncoLogic program analysis; In addition, there is uncertainty due to lack of data for this substance; carcinogenic effects cannot be ruled out.**		
	OncoLogic Results	Marginal; likely to have equivocal carcinogenic activity.	Professional judgment	Data are for CASRN 56803-37-3, 65652-41-7 and 78-33-1.
	Carcinogenicity (Rat and Mouse)			No data located.
	Combined Chronic Toxicity/Carcinogenicity			No data located.
	Other			No data located.

Tris (p-t-butylphenyl) phosphate (TBPP) CASRN 78-33-1				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Genotoxicity		**LOW: Based on experimental data for individual isomers and mixture components of TBPP, which were negative for *in vitro* gene mutations and chromosomal aberrations. No *in vivo* data were located.**		
	Gene Mutation *in vitro*	Negative, *Salmonella typhimurium* strains TA97, TA98, TA100, TA1535, TA137 with and without metabolic activation	Zeiger et al., 1987	Data are for CASRN 56803-37-3.
		Negative, *Salmonella typhimurium* TA98, TA100, TA1535, TA1537, or TA1538, and *Saccharomyces cerevisiae* D4 with or without metabolic activation	Submitted confidential study; Environment Agency, 2009	Data are for Phosflex 51B; 75-80 percent w/w tertbutylphenyl diphenyl phosphate (CASRN 56803-37-3), 20-25 percent w/w triphenyl phosphate (CASRN 115-86-6). Study details reported in a secondary source.
		Negative, forward gene mutations, cultured mouse lymphoma L5178Y/TK+/- cells with or without metabolic activation	Submitted confidential study; Environment Agency, 2009	Data are for Phosflex 51B; 75-80 percent w/w tertbutylphenyl diphenyl phosphate (CASRN 56803-37-3), 20-25 percent w/w triphenyl phosphate (CASRN 115-86-6). Study details reported in a secondary source.
	Gene Mutation *in vivo*			No data located.
	Chromosomal Aberrations *in vitro*	Negative, sister chromatid exchanges in cultured mouse lymphoma L5178Y/TK+/- cells with or without metabolic activation	Submitted confidential study; Murphy, 1979; Environment Agency, 2009	Data are for Phosflex 51B; 75-80 percent w/w tertbutylphenyl diphenyl phosphate (CASRN 56803-37-3), 20-25 percent w/w triphenyl phosphate (CASRN 115-86-6).
		Negative, chromosomal aberrations in cultured mouse lymphoma L5178Y/TK+/-cells with or without metabolic activation	Submitted confidential study; Murphy, 1979; Environment Agency, 2009	Data are for Phosflex 51B; 75-80 percent w/w tertbutylphenyl diphenyl phosphate (CASRN 56803-37-3), 20-25 percent w/w triphenyl phosphate (CASRN 115-

Tris (p-t-butylphenyl) phosphate (TBPP) CASRN 78-33-1				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
				86-6).
	Chromosomal Aberrations *in vivo*			No data located.
	DNA Damage and Repair			No data located.
	Other			No data located.
Reproductive Effects		**MODERATE: Based on experimental data for individual isomers of TBPP and its mixture components. No adverse reproductive effects were observed in rats fed diets containing CASRN 56803-37-3 at doses up to 1600 ppm (107.5 mg/kg-day; LOAEL not established), while abnormal reproductive cycles and liver effects were noted in rats administered BTP (CASRN 220352-35-2) at a dose of 1.7 g/kg (1700 mg/kg-day, only dose tested). A NOAEL of 170 mg/kg-day (without an established LOAEL) leaves uncertainty as to what dose adverse effects could occur; it is possible that effects could occur between 107.5 mg/kg-day and 250 mg/kg-day which falls within the DfE Moderate criteria range. Using a conservative approach, a Moderate hazard designation was assigned.**		
	Reproduction/Developmental Toxicity Screen			No data located.
	Combined Repeated Dose with Reproduction/ Developmental Toxicity Screen			No data located.

Tris (p-t-butylphenyl) phosphate (TBPP) CASRN 78-33-1				
PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
	Reproduction and Fertility Effects	In an oral study, groups of intact and ovariectomized female rats were administered BTP at doses of 0 or 1.7 g/kg (0 or 1700 mg/kg) via oral gavage in sesame oil vehicle or as neat BTP for 20, 40 or 60 days. Abnormal reproductive cycles in treated females that were significantly prolonged in diestrus. Abnormal reproductive cycles and liver effects suggest fecundity could be affected as a result of altered liver metabolism. NOAEL: Not established LOAEL: 1.7 g/kg-day (1,700 mg/kg-day; only dose tested)	Latendresse et al., 1995	Data are for CASRN 220352-35-2; Only one dose tested; there is uncertainty as to if adverse effects may have occurred at a lower dose.
		In a reproductive study, groups of breeding pairs of F344 rats were administered 0, 0.6, or 1.0 g (0, 600, 1,000 mg) BTP/kg via oral gavage in sesame oil or 1.7 g (1,700 mg) neat BTP/kg for up to 135 days. Significantly decreased fertility index and number of live litters (1.0 and 1.7 g/kg-day); decreased uterine weight (1.0 g/kg-day). No adverse effects on testicular or epididymal weights. NOAEL: 600 mg/kg-day LOAEL: 1,000 mg/kg-day	Latendresse et al., 1994b; Environment Agency, 2009	Data are for a butylated triphenyl phosphate-based hydraulic fluid (CASRN 115-86-6) reported to contain predominantly p-t-butylphenyl phenyl phosphates (84 percent wt., CASRN 220352-35-2), with lesser amounts of triphenyl phosphate (13 percent wt., CASRN 115-86-6). This study is described as invalid, based on unknown impurities present in the test compound and the possibility of incorrect dosing of animals.
		Sprague-Dawley rats (12/sex/group) were administered Phosflex 61B at doses of 0, 50, 250 or 1,000 mg/kg-day	Environment Agency, 2009	Data are for Phosflex 61B; a commercial mixture of tertbutylphenyl diphenyl

Tris (p-t-butylphenyl) phosphate (TBPP) CASRN 78-33-1				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		via oral gavage for two weeks prior to mating, during the two-week mating period and throughout gestation and lactation (total of ~8 weeks). No changes in reproductive organ weights. Histological changes in the reproductive organs were considered to be not treatment-related, however they were not described in detail. No significant difference in litter size or number of live pups. NOAEL ≥ 1,000 mg/kg-day (highest dose tested) LOAEL: Not established		phosphate (CASRN 56803-37-3). Purity and composition of test substance is not provided and study details are insufficient to assess robustness of results.
	Other	In a 90-day study, Sprague-Dawley rats (20/sex/group) were fed diets containing 0, 100, 400, or 1,600 ppm (average intakes of 0, 6.6, 26.7 or 107.5 mg/kg-day in males and 0, 7.7, 30.0 or 124.8 mg/kg-day in females) test substance. No adverse effect on histopathology or weights of reproductive organs in males or females. NOAEL: 1600 ppm (107.5 mg/kg-day for males and 124.8 mg/kg-day for females; highest dose tested) LOAEL: Not established	Submitted confidential study	Data are for CASRN 56803-37-3; there is uncertainty as to if adverse effects may have occurred within the Moderate hazard criteria range (50 - 250 mg/kg-day).
		Rats were administered ML-H-19457C (CASRN 28777-70-0) and tricresyl phosphate (TCP) daily via oral gavage for up to 10 weeks (doses not specified).	Dodd and Smith, 1994	Data are for MIL-H-19457C hydraulic fluid (CASRN 28777-70-0). Limited study details reported in a secondary source;

Tris (p-t-butylphenyl) phosphate (TBPP) CASRN 78-33-1				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		The estrous cycle was extended for high dose females administered ML-ML-H-19457C and relative testes weight was increased. Effects were reversed at 5 and 10 weeks post-treatment.		doses not specified.
		Rats, hamsters and rabbits were exposed to MIL-H-19457C hydraulic fluid (CASRN 28777-70-0) via inhalation 6 hours/day at a concentration of 250 mg/m^3 for 21 days or 0, 10 and 100 mg/m^3 for 90 days. Effects were only observed in rats and consisted lesions in the ovaries after 90 days of exposure (no further details provided).	Dodd and Smith, 1994	Data are for MIL-H-19457C hydraulic fluid (CASRN 28777-70-0).
Developmental Effects		**LOW: Based on experimental data for mixture components of TBPP. In two studies using Santicizer 154 (a mixture containing TBPP and CASRN 56803-37-3), no biologically significant treatment-related effects were observed in rats gavaged with up to 3,000 mg/kg-day undiluted test substance, while a decrease in viable fetuses and increase in mean post implantation loss was noted at a dose of 5,000 mg/kg-day (NOAEL= 1,000 mg/kg-day). In a study using Phosflex 51B (a mixture containing 75-80% CASRN 56803-37-3), embryotoxicity was indicated by reduced fetal body weight at a dose of 1,000 mg/kg-day; however, this response was considered to be secondary to maternal toxicity. There were no data located for the developmental neurotoxicity endpoint. Decreased cholinesterase activity in pregnant lab animals has been shown to have a negative impact on fetal brain development. As a result, there is uncertain potential for developmental neurotoxicity for this substance.**		

Tris (p-t-butylphenyl) phosphate (TBPP) CASRN 78-33-1				
PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
	Reproduction/ Developmental Toxicity Screen	Groups of 25 pregnant CD rats received 2.5 mL of water or undiluted test substance at doses of 300, 1,000, or 3,000 mg/kg-day via oral gavage on GD 6-19. No adverse effect on maternal survival, behavior, body weight gain, the incidence of gross necropsy findings, or most reproductive/developmental parameters. Slight increase in yellow staining and matting in the anogenital area with or without staining in the abdominal and thoracic areas (1,000 and 3,000 mg/kg-day). Increase in dried red matter in the nasal region on forepaws (3,000 mg/kg-day). Slight, non dose-related increase in the percentage of litters with skeletal malformations at 3,000 mg/kg-day (effect was not considered to be biologically significant). Maternal toxicity: NOAEL: 300 mg/kg-day LOAEL: 1,000 mg/kg-day Developmental toxicity: NOAEL: 3,000 mg/kg-day (highest dose tested) LOAEL: Not established	Submitted confidential study; Bowman, 1981; Keller, 1984	Data are for Santicizer 154; a mixture containing 43.2% t-butyl phenyl diphenyl phosphate (CASRN 56803-37-3), 40.2% triphenyl phosphate (CASRN 115-86-6), 14% di-t-butylphenyl phenyl phosphate (CASRN 2528-36-1) and 2% tri-t-butyl phenyl phosphate (CASRN 78-33-1).
		In a pilot study, pregnant CD rats (5/group) received undiluted Santicizer 154 at doses of 250, 500, 1,000, 2,500,	Submitted confidential study; Bowman, 1981	Data are for Santicizer 154; a mixture containing 43.2% t-butyl phenyl diphenyl phosphate

Tris (p-t-butylphenyl) phosphate (TBPP) CASRN 78-33-1				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		or 5,000 mg/kg-day via oral gavage on gestational days (GD) 6-19. Anogenital staining was observed in all test groups and red and/or brown matter around the nose, mouth, and forelimbs in all receiving 5,000 mg/kg-day. Dose-related reductions in body weight gain for GD 0-20 were observed at ≥ 1,000 mg/kg-day but were only biologically significant at the highest dose. Decreases in viable fetuses and increases in mean post implantation losses (5,000 mg/kg-day) Maternal toxicity: NOAEL: 500 mg/kg-day LOAEL: 1,000 mg/kg-day Developmental toxicity: NOAEL: 2,500 mg/kg-day LOAEL: 5,000 mg/kg-day (reduced body weight gain; decreased number of viable fetuses; increased mean post implantation losses)		(CASRN 56803-37-3), 40.2% triphenyl phosphate (CASRN 115-86-6), 14% di-t-butylphenyl phenyl phosphate (CASRN 2528-36-1) and 2% tri-t-butyl phenyl phosphate (CASRN 78-33-1).
	Combined Repeated Dose with Reproduction/ Developmental Toxicity Screen			No data located.

Tris (p-t-butylphenyl) phosphate (TBPP) CASRN 78-33-1				
PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
	Prenatal Development	Pregnant rats were administered BPDP at doses of 0, 100, 400 and 1,000 mg/kg-day (dosing volume of 5 ml) as a solution in corn on GDs 6-20. Dose-related increase in maternal liver weight. Reduced food consumption on gravid days 6-9 at the high dose. No adverse effects on litter size or fetal weights. No evidence of structural teratogenicity at any dose. Embryotoxicity as indicated by reduced fetal body weight at 1,000 mg/kg; this response was considered secondary to maternal toxicity. Maternal toxicity: NOAEL: 400 mg/kg-day LOAEL: 1,000 mg/kg-day Developmental toxicity: NOAEL: 1,000 mg/kg-day (highest dose tested) LOAEL: Not established	Keller, 1984	Data are for Phosflex 51B; 75-80 percent w/w tertbutylphenyl diphenyl phosphate (CASRN 56803-37-3), 20-25 per cent w/w triphenyl phosphate (CASRN 115-86-6).
	Postnatal Development			No data located.
	Prenatal and Postnatal Development			No data located.

Tris (p-t-butylphenyl) phosphate (TBPP) CASRN 78-33-1				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Developmental Neurotoxicity	There were no data located for the developmental neurotoxicity endpoint. Decreased cholinesterase activity in pregnant lab animals has been shown to have a negative impact on fetal brain development. As a result, there is uncertain potential for developmental neurotoxicity for this substance.	Professional judgment	No data located.
	Other			No data located.
Neurotoxicity		**MODERATE: Based on a 3-week dermal study in rats exposed to Santicizer 154 where cholinesterase inhibition was the major effect at 100 mg/kg-day (NOAEL = 10 mg/kg-day). Experimental data for individual isomers and mixture components of TBPP and analogy to closely related compounds yielded negative results for neurotoxicity in hens and rats. There is a structural alert for the neurotoxicity endpoint based on organophosphates; however, TBPP is not expected to form intermolecular intermediates that may result in neurotoxic mechanisms of action.**		
	Neurotoxicity Screening Battery (Adult)	MIL-H-19457C hydraulic fluid (CASRN 28777-70-0) was found to have minimal toxicity in an acute delayed neurotoxicity test.	Dodd and Smith, 1994	Data are for MIL-H-19457C hydraulic fluid (CASRN 28777-70-0). Limited study details reported in a secondary source. No data on test species, route of exposure, or exposure concentrations.
		In two acute delayed neurotoxicity studies, hens were treated via oral gavage with 1,000 mg/kg test substance 5-7 times per day for 5 days. No adverse effects on mortality or body weight gain. No signs of ataxia; egg production was 50-70% of controls. NOAEL: 1,000 mg/kg (only dose tested) LOAEL: Not established	Submitted confidential study	Data are for CASRN 56803-37-3; only one dose tested.

Tris (p-t-butylphenyl) phosphate (TBPP) CASRN 78-33-1				
PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
		In an acute delayed neurotoxicity study, White Leghorn chickens were treated via oral gavage with 10,000 mg/kg test substance twice a day for 3 days. No signs of ataxia or neurohistopathological lesions. NOAEL: 10,000 mg/kg (only dose tested) LOAEL: Not established	Submitted confidential study	Data are for CASRN 56803-37-3; only one dose tested.
	Other	In a 3-week dermal study, test substance was applied to the intact and abraded skin of New Zealand White rabbits (10/sex/group) at doses levels of 10, 100, or 1,000 mg/kg-day, 5 days/week. No deaths or treatment-related changes in clinical signs, body weight, hematology, clinical chemistry, organ weights, gross or microscopic lesions. Edema and fissuring (1,000 mg/kg-day); atonia (≥ 100 mg/kg-day); desquamation (≥ 10 mg/kg-day); increased blood urea nitrogen (1,000 mg/kg-day); depression of plasma cholinesterase (≥ 100 mg/kg-day); depression of erythrocyte and brain cholinesterase (≥ 10 mg/kg-day). NOAEL: 10 mg/kg-day LOAEL: 100 mg/kg-day (based on cholinesterase inhibition)	Submitted confidential study; Hollister, 1979; Keller, 1984	Data are for Santicizer 154; a mixture containing 43.2% t-butyl phenyl diphenyl phosphate (CASRN 56803-37-3), 40.2% triphenyl phosphate (CASRN 115-86-6), 14% di-t-butylphenyl phenyl phosphate (CASRN 2528-36-1) and 2% tri-t-butyl phenyl phosphate (CASRN 78-33-1).
		In a 90-day study, Sprague-Dawley rats (20/sex/group) were fed diets containing	Submitted confidential study	Data are for CASRN 56803-37-3.

Tris (p-t-butylphenyl) phosphate (TBPP) CASRN 78-33-1				
PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
		0, 100, 400, or 1,600 ppm (average intakes of 0, 6.6, 26.7 or 107.5 mg/kg-day in males and 0, 7.7, 30.0 or 124.8 mg/kg-day in females) test substance. No neurohistopathology and no inhibition of brain cholinesterase activity. NOAEL: 1,600 ppm (107.5 mg/kg-day males, 124.8 mg/kg-day female; highest dose tested) LOAEL: Not established		
		No signs of neurotoxicity in rats following acute gavage administration of Durad 220B at dose levels as high as 5,000 mg/kg	ATSDR, 1997	Data are for Durad 200B (CASRN 28777-70-0); a t-Butylphenyl diphenyl phosphate mixture containing t-Butylphenyl phenyl phosphate (CASRN 220352-35-2) and triphenyl phosphate (CASRN 115-86-6).
		Not neurotoxic by analogy to a closely related compound which yielded negative results in all reliable oral assays for delayed acute neurotoxicity in hens and subchronic neurobehavioral assays in rats	Professional judgment	Data are for CASRN 78-33-1.

Tris (p-t-butylphenyl) phosphate (TBPP) CASRN 78-33-1				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Repeated Dose Effects		**HIGH: Based on weight of evidence for individual isomers and commercial formulation components containing TBPP and CASRN 56803-37-3). In a 90-day inhalation study, rats exposed to Santicizer 154 aerosol showed clinical signs of toxicity, increased liver-body weight-ratios and changes in urinalysis parameters at a concentration of 100 mg/m^3 (0.1 mg/L; NOAEL= 0.01 mg/L). In a 3-week dermal study in rats exposed to Santicizer 154, cholinesterase inhibition was the major effect at 100 mg/kg-day (NOAEL= 10 mg/kg-day). The adrenal gland appeared to be a target organ in some inhalation and oral studies (effects included lesions and increased weight). Several oral toxicity studies using CASRN 56803-37-3, Phosflex 51B (a mixture containing CASRN 56803-37-3) and MIL-H-19457C hydraulic fluid (CASRN 28777-70-0) indicate low concern for toxicity via this route of exposure.**		
		In a 90-day inhalation study, rats (15/sex/group) were exposed to Santicizer-154 aerosol at concentrations of 0, 10 and 100 mg/m^3 (actual) analytical concentrations: 0, 10.1 and 101.1 mg/m^3). No deaths attributed to treatment. Clinical signs of toxicity at the high dose included ptosis, ruffled and discolored fur, rhinitis, sneezing, hemorrhagic conjunctivitis and wheezing. No effect on body weight gain or clinical chemistry. Elevated SGOT and SAP values upon urinalysis of one high dose animal. Increased liver-body weight-ratio in high dose males. No gross or microscopic tissue changes. NOAEL: 10 mg/m^3 (0.01 mg/L) LOAEL: 100 mg/m^3 (0.1 mg/L)	Clayton, 1983; Keller, 1984	Data are for Santicizer 154; a mixture containing 43.2% t-butyl phenyl diphenyl phosphate (CASRN 56803-37-3), 40.2% triphenyl phosphate (CASRN 115-86-6), 14% di-t-butylphenyl phenyl phosphate (CASRN 2528-36-1) and 2% tri-t-butyl phenyl phosphate (CASRN 78-33-1).
		In a 3-week dermal study, test substance was applied to the intact and abraded skin of New Zealand White rabbits (10/sex/group) at doses levels of 10,	Submitted confidential study; Hollister, 1979; Keller, 1984	Data are for Santicizer 154; a mixture containing 43.2% t-butyl phenyl diphenyl phosphate (CASRN 56803-37-3), 40.2%

Tris (p-t-butylphenyl) phosphate (TBPP) CASRN 78-33-1				
PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
		100, or 1,000 mg/kg-day, 5 days/week. No deaths or treatment-related changes in clinical signs, body weight, hematology, clinical chemistry, organ weights, gross or microscopic lesions. Edema and fissuring (1,000 mg/kg-day); atonia (≥ 100 mg/kg-day); desquamation (≥ 10 mg/kg-day); increased blood urea nitrogen (1,000 mg/kg-day); depression of plasma cholinesterase (≥ 100 mg/kg-day); depression of erythrocyte and brain cholinesterase (≥ 10 mg/kg-day). NOAEL: Not established LOAEL: 10 mg/kg-day (Lowest dose tested; desquamation, decreased erythrocytes and brain cholinesterase)		triphenyl phosphate (CASRN 115-86-6), 14% di-t-butylphenyl phenyl phosphate (CASRN 2528-36-1) and 2% tri-t-butyl phenyl phosphate (CASRN 78-33-1).
		In a 90-day study, Sprague-Dawley rats (20/sex/group) were fed diets containing 0, 100, 400, or 1,600 ppm (average intakes of 0, 6.6, 26.7 or 107.5 mg/kg-day in males and 0, 7.7, 30.0 or 124.8 mg/kg-day in females) test substance. No significant effect on survival, food consumption, body weight gain, hematology or clinical chemistry parameters, cholinesterase values, or the incidence of gross or microscopic lesions. Increased liver, kidney, and adrenal gland weight (1600 ppm). NOAEL: 400 ppm (26.7 mg/kg-day for	Submitted confidential study; Keller, 1984; Environment Agency, 2009	Data are for Phosflex 51B; 75-80 percent w/w tertbutylphenyl diphenyl phosphate (CASRN 56803-37-3), 20-25 percent w/w triphenyl phosphate (CASRN 115-86-6).

Tris (p-t-butylphenyl) phosphate (TBPP) CASRN 78-33-1				
PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
		males and 30 mg/kg-day for females) LOAEL: 1600 ppm (107.5 mg/kg-day for males and 124.8 mg/kg-day for females); (based on organ weight changes)		
		In a 30-day study, Sprague-Dawley rats (10/sex/group) were fed diets containing 0, 250, 500, 750, 1,000, or 2,000 mg/kg-day (nominal doses of 213, 442, 660, 898, and 1,710 mg/kg-day for males and 234, 454, 690, 898, and 1,867 mg/kg-day for females) test chemical. No deaths. Reduced food consumption (2,000 mg/kg-day) and body weight gain (≥750 mg/kg-day); hepatic enlargement (all doses); discoloration of kidneys (≥500 mg/kg-day) NOAEL: Not established LOAEL: 250 mg/kg-day (hepatic enlargement; lowest dose tested)	Submitted confidential study; Keller, 1984	Data are for CASRN 56803-37-3; study deficiencies include lack of examinations for histopathology, hematology, or clinical chemistry.
		In a 90-day dietary study, CD rats were fed 0 or 5 mg/kg-day test substance. There were no compound-related effects on any parameter tested. NOAEL: 5 mg/kg-day (only dose tested) LOAEL: Not established	Keller, 1984	Data are for CASRN 56803-37-3.
		In a 90-day dietary study, rats were fed BPDP at concentrations of 0, 100, 300 or 1,000 ppm (11, 32, and 110 mg/kg-day). There were no clinical signs of	Matheson, 1980	Data are for CASRN 56803-37-3. Doses were reported as ppm in the diet but were converted to mg/kg-day using EPA 1988 reference

Tris (p-t-butylphenyl) phosphate (TBPP) CASRN 78-33-1				
PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
		toxicity. No effect on hematology, clinical chemistry, or urinalysis parameters. No gross pathologic or microscopic lesions attributed to the BPDP. NOAEL: 1,000 ppm (110 mg/kg-day; highest dose tested) LOAEL: Not established		values for body weight and food consumption.
		In a 90-day dietary study, albino rats were fed diets containing 0, 200, 1,000 or 5,000 ppm (0, 21, 110, and 530 mg/kg-day) test substance. No deaths or effect on body weight gain, food intake, hematology, clinical chemistry or urinalysis parameters. Increased mean liver and kidney weight with no associated histopathologic findings. NOAEL: 5,000 ppm (530 mg/kg-day; highest dose tested) LOAEL: Not established	Keller, 1984	Data are for CASRN 56803-37-3. Doses were reported as ppm in the diet but were converted to mg/kg-day using EPA 1988 reference values for body weight and food consumption.
		Rats, hamsters and rabbits were exposed to MIL-H-19457C hydraulic fluid (CASRN 28777-70-0) via inhalation 6 hours/day at a concentration of 250 mg/m^3 for 21 days or 0, 10 and 100 mg/m^3 for 90 days. Effects were only observed in rats and consisted of increased liver and kidney weight (100 and 250 mg/m^3) and lesions in the adrenal glands and ovaries (90 day	Dodd and Smith, 1994	Data are for MIL-H-19457C hydraulic fluid (CASRN 28777-70-0).

Tris (p-t-butylphenyl) phosphate (TBPP) CASRN 78-33-1				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		exposure).		
		Rats were administered ML-H-19457C (CASRN 28777-70-0) and tricresyl phosphate (TCP) daily via oral gavage for up to 10 weeks (doses not specified). No mortality occurred and there was no effect on body weight gain in either sex. Target organs were the adrenal gland and the liver. The estrous cycle was extended for high dose females administered ML-ML-H-19457C and relative testes weights were increased. Effects were reversed at 5 and 10 weeks post-treatment.	Dodd and Smith, 1994	Data are for MIL-H-19457C hydraulic fluid (CASRN 28777-70-0); doses not specified.
		Potential for systemic effects by analogy to triphenyl phosphate (115-86-6), including 28-d repeated-dose study (inadequate), rats, diet, liver effects at 0.5%. NOAEL: 0.1%	Professional judgment	Estimated by analogy to Triphenyl Phosphate (115-86-6); Study was determined to be inadequate and does not satisfy standard guidelines.
Skin Sensitization		**MODERATE: TBPP is expected to have low concern for sensitization by analogy to closely related compounds.**		
	Skin Sensitization	Moderate concern for sensitization by analogy to isobutylphenyl phosphate (68937-40-6) (Estimated based on analogy)	Professional judgment	Estimated based on analogy to Isobutylphenyl phosphate (68937-40-6).
Respiratory Sensitization		**No data located.**		
	Respiratory Sensitization			No data located.

Tris (p-t-butylphenyl) phosphate (TBPP) CASRN 78-33-1				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Eye Irritation		**LOW: Based on experimental data for mixture components of TBPP. Phosflex 51B (a commercial mixture containing 75-80% CASRN 56803-37-3), produced slight irritation in rabbit eyes which cleared within 72 hours. Additional studies with CASRN 56803-37-3 were negative for irritation.**		
	Eye Irritation	Slightly irritating, rabbits. Mild redness of the conjunctiva 24- and 48-hours after treatment; no irritation at 72- or 96-hours or 7 days after treatment.	Environment Agency, 2009	Data are for Phosflex 51B; 75-80 percent w/w tertbutylphenyl diphenyl phosphate (CASRN 56803-37-3), 20-25 percent w/w triphenyl phosphate (CASRN 115-86-6); study details reported in a secondary source.
		Not irritating, rabbits	Submitted confidential study; Bowman, 1981	Data are for CASRN 56803-37-3.
		Not irritating, rabbits. Mild conjunctival inflammation 1 hour after exposure, but no evidence of irritation by 24 hours.	Submitted confidential study; Murphy, 1979	Data are for CASRN 56803-37-3; conducted in accordance with OECD Guideline 405
Dermal Irritation		**MODERATE: Based on weight of evidence from experimental data for mixture components of TBPP. Phosflex 51B (a commercial mixture containing 75-80% CASRN 56803-37-3), produced mild irritation in rabbits, which cleared within 72 hours. Additional studies using CASRN 56803-37-5 resulted in very slight or well-defined erythema in rabbits that persisted for 8-10 days and slight destruction of guinea pig skin, but only when the test substance was dissolved in Stoddard`s solution. A study using mixture component 78-33-1 was not irritating to rabbits.**		
	Dermal Irritation	Mildly irritating, rabbits. Mild to moderate erythema 24 hours after treatment; mild erythema at 48 hours; no irritation at 72 hours	Environment Agency, 2009	Data are for Phosflex 51B; 75-80 percent w/w tertbutylphenyl diphenyl phosphate (CASRN 56803-37-3), 20-25 percent w/w triphenyl phosphate (CASRN 115-86-6)
		Very slight or well-defined erythema (with or without very slight edema) persisting though day 8 and day 10 in rabbits	Submitted confidential study; Latendresse, 1994	Data are for CASRN 56803-37-3; conducted in accordance with OECD Guideline 404
		Not irritating, rabbits. Phosphen	Hagerman, 1984	Data are for CASRN 78-33-1;

Tris (p-t-butylphenyl) phosphate (TBPP) CASRN 78-33-1				
PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
		plasticiser P-7 applied as a 10% solution in butyl carbitol acetate to the shaven ear and belly. Very slight irritation on the belly, but only after repeated and prolonged exposure.		phosphen plasticiser P-7
		Not irritating, rabbits	Submitted confidential study; Bowman, 1981	Data are for CASRN 56803-37-3
		Not irritating, rabbits	ATSDR, 1997	Data are for Durad 200B (CASRN 28777-70-0); a t-Butylphenyl diphenyl phosphate mixture containing t-Butylphenyl phenyl phosphate (CASRN 220352-35-2) and triphenyl phosphate (CASRN 115-86-6)
		CASRN 56803-37-5 produced slight destruction of tissue in guinea pig skin when dissolved in Stoddard's solution. No irritation occurred when the test substance was dissolved in ethyl alcohol or tertiary butyl alcohol.	Fabian, 1982	Data are for CASRN 56803-37-5

Tris (p-t-butylphenyl) phosphate (TBPP) CASRN 78-33-1			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
Endocrine Activity	**No data were available for TBPP. Rats exposed to hydraulic BTP (mixture of p-t-butylphenyl phenyl phosphates (84%), triphenyl phosphate, and m-t-phenyl phosphate), had significantly prolonged diestrus, hypertrophy and cholesteryl lipidosis of adrenocortical and ovarian interstitial cells and minimal degeneration in the adrenal cortex and ovary. Lesions on the adrenal glands and ovaries were observed in rats, hamsters and rabbits and relative testes weight was increased in rats following inhalation exposure to MIL-H-19457C hydraulic fluid (CASRN 28777-70-0). Adrenal weights were increased in rats after dietary exposure to Phosflex 51B.**		
	In an oral study, male and female rats were administered hydraulic BTP at doses of 0 or 1.7 g/kg-day (0 or 1,700 mg/kg-day) via gavage in sesame oil or 2.8 g/kg (2,800 mg/kg) neat hydraulic BTP for 20, 40 and 60 days. Hypertrophy and cholesteryl lipidosis of adrenocortical and ovarian interstitial cells; minimal degeneration in the adrenal cortex and ovary. No decreased testicular weight or degeneration of seminiferous tubules.	Latendresse et al., 1994a	Data are for CASRN 220352-35-2; mixture of p-t-butylphenyl phenyl phosphates (84%), triphenyl phosphate, and m-t-phenyl phosphate.
	In an oral study, groups of intact and ovariectomized female rats were administered BTP at doses of 0 or 1.7 g/kg-day (0 or 1,700 mg/kg-day) via oral gavage in sesame oil vehicle or as neat BTP for 20, 40 or 60 days. Cholesteryl lipidosis in AC and OI cells; elevated estradiol levels (14.5 times greater than controls). No effect on serum concentrations of androstenedione and corticosterone. Abnormal reproductive cycles in treated females that were significantly prolonged in diestrus. Increased liver	Latendresse et al., 1993; Latendresse, 1994	Data are for CASRN 220352-35-2; mixture of p-t-butylphenyl phenyl phosphates (84%), triphenyl phosphate, and m-t-phenyl phosphate.

Tris (p-t-butylphenyl) phosphate (TBPP) CASRN 78-33-1			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	weights (134% that of controls) and P-450 enzymes (3 times greater than controls).		
	Rats were administered ML-H-19457C (CASRN 28777-70-0) and TCP daily via oral gavage for up to 10 weeks (doses not specified). No mortality occurred and there was no effect on body weight gain in either sex. Target organs were the adrenal gland and the liver. The estrous cycle was extended for high dose females administered ML-ML-H-19457C and relative testes weights were increased. Effects were reversed at 5 and 10 weeks post-treatment.	Dodd and Smith, 1994	Data are for MIL-H-19457C hydraulic fluid (CASRN 28777-70-0); doses not specified.
	Rats, hamsters and rabbits were exposed to MIL-H-19457C hydraulic fluid (CASRN 28777-70-0) via inhalation 6 hours/day at a concentration of 250 mg/m^3 for 21 days or 0, 10 and 100 mg/m^3 for 90 days. Effects were only observed in rats; lesions in the adrenal glands and ovaries (90 day exposure).	Dodd and Smith, 1994	Data are for MIL-H-19457C hydraulic fluid (CASRN 28777-70-0).
	In a 90-day study, Sprague-Dawley rats (20/sex/group) were fed diets containing 0, 100, 400, or 1,600 ppm (average intakes of 0, 6.6, 26.7 or 107.5 mg/kg-day in males and 0, 7.7, 30.0 or 124.8 mg/kg-day in females) test substance. Adrenal weight was increased at 1,600 ppm.	Submitted confidential study; Keller, 1984; Environment Agency, 2009	Data are for Phosflex 51B; 75-80 percent w/w tertbutylphenyl diphenyl phosphate (CASRN 56803-37-3), 20-25 percent w/w triphenyl phosphate (CASRN 115-86-6).

Tris (p-t-butylphenyl) phosphate (TBPP) CASRN 78-33-1			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	NOAEL: 400 ppm (26.7 mg/kg-day for males and 30 mg/kg-day for females) LOAEL: 1600 ppm (107.5 mg/kg-day for males and 124.8 mg/kg-day for females); (based on organ weight changes)		
Immunotoxicity	**No data located.**		
Immune System Effects			No data located.
ECOTOXICITY			
ECOSAR Class			
Acute Aquatic Toxicity	**VERY HIGH: Based on experimental data for mixture components of TBPP for fish and daphnia. Experimental data for algae indicates HIGH hazard concern. The reported water solubility values from studies on commercial mixtures may not adequately represent all components of the mixture. The TBPP isomers and t-butyl substituted phenyl phosphate esters anticipated to be present in the commercial product are expected to have a range of water solubility values. Therefore NES may be predicted for some components but not others.**		
Fish LC_{50}	Freshwater fish (*Ictalurus punctatus*) 96-hour LC_{50} = 0.8 mg/L static test conditions (Experimental)	Cleveland et al., 1986 (as cited in Environment Agency, 2009)	Data are for a commercial tertbutylphenyl diphenyl phosphate product consisting of 15 - 20 percent triphenyl phosphate (CASRN 115-86-6) with the remainder consisting mainly of a mixture of isomers of tertbutylphenyl diphenyl phosphate (CASRN 56803-37-3) , along with isomers of di-tertbutylphenyl diphenyl phosphate (CASRN 65652-41-7).
	Freshwater fish (*Oncorhynchus mykiss*) 96-hour LC_{50} = 1.1 mg/L (Experimental)	Submitted confidential study	Data are for t-Butylphenyl diphenyl phosphate (CASRN 56803-37-3). The available acute toxicity data for fish, aquatic

Tris (p-t-butylphenyl) phosphate (TBPP) CASRN 78-33-1			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
			invertebrates, and algae were judged inadequate to meet the endpoints; summary did not provide sufficient information regarding study conditions, including test substance purity or water solubility, to allow for an independent evaluation of the studies.
	Freshwater fish (*Oncorhynchus mykiss*) 96-hour LC_{50} = 2.0 mg/L static test conditions (Experimental)	Cleveland et al., 1986 (as cited in Environment Agency, 2009)	Data are for a commercial tertbutylphenyl diphenyl phosphate product consisting of 15 - 20 percent triphenyl phosphate (CASRN 115-86-6) with the remainder consisting mainly of a mixture of isomers of tertbutylphenyl diphenyl phosphate (CASRN 56803-37-3) , along with isomers of di-tertbutylphenyl diphenyl phosphate (CASRN 65652-41-7).
	Freshwater fish (*Salmo gairdneri*) 96-hour LC_{50} = 2.0 mg/L 96-hour NOEC = 0.56 mg/L 24-hour LC_{50} = 26 mg/L 48-hour LC_{50} = 13 mg/L (Experimental)	Bucafusco, 1976b	Data are for Santicizer 154; a mixture containing 43.2% t-butyl phenyl diphenyl phosphate (CASRN 56803-37-3), 40.2% triphenyl phosphate (CASRN 115-86-6), 14% di-t-butylphenyl phenyl phosphate (CASRN 2528-36-1) and 2% tri-t-butyl phenyl phosphate (CASRN 78-33-1).
	Freshwater fish (*Pimephales promelas*) 96-hour LC_{50} = 2.3 mg/L static test conditions	Cleveland et al., 1986 (as cited in Environment Agency, 2009)	Data are for a commercial tertbutylphenyl diphenyl phosphate product consisting of

Tris (p-t-butylphenyl) phosphate (TBPP) CASRN 78-33-1			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	(Experimental)		15 - 20 percent triphenyl phosphate (CASRN 115-86-6) with the remainder consisting mainly of a mixture of isomers of tertbutylphenyl diphenyl phosphate (CASRN 56803-37-3), along with isomers of di-tertbutylphenyl diphenyl phosphate (CASRN 65652-41-7).
	Freshwater fish (*Oncorhynchus mykiss*) 96-hour LC_{50} = 2.4 - 5.4 mg/L static test conditions (Experimental)	Akzo Nobel, 2003 (as cited in Environment Agency, 2009)	Data are for t-Butylphenyl diphenyl phosphate (CASRN 56803-37-3).
	Freshwater fish (*Lepomis macrochirus*) 96-hour LC_{50} = 3.1 mg/L static test conditions (Experimental)	Cleveland et al., 1986 (as cited in Environment Agency, 2009)	Data are for a commercial tertbutylphenyl diphenyl phosphate product consisting of 15 - 20 percent triphenyl phosphate (CASRN 115-86-6) with the remainder consisting mainly of a mixture of isomers of tertbutylphenyl diphenyl phosphate (CASRN 56803-37-3), along with isomers of di-tertbutylphenyl diphenyl phosphate (CASRN 65652-41-7).
	Freshwater fish (*Pimephales promelas*) 96-hour LC_{50}= 3.4 mg/L 96-hour NOEC < 1.0 mg/L 24-hour LC_{50} > 10 < 32 mg/L 48-hour LC_{50} = 4.0 mg/L (Experimental)	Monsanto, 1976	Data are for Santicizer 154; a mixture containing 43.2% t-butyl phenyl diphenyl phosphate (CASRN 56803-37-3), 40.2% triphenyl phosphate (CASRN 115-86-6), 14% di-t-butylphenyl phenyl phosphate (CASRN 2528-36-1) and 2% tri-t-butyl phenyl

Tris (p-t-butylphenyl) phosphate (TBPP) CASRN 78-33-1			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
			phosphate (CASRN 78-33-1).
	Freshwater fish (*Pimephales promelas*) 96-hour LC_{50} > 0.268 - 0.647 mg/L Measured exposure concentrations were not high enough to cause 50% mortality. The highest concentrations in clean and sediment pond tests were 0.286 - 0.647 mg/L. (Experimental)	Adams et al., 1983	Data are for Santicizer 154; a mixture containing 43.2% t-butyl phenyl diphenyl phosphate (CASRN 56803-37-3), 40.2% triphenyl phosphate (CASRN 115-86-6), 14% di-t-butylphenyl phenyl phosphate (CASRN 2528-36-1) and 2% tri-t-butyl phenyl phosphate (CASRN 78-33-1).
	Freshwater fish (*Cyprinodon variegatus*) 96-hour LC_{50} ≥1 mg/L NOEC = 1 mg/L static-renewal test conditions (Experimental)	Akzo Nobel, 2001	Data are for CASRN 220352-35-2 (75-80% w/w; impurity: 20-25% w/w triphenyl phosphate (CASRN 115-86-6)). Study was conducted according to OECD Guideline 203; details reported in a secondary source.
	Freshwater fish (*Lepomis macrochirus*) 96-hour LC_{50} > 10 < 12 mg/L 24-hour LC_{50} = 35 mg/L 48-hour LC_{50} = 14 mg/L (Experimental)	Bucafusco, 1976a	Data are for Santicizer 154; a mixture containing 43.2% t-butyl phenyl diphenyl phosphate (CASRN 56803-37-3), 40.2% triphenyl phosphate (CASRN 115-86-6), 14% di-t-butylphenyl phenyl phosphate (CASRN 2528-36-1) and 2% tri-t-butyl phenyl phosphate (CASRN 78-33-1); values are well above reported water solubility values; NES may be predicted.
	Freshwater fish 96-hour LC_{50} < 0.001 mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	Data are for Tris(p-t-butylphenyl) phosphate (CASRN 78-33-1). NES: The log K_{ow} of 10 for this chemical exceeds the SAR

Tris (p-t-butylphenyl) phosphate (TBPP) CASRN 78-33-1			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
			limitation for the log K_{ow} of 5.0; NES are predicted for these endpoints. Estimate for the Esters class was provided for comparative purposes. See Section 5.5.1.
	Freshwater fish (*Lepomis macrochirus*) 96-hour LC_{50} = 1.0 mg/L (Experimental)	Submitted confidential study	Data are for t-Butylphenyl diphenyl phosphate (CASRN 56803-37-3). The available acute toxicity data for fish, aquatic invertebrates, and algae were judged inadequate to meet the endpoints; summary did not provide sufficient information regarding study conditions, including test substance purity or water solubility, to allow for an independent evaluation of the studies.
	Freshwater fish (*Oncorhynchus mykiss*) 96-hour LC_{50} = 5.4 mg/L static test conditions (Experimental)	Union Carbide, 1978 (as cited in Environment Agency, 2009)	Data are for t-Butylphenyl diphenyl phosphate (CASRN 56803-37-3; Fyrquel GT). The test report indicates that the test substance formed an oily film on the surface of the water for all concentrations tested and the result is considered to be invalid as undissolved test material appeared to be present.
	Freshwater fish (*Oncorhynchus mykiss*)	IUCLID, 2001 (as cited in	Data are for t-Butylphenyl

Tris (p-t-butylphenyl) phosphate (TBPP) CASRN 78-33-1			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	96-hour LC_{50} = 13.7 mg/L flow-through test conditions (Experimental)	Environment Agency, 2009)	diphenyl phosphate (CASRN 56803-37-3). The reported LC_{50} is well above the water solubility of the test substance; effect level is well above the estimated water solubility therefore NES can be predicted.
	Freshwater fish 96-hour LC_{50} = 0.77 mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	Data are for t-Butylphenyl diphenyl phosphate (CASRN 56803-37-3). NES: The log K_{ow} of 5.12 for this chemical exceeds the SAR limitation for the log K_{ow} of 5.0; NES are predicted for these endpoints. Estimate for the Esters class was provided for comparative purposes. See Section 5.5.1.
	Freshwater fish 96-hour LC_{50} = 0.009 mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	Data are for Bis(t-butylphenyl) phenyl phosphate (CASRN 65652-41-7). NES: The log K_{ow} of 8.5 for this chemical exceeds the SAR limitation for the log K_{ow} of 5.0; NES are predicted for these endpoints. Estimate for the Esters class was provided for comparative purposes. See Section 5.5.1.

Tris (p-t-butylphenyl) phosphate (TBPP) CASRN 78-33-1			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
Daphnid LC_{50}	*Daphnia magna* 48-hour EC_{50} = 0.25 mg/L (Experimental)	Adams and Heidolph, 1985 (as cited in Environment Agency, 2009)	Data are for TB220-H; tertbutylphenyl phosphate (CASRN 78-33-1) with 18 percent triphenyl phosphate (115-86-6); effect level higher than the estimated water solubility therefore NES can be predicted.
	Daphnia magna 48-hour EC_{50} = 0.289 - 0.321 mg/L, mean measured values field tests from sediment or clean ponds, static conditions. (Experimental)	Adams et al., 1983	Data are for Santicizer 154; a mixture containing 43.2% t-butyl phenyl diphenyl phosphate (CASRN 56803-37-3), 40.2% triphenyl phosphate (CASRN 115-86-6), 14% di-t-butylphenyl phenyl phosphate (CASRN 2528-36-1) and 2% tri-t-butyl phenyl phosphate (CASRN 78-33-1).
	Daphnia magna 48-hour LC_{50} = 0.30 mg/L (Experimental)	Submitted confidential study	Data are for CASRN 56803-37-3; tertbutylphenyl diphenyl phosphate (purity not given); effect level higher than the estimated water solubility therefore NES can be predicted.
	Daphnia magna 48-hour EC_{50} = 0.30 mg/L (Experimental)	Ziegenfuss et al., 1986 (as cited in Environment Agency, 2009)	Data are for Santicizer 154; a mixture of tertbutylphenyl diphenyl phosphate (CASRN 56803-37-3), di-tertbutylphenyl phenyl phosphate (65652-41-7) and triphenyl phosphate (115-86-6).
	Daphnia magna 48-hour EC_{50} = 1.1 mg/L (Experimental)	Adams and Heidolph, 1985 (as cited in Environment Agency, 2009)	Data are for TB220-L; tertbutylphenyl diphenyl phosphate (CASRN 56803-37-3) with less than 1 percent triphenyl

Tris (p-t-butylphenyl) phosphate (TBPP) CASRN 78-33-1			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
			phosphate (115-86-6); effect level higher than the estimated water solubility therefore NES can be predicted.
	Daphnia magna 48-hour EC_{50} = 2.9 mg/L (Experimental)	Sanders et al., 1985 (as cited in Environment Agency, 2009)	Data are for Fyrquel GT; commercial tertbutylphenyl diphenyl phosphate product (purity not given).
	Daphnia magna 48-hour EC_{50} = 5.0 mg/L (Experimental)	Sanders et al., 1981	Data are for Santicizer 154; a mixture containing 43.2% t-butyl phenyl diphenyl phosphate (CASRN 56803-37-3), 40.2% triphenyl phosphate (CASRN 115-86-6), 14% di-t-butylphenyl phenyl phosphate (CASRN 2528-36-1) and 2% tri-t-butyl phenyl phosphate (CASRN 78-33-1); effect level marginally higher than the estimated water solubility of the commercial mixture, therefore NES may be predicted.
	Daphnia magna 48-hour LC_{50} = 1.15 mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	Data are for t-Butylphenyl diphenyl phosphate (CASRN 56803-37-3). NES: The log K_{ow} of 5.12 for this chemical exceeds the SAR limitation for the log K_{ow} of 5.0; NES are predicted for these endpoints. Estimate for the Esters class was provided for comparative purposes.

Tris (p-t-butylphenyl) phosphate (TBPP) CASRN 78-33-1			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
			See Section 5.5.1.
	Daphnia magna 48-hour LC_{50} = 0.009 mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	Data are for Bis(t-butylphenyl) phenyl phosphate (CASRN 65652-41-7). NES: The log K_{ow} of 8.5 for this chemical exceeds the SAR limitation for the log K_{ow} of 5.0; NES are predicted for these endpoints. Estimate for the Esters class was provided for comparative purposes. See Section 5.5.1.
	Daphnia magna 48-hour LC_{50} < 0.001 mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	Data are for Tris(p-t-butylphenyl) phosphate (CASRN 78-33-1). NES: The log K_{ow} of 10 for this chemical exceeds the SAR limitation for the log K_{ow} of 5.0; NES are predicted for these endpoints. Estimate for the Esters class was provided for comparative purposes. See Section 5.5.1.
Other Invertebrate LC_{50}	Mysid shrimp (*Mysidopsis bahia*) 96-hour EC_{50} = 0.39 mg/L NOEC = 0.22 mg/L (Experimental)	Akzo Nobel, 2001	Data are for CASRN 220352-35-2 (75-80% w/w; impurity: 20-25% w/w triphenyl phosphate (CASRN 115-86-6)). Study conducted according to OECD Guide-line 202, part 1; details reported in a

Tris (p-t-butylphenyl) phosphate (TBPP) CASRN 78-33-1			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
			secondary source.
Green Algae EC_{50}	Green algae (*Selenastrum capricornutum*) 96-hour EC_{50} (total biomass) = 2.6 mg/L 96-hour EC_{50} (chlorophyll A) = 3.0 mg/L (Experimental)	IUCLID, 2001 (as cited in Environment Agency, 2009)	Data are for CASRN 220352-35-2 (75-80% w/w; impurity: 20-25% w/w triphenyl phosphate (CASRN 115-86-6)). Study details reported in a secondary source.
	Green algae (*Selenastrum capricornutum*) 96-hour EC_{50} = 3.0 mg/L 24-hour EC_{50} > 10 mg/L 48-hour EC_{50} = 5.9 mg/L 72-hour EC_{50} = 3.4 mg/L (Experimental)	Hollister, 1979	Data are for Santicizer 154; a mixture containing 43.2% t-butyl phenyl diphenyl phosphate (CASRN 56803-37-3), 40.2% triphenyl phosphate (CASRN 115-86-6), 14% di-t-butylphenyl phenyl phosphate (CASRN 2528-36-1) and 2% tri-t-butyl phenyl phosphate (CASRN 78-33-1).
	Green algae (*Selenastrum capricornutum*) 14-day NOEC = 1 mg/L 14-day LOEC = 10 mg/L (Experimental)	Sanders et al., 1985 (as cited in Environment Agency, 2009)	Data are for Fyrquel GT, a commercial tertbutylphenyl diphenyl phosphate product (composition not given).
	Green algae 96-hour LC_{50} = 0.30 mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	Data are for t-Butylphenyl diphenyl phosphate (CASRN 56803-37-3); The log K_{ow} of 5.1 for this chemical exceeds the SAR limitation for the log K_{ow} of 6.4; Estimate for the Esters class was provided for comparative

Tris (p-t-butylphenyl) phosphate (TBPP) CASRN 78-33-1			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
			purposes. See Section 5.5.1.
	Green algae 96-hour LC_{50} = 0.001 mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	Data are for Bis(t-butylphenyl) phenyl phosphate (CASRN 65652-41-7). NES: The log K_{ow} of 8.5 for this chemical exceeds the SAR limitation for the log K_{ow} of 6.4; NES are predicted for these endpoints. Estimate for the Esters class was provided for comparative purposes. See Section 5.5.1.
	Green algae 96-hour LC_{50} < 0.001 mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	Data are for Tris(p-t-butylphenyl) phosphate (CASRN 78-33-1). NES: The log K_{ow} of 10 for this chemical exceeds the SAR limitation for the log K_{ow} of 6.4; NES are predicted for these endpoints. Estimate for the Esters class was provided for comparative purposes. See Section 5.5.1.

Tris (p-t-butylphenyl) phosphate (TBPP) CASRN 78-33-1			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
Chronic Aquatic Toxicity	**VERY HIGH: Based on experimental NOEC values for mixture components of TBPP for fish and daphnia. The reported water solubility values from studies on commercial mixtures may not adequately represent all components of the mixture. The TBPP isomers and t-butyl substituted phenyl phosphate esters components anticipated to be present in the commercial product are expected to have a range of water solubility values. Therefore NES may be predicted for some components but not others.**		
Fish ChV	Freshwater fish (*Pimephales promelas*) 30-day NOEC (mortality) = 0.093 mg/L 30-day NOEC (growth) = 0.194 mg/L (Experimental)	Cleveland et al., 1986 (as cited in Environment Agency, 2009)	Data are for a commercial tertbutylphenyl diphenyl phosphate product consisting of 15 - 20 percent triphenyl phosphate (CASRN 115-86-6) with the remainder consisting mainly of a mixture of isomers of tertbutylphenyl diphenyl phosphate (CASRN 56803-37-3), along with isomers of di-tertbutylphenyl diphenyl phosphate (CASRN 65652-41-7).
	Freshwater fish ChV = 0.03 mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	Data are for t-Butylphenyl diphenyl phosphate (CASRN 56803-37-3) Estimate for the Esters class was provided for comparative purposes. See Section 5.5.1.
	Freshwater fish ChV < 0.001 mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	Data are for Bis(t-butylphenyl) phenyl phosphate (CASRN 65652-41-7). NES: The log K_{ow} of 8.5 for this chemical exceeds the SAR limitation for the log K_{ow} of 8.0; NES are predicted for these endpoints. Estimate for the Esters class was

Tris (p-t-butylphenyl) phosphate (TBPP) CASRN 78-33-1			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
			provided for comparative purposes. See Section 5.5.1.
	Freshwater fish ChV < 0.001 mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	Data are for Tris(p-t-butylphenyl) phosphate (CASRN 78-33-1). NES: The log K_{ow} of 10 for this chemical exceeds the SAR limitation for the log K_{ow} of 8.0; NES are predicted for these endpoints. Estimate for the Esters class was provided for comparative purposes. See Section 5.5.1.
Daphnid ChV	*Daphnia magna* 21-day LOEC (mortality) < 0.1 mg/L NOEC (mortality and reproduction) = 0.04 mg/L (Experimental)	Akzo Nobel, 2001	Data are for CASRN 220352-35-2 (75-80% w/w; impurity: 20-25% w/w triphenyl phosphate (CASRN 115-86-6)). Study details reported in a secondary source.
	Daphnia magna 21-day NOEC (survival and reproduction) = 0.01 mg/L (Experimental)	Sanders et al., 1985 (as cited in Environment Agency, 2009)	Data are for Santicizer 154; a commercial tertbutylphenyl diphenyl phosphate product (purity not given).
	Daphnia magna 21-day NOEC = 0.03 mg/L (Experimental)	Sanders et al., 1985 (as cited in Environment Agency, 2009)	Data are for TB220-L; tertbutylphenyl diphenyl phosphate (CASRN 56803-37-3) with less than 1 percent triphenyl phosphate (115-86-6); effect level higher than the estimated water

Tris (p-t-butylphenyl) phosphate (TBPP) CASRN 78-33-1			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
			solubility therefore NES can be predicted.
	Daphnia magna 21-day NOEC = 0.03 mg/L (Experimental)	Sanders et al., 1985 (as cited in Environment Agency, 2009)	Data are for TB220-H; tertbutylphenyl phosphate (CASRN 78-33-1) with 18 percent triphenyl phosphate (115-86-6).
	Daphnia magna 21-day NOEC (survival and reproduction) = 0.032 mg/L (Experimental)	Sanders et al., 1985 (as cited in Environment Agency, 2009)	Data are for Fyrquel GT; a commercial tertbutylphenyl diphenyl phosphate product (purity not given).
	Daphnia magna 21-day NOEC = 0.04 mg/L (Experimental)	Adams and Heidolph et al., 1985 (as cited in Environment Agency, 2009)	Data are for Santicizer 154; a mixture of tertbutylphenyl diphenyl phosphate (CASRN 56803-37-3), di-tertbutylphenyl phenyl phosphate (65652-41-7) and triphenyl phosphate (115-86-6).
	Daphnia magna 21-day NOEC >0.204 - 0.461 mg/L, mean measured values 21-day MATC > 0.0236 - 0.0524 mg/L, field tests from sediment or clean ponds, static conditions (Experimental)	Adams et al., 1983	Data are for Santicizer 154; a mixture containing 43.2% t-butyl phenyl diphenyl phosphate (CASRN 56803-37-3), 40.2% triphenyl phosphate (CASRN 115-86-6), 14% di-t-butylphenyl phenyl phosphate (CASRN 2528-36-1) and 2% tri-t-butyl phenyl phosphate (CASRN 78-33-1).
	Daphnia magna ChV = 0.32 mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	Data are for t-Butylphenyl diphenyl phosphate (CASRN 56803-37-3). Estimate for the Esters class was provided for comparative purposes.

Tris (p-t-butylphenyl) phosphate (TBPP) CASRN 78-33-1			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
			See Section 5.5.1.
	Daphnia magna ChV < 0.001 mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	Data are for Tris(p-t-butylphenyl) phosphate (CASRN 78-33-1). NES: The log K_{ow} of 10 for this chemical exceeds the SAR limitation for the log K_{ow} of 8.0; NES are predicted for these endpoints. Estimate for the Esters class was provided for comparative purposes. See Section 5.5.1.
	Daphnia magna 48-hour ChV < 0.001 mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	Data are for Bis(t-butylphenyl) phenyl phosphate (CASRN 65652-41-7). NES: The log K_{ow} of 8.5 for this chemical exceeds the SAR limitation for the log K_{ow} of 8.0; NES are predicted for these endpoints. Estimate for the Esters class was provided for comparative purposes. See Section 5.5.1.

Tris (p-t-butylphenyl) phosphate (TBPP) CASRN 78-33-1			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
Green Algae ChV	Green algae (*Selenastrum capricornutum*) 14-day NOEC = 1 mg/L 14-day LOEC = 10 mg/L (Experimental)	Sanders et al., 1985 (as cited in Environment Agency, 2009)	Data are for Fyrquel GT, a commercial tertbutylphenyl diphenyl phosphate product (composition not given).
	Green algae ChV = 0.21 mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	Data are for t-Butylphenyl diphenyl phosphate (CASRN 56803-37-3) Estimate for the Esters class was provided for comparative purposes. See Section 5.5.1.
	Green algae ChV = 0.003 mg/L (Estimated) ECOSAR: Esters	ECOSAR v1.11	Data are for Bis(t-butylphenyl) phenyl phosphate (CASRN 65652-41-7). NES: The log K_{ow} of 8.5 for this chemical exceeds the SAR limitation for the log K_{ow} of 8.0; NES are predicted for these endpoints. Estimate for the Esters class was provided for comparative purposes. See Section 5.5.1.
	Green algae ChV < 0.001 mg/L (Estimated) ECOSAR: Ester	ECOSAR v1.11	Data are for Tris(p-t-butylphenyl) phosphate (CASRN 78-33-1). NES: The log K_{ow} of 10 for this chemical exceeds the SAR limitation for the log K_{ow} of 8.0;

Tris (p-t-butylphenyl) phosphate (TBPP) CASRN 78-33-1				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
				NES are predicted for these endpoints. Estimate for the Esters class was provided for comparative purposes. See Section 5.5.1.
ENVIRONMENTAL FATE				
Transport		**Level III fugacity models incorporating available physical and chemical property data indicate that at steady state, TBPP is expected to be found primarily in soil and to a lesser extent, water. TBPP is expected to have negligible mobility in soil based on the estimated K_{OC} value. There is low to moderate potential for volatilization from water or moist soil surfaces based upon the estimated Henry`s Law constant; however adsorption to soil is expected to attenuate this process. TBPP is not expected to volatilize from dry soil surfaces based upon the extrapolated and measured vapor pressures. In the atmosphere, TBPP is expected to exist primarily in the particulate phase. Particulate phase TBPP will be removed from air by wet or dry deposition.**		
	Henry's Law Constant (atm-m^3/mole)	$6.9x10^{-7}$ for tris (p-t-butylphenyl) phosphate; $2.7x10^{-7}$ for di-t-butylphenyl phenyl phosphate; $1x10^{-7}$ for t-butylphenyl diphenyl phosphate (Estimated)	EPI v4.11	Estimated using representative structures indicated in the SMILES section for components of the mixture using the HENRYWIN (v3.20) Program.
		$8.8x10^{-7}$ (Measured)	ChemID, 2013c	Reported for CASRN 56803-37-3 in secondary source.
	Sediment/Soil Adsorption/Desorption - K_{oc}	3,400 for t-butylphenyl diphenyl phosphate using the MCI method (Estimated)	EPI v4.11	Estimated using the representative structure for t-butylphenyl diphenyl phosphate indicated in the SMILES section.
		>30,000 (Estimated)	EPI v4.11; EPA, 2005	Cutoff value for nonmobile compounds. Estimated for both tris (p-t-butylphenyl) phosphate

Tris (p-t-butylphenyl) phosphate (TBPP) CASRN 78-33-1				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
				and for di-t-butylphenyl phenyl phosphate.
	Level III Fugacity Model	Air = 0.1% Water = 5% Soil = 93.2% Sediment = 1.67% (Estimated)	EPI v4.11	Estimated for tris (p-t-butylphenyl) phosphate.
Persistence		**MODERATE: Based on primary and ultimate biodegradation in nonguideline experimental studies using CASRN 56803-37-3 in river and pond water and sediment samples. These results indicate a half-life for ultimate degradation of <60 days but ≥16 days in the environment and are consistent with inherent degradation. 100% primary degradation of CASRN 56803-37-3 was reported after approximately 11 days in a river die-away study and 93% primary degradation after 9 weeks in a SCAS test using activated sludge inoculum under aerobic conditions. CASRN 56803-37-3 was found to have half-lives based on disappearance of the parent compound of 4.2 and 8.4 days in pond and river sediment, respectively, and showed mineralization of 1.7-37.2% after 8 weeks in water-sediment microcosms. Hydrolysis in alkaline waters may be an important fate process based on experimental half-lives for TBPP but slower under neutral conditions. In a nonguideline photolysis study, no transformation products were identified from a commercial mixture of TBPP in filtered Mississippi River water after exposure to sunlight for 14 days.**		
Water	**Aerobic Biodegradation**	Study results: 93%/9 weeks Test method: Biological Treatment Simulation SCAS test. 93% primary degradation after 9 weeks in domestic activated sludge at a test substance addition rate of 3 mg/L every 24 hours. (Measured)	Saeger et al., 1979	Nonguideline study reported for CASRN 56803-37-3.
		Study results: 100%/~11 days Test method: Die-Away Complete primary degradation occurred after about 11 days in a river water die-away study. (Measured)	Saeger et al., 1979	Nonguideline study reported for CASRN 56803-37-3.
		Study results: 50%/7 days	Saugar, 1983	Guideline test performed on a

Tris (p-t-butylphenyl) phosphate (TBPP) CASRN 78-33-1				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		Test method: Die-Away Reported as the disappearance of the parent compound. TPP: 50%/<0.5 days DTBPPP: 50%/1 day TBPDPP: 50%/7 days Mississippi River water over 27 days (Measured)		commercial product consisting of TPP (CASRN 115-86-6), di(t-butylphenyl)phenyl phosphate (DTBPPP) and t-butylphenyldiphenyl phosphate (TBPDPP).
	Volatilization Half-life for Model River	79 days (Estimated)	EPI v4.11	Estimated for tris (p-t-butylphenyl) phosphate.
		54 days (Estimated)	EPI v4.11	Estimated using the representative structure for p-(t-butylphenyl) diphenyl phosphate.
		190 days (Estimated)	EPI v4.11	Estimated using the representative structure for di-t-butylphenyl phenyl phosphate.
	Volatilization Half-life for Model Lake	>1 year (Estimated)	EPI v4.11	Estimated for tris (p-t-butylphenyl) phosphate.
		>1 year (Estimated)	EPI v4.11	Estimated using the representative structure for p-(t-butylphenyl) diphenyl phosphate.
		>1 year (Estimated)	EPI v4.11	Estimated using the representative structure for di-t-butylphenyl phenyl phosphate.
Soil	**Aerobic Biodegradation**			No data located.
	Anaerobic Biodegradation	Not probable (Anaerobic-methanogenic biodegradation probability model)	EPI v4.11	Estimated for tris (p-t-butylphenyl) phosphate.
	Soil Biodegradation with Product Identification			No data located.

Tris (p-t-butylphenyl) phosphate (TBPP) CASRN 78-33-1				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Sediment/Water Biodegradation	Mineralization of the test substance (2 mg) ranged from 1.7 to 37.2% after 8 weeks in microcosms containing sediment and water from lacustrine, riverine, and estuarine ecosystems. The rate of degradation was related to the nutrient level and contaminant (Measured)	Heitkamp and Cerniglia, 1986; Heitkamp et al., 1986	Nonguideline study reported for CASRN 56803-37-3.
		50%/4.2 days at 25°C in pond sediment. Half-life = 8.4 days at 25°C in river sediment based on disappearance of the parent compound from the sediment phase. ^{14}C-labelled test substance was subject to static river and pond sediment-water incubations in respirometer flasks at temperatures and redox conditions typical of aquatic environments. (Measured)	Muir et al., 1989	Nonguideline study reported for CASRN 56803-37-3.
Air	**Atmospheric Half-life**	0.7 days for t-butylphenyl diphenyl phosphate; 0.74 tri-t-butylphenyl phosphate 0.81 for di-t-butylphenyl phenyl phosphate; (Estimated)	EPI v4.11	Estimated using representative structures indicated in the SMILES section.
		$k_1 = 3.9x10^6$ Thin film oxidation test analyzed by Gel Permeation chromatography (GPC) Hydrocarbon portion of the phosphate oxidizes in the first step; oxidized material undergoes condensation (Measured)	Cho and Klaus, 1981	Nonguideline study providing supporting information.
Reactivity	**Photolysis**	0%/14 days No transformation products were identified in filtered Mississippi River	Sauger, 1983	Nonguideline study on a commercial mixture.

Tris (p-t-butylphenyl) phosphate (TBPP) CASRN 78-33-1				
PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
		water after exposure to sunlight for 14 days in a sealed quartz tube; analysis with GC (Measured)		
	Hydrolysis	pH 5: 50%/>100 days pH 7: 50%/31 days pH 9: 50%/19 days (Measured)	Michael, 1978	Reported for tri t-butylphenyl phenyl phosphate.
		pH 5: 50%/>100 days pH 7: 50%/57 days pH 9: 50%/10 days (Measured)	Michael, 1978	Reported for CASRN 56803-37-3.
		pH 7: 50%/3.5 years pH 5: 50%/341 years pH 6: 50%/35 years pH 8: 50%/127 days pH 9: 50%/13 days pH 10: 50%/1.3 days (Estimated)	EPI v4.11	Estimated for tris (p-t-butylphenyl) phosphate.
Environmental Half-life		0.44 day in pond water 39 days in bottom sediment Field study; 360 days following the addition of 50 µg/L of the test substance to artificial ponds of 5 cubic meter volume (Measured)	Muir et al., 1985	Reported for CASRN 56803-37-3.
		360 days (Estimated)	PBT Profiler	Half-life estimated for tris (p-t-butylphenyl) phosphate in the predominant compartment, soil, as determined by EPI methodology.

Tris (p-t-butylphenyl) phosphate (TBPP) CASRN 78-33-1				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Bioaccumulation		**HIGH: The bioaccumulation designation is based on the measured BCF values for t-butylphenyl diphenyl phosphate (CASRN 56803-37-3); BCF results >1,000 are from two different species. The estimated BAF values for the di and tri-t-butylphenyl phosphate also indicate high potential for bioaccumulation. The low estimated BCF values were determined from the estimated log Kow values, which are >6.6.**		
	Fish BCF	1,096 whole fish, short-term static exposure of 50 and 5 µg/L in Rainbow trout (Measured)	Muir et al., 1983	Nonguideline study reported for >98% pure CASRN 56803-37-3.
		1,010 Whole fish, short-term static exposure of 50 and 5 µg/L in Fathead minnow (Measured)	Muir et al., 1983	Nonguideline study reported for >98% pure CASRN 56803-37-3.
		42 (Estimated)	EPI v4.11	Estimated for tris (p-t-butylphenyl) phosphate.
		170 (Estimated)	EPI v4.11	Estimated using the representative structure for p-(t-butylphenyl) diphenyl phosphate.
		360 (Estimated)	EPI v4.11	Estimated using the representative structure for di-t-butylphenyl phenyl phosphate.
	Other BCF			No data located.
	BAF	100,000 (Estimated)	EPI v4.11	Estimated for tris (p-t-butylphenyl) phosphate. Given the limited water solubility, this BAF value may be overestimated.
		460,000 (Estimated)	EPI v.411	Estimated using the representative structure for di-t-butylphenyl phenyl phosphate.
		540 (Estimated)	EPI v4.11	Estimated using the representative structure for p-(t-butylphenyl) diphenyl phosphate.
	Metabolism in Fish			No data located.

Tris (p-t-butylphenyl) phosphate (TBPP) CASRN 78-33-1			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
ENVIRONMENTAL MONITORING AND BIOMONITORING			
Environmental Monitoring	t-Butylphenyl diphenyl phosphate (CASRN 56803-37-3) has been found in river sediments in industrial areas (Muir et al., 1989).		
Ecological Biomonitoring	No data located.		
Human Biomonitoring	t-Butylphenyl diphenyl phosphate (CASRN 56803-37-3) was detected in human adipose samples. TBPP was not included in the NHANES biomonitoring report (LeBel and Williams, 1983; CDC, 2009).		

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ChemID (2013c) t-Butylphenyl diphenyl phosphate RN: 56803-37-3. ChemID plus. National Library of Medicine. http://chem.sis.nlm.nih.gov/chemidplus/.

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