

REPORT FOR INTERNATIONAL COOPERATION ON COSMETIC REGULATION (ICCR)

Principles for the handling of traces of impurities and/or contaminants in cosmetic products

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1. PURPOSE AND SCOPE

Due to the ever increasing sensitivity of analytical methods, lower levels of traces of unwanted substances may be detected in cosmetic products, even if they are produced according to state of the art sourcing and manufacturing practices. These traces can originate from a variety of sources. Some trace substances are prohibited or restricted in different jurisdictions around the world. The final responsibility for ensuring the safety and regulatory compliance of a cosmetic product (including any trace substances it may contain) lies with the entity responsible for placing the product on the market (i.e. manufacturer, distributor and/or importer). Appropriate management of traces in cosmetic products is thus required.

Any management approach for traces should be primarily based on safety considerations and on the applicable regulatory requirements. Additional elements can be considered when taking further management measures.

This document may serve as a guidance tool for any person responsible for handling traces in cosmetic products. It includes a number of definitions and describes important management principles for traces in cosmetic products.

The principles outlined in this document will also help guide the development of any recommendations for trace impurity limits set out by the International Cooperation on Cosmetic Regulation (ICCR).

2. ACRONYMS AND DEFINITIONS

Raw materials can be made of one or numerous substances. In general a substance is made of constituents (one constituent or multi constituents if well characterized), impurities and additives.

Impurities are generally minor constituents of a substance or a raw material that can originate from:

- constituents themselves
- the manufacturing process
- chemical synthesis or interaction within the product that could occur under normal storage conditions
- potential migration from the final packaging to the product
- potential chemical changes caused by instability of the product in contact with the final packaging

Contaminants are defined as unintended substances that can originate from sources outside the chemical pathway, chemical processes, unexpected situations such as bad storage of primary substances or instability of the primary packaging.

Impurities and/or contaminants can be present at trace levels in a finished product.

Traces, for the scope of this document, refer to very low amounts of impurities and/or contaminants in a finished product.

3. RESPONSIBILITIES

This report for ICCR has been prepared by the ICCR Working Group on Traces :

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- Neil Wilcox, United States, Food and Drug Administration (*Replaced by John Gasper in April*).
- John Bailey; United States, PCPC.

It is presented for discussion and adoption at the ICCR-5 meeting on June 29, 2011 in Paris.

4. DISCUSSION

Key management principles for traces in cosmetic products

- The final responsibility for ensuring the safety and regulatory compliance of a cosmetic product (including any trace substances it may contain) lies with the entity responsible for placing the product on the market (i.e. manufacturer, distributor and/or importer). Trace substances that may present a potential safety issue must be considered in the cosmetic product safety assessment and it may be appropriate to set a maximum acceptable concentration in the finished product.
- The identification of an unwanted trace substance should be based on a thorough understanding of the raw material source (e.g. synthetic, natural or

other origin) and the manufacturing process (e.g. route of synthesis and the process of extraction including the used solvent).

Compatibility studies allow testing of the potential transfer of small amounts of substances from the primary packaging material to the product. The stability of inner packaging materials and ingredients in contact with these materials can also be determined. These tests are performed under specific and relevant test conditions and depend on the specific situation. An appropriate assessment can also be made based on the knowledge of the formulation and primary packaging materials and experienced expert judgment.

- Ingredients should be assessed for their potential to introduce trace substances into the finished cosmetic products and whether or not management steps are required to control traces of concern. This should include an evaluation of the source of the ingredient, the method of manufacture and/or the interaction with the primary packaging material.
- For trace substances that have been identified (which by definition are not intended cosmetic ingredients), the toxicological relevance of the substance should be assessed. In case of traces of substances with known safety concern, particular attention should be posed in determining if the levels in the finished product are below a level that is considered sufficiently protective for human health, based on reasonable evidence such as available safety data.
- Safety must be the key aspect of traces management. The safe level of a trace substance of safety concern (i.e., a level that is considered sufficiently protective for human health), must be determined. The assessment should start from the hazard profile of the substance and take into consideration available safety data and finished product usage. The safe level must be established based on the acceptable safe exposure level of the unwanted trace substance and takes into consideration exposure of the consumer to the trace substance, including cumulative exposure from other products and environmental sources, as appropriate. One safe trace limit for all cosmetic product categories may be preferable from a management and control perspective, when acceptable from a safety point of view. Several key elements to determine safe levels of a trace substance of safety concern are listed hereafter:
 - First, it is necessary to identify maximum acceptable trace exposures (maximum acceptable daily exposures in appropriate units—mg/kg/day or mg/cm²/day).
 - If an acceptable safety exposure level has already been established by a regulatory agency or recognised scientific organization, this acceptable exposure level can be considered for adoption if relevant to the product class and/or use pattern. If different regulatory requirements exist, the available safety data should be used to determine the most appropriate level to use.

- If no externally established acceptable exposure levels are available, maximum acceptable trace exposures can be established based on available toxicological data and appropriate risk-assessment methods.
 - If no adequate data on the specific trace material is available, the application of alternative approaches may be considered provided that they give a reasonable level of confidence in the calculation of an acceptable trace exposure or safety assessment. For example, acceptable exposure levels could be derived based toxicity data from structurally related chemicals (structural analogs) using a read-across approach.
 - In those situations where the available data for assessing the safety and exposure to a trace material is incomplete, the responsible individuals may consider the application of additional alternative approaches. This is not usually the situation for those trace substances that have been known and assessed for many years. For example, the Threshold of Toxicological Concern (TTC)² approach, as well as other approaches, have been proposed in some instances but remain investigational tools.
- Set safe trace limit in product/product category
- After determining the potential categories of product use, consumer habits and practices data are applied to estimate the consumer exposure level to the trace substance through the use of the product. Different exposure routes, such as dermal, oral and inhalation exposure routes may be taken into account where relevant when determining the consumer exposure level. Appropriate physical/chemical characteristics of the substance should be taken into consideration, as well as the physiological characteristics of the most sensitive sub-population likely to use the product in question.
 - Appropriate dermal bioavailability data should be used when available.
 - The safe product trace limit for a specific product category can then be calculated based on the maximum acceptable trace exposure, and consumer use habits and practices for the product.
 - If acceptable from a safety point of view, it is advisable to determine one single safe trace limit for all product categories. The safe product trace limit may be different for different product categories, due to the differences in consumer uses and exposures. If not acceptable otherwise,

² See R. Kroes et al., Application of the Threshold of Toxicological Concern (TTC) to the Safety Evaluation of Cosmetic Ingredients, *Food and Chemical Toxicology* 45 (2007) 2533–262.

the safe limit could potentially be grouped into exposure tiers such as rinse off, leave on, oral care, aerosol product etc.

- For certain trace substances, levels have been specified in legislation applying to cosmetics in different regions of the world. A brief overview of the regulatory structure for each of the four ICCR jurisdictions is given in Annex I. It is the responsibility of the entity placing the cosmetic product on the market (i.e. manufacturer, distributor and/or importer) to comply with the local or regional regulations or regulatory guidance/policy.
- Each manufacturer should ensure that levels of unwanted trace substances are below the recognized safe limit and the product meets the applicable regulatory requirements. A company should consider further reasonable and practical reductions based on a number of factors related to regulatory requirements and other appropriate considerations. For example, this could be driven by factors such as currently achievable levels, external relations issues, currently achievable quality under Good Manufacturing Practices (GMP)³ and the quality of the raw material and analytical testing capability. With deference to the recognized safe trace limits, the “As Low As Reasonably Achievable” (ALARA)⁴ principle must always be evaluated as part of the deliberations. ALARA levels reflect quality of the raw materials and manufacturing practices, and are normally below levels related to safety criteria and may differ by manufacturer and region. They are part of a continuing process and can evolve over time, even within a company.
- Control at the finished product level is the essential element for management of traces. This can be effectively accomplished through testing of the finished product intended for market. Alternatively, the manufacturer can control traces through suitable selection of raw materials used to manufacture the product. Either approach is acceptable as long as it can be assured that the traces levels in the finished product are adequately managed.
- Given the challenges associated with developing analytical methods for the detection of trace substances in different finished products, the management of traces may be driven mainly by raw material control including working with suppliers. There is a very wide variety of different cosmetic formulations and thus product matrices in which the trace substance must be considered. Different analytical methods for different product matrices may be available. Methods should be adapted as necessary and the appropriate analytical method should be chosen considering the product formulation.

³ In certain jurisdictions, reference is made to GMP in the context of traces in the cosmetics legislation.

⁴ As Low As Reasonably Achievable (ALARA) means those levels of traces that can be achieved through reasonable and practical approaches to control of raw materials and the manufacturing process. It does not encompass extraordinary efforts beyond these ordinary steps.

Standardization of analytical methods can be envisaged and development of globally-aligned analytical approaches is encouraged. However, due to the large variety of different formulations and matrices, standardization of specific methods for each matrix of interest is not always achievable. If in-house methods are developed and applied, then the results obtained by those methods should be validated.

6. CONCLUSIONS

Further perspectives

Trace substances and trace levels are topics of interest for both the industry and regulatory authorities worldwide.

Industry and regulators are working together at the ICCR level on traces in cosmetic products to maintain the highest level of global consumer protection, to facilitate convergence to the fullest extent possible and to minimize barriers to international trade. The ICCR recommendations may be taken and/or adopted by ICCR members for implementation as appropriate, respecting the boundaries of their legal and institutional constraints. The ICCR recommendations are considered to be non-binding on the members.

Annex I: Regulatory overview in the ICCR jurisdictions

In this Annex is a brief overview of the regulatory structure with regard to traces in cosmetic products for each of the four ICCR jurisdictions.

The United States

FDA regulates cosmetic safety under the authority of the Federal Food, Drug, and Cosmetic Act (FD&C Act). The FD&C Act prohibits any product or ingredient that is a “poisonous or deleterious substance which may render [the product] injurious to users under the conditions of use prescribed in the labeling.” The FD&C Act also prohibits any products that are “filthy, putrid, or decomposed substance”, products “prepared, packed, or held under insanitary conditions whereby it may have become contaminated with filth, or whereby it may have been rendered injurious to health” and products whose “container is composed, in whole or in part, of any poisonous or deleterious substance which may render the contents injurious to health.” FDA addresses the presence of trace impurities in cosmetics on a case-by-case basis. Requirements for specific cosmetics are listed in 21 CFR part 700. For heavy metals, FDA has set a limit of 1 ppm mercury in most cosmetics under 21 CFR 700.13 (a limit of 65 ppm is permitted in certain eye area cosmetics) and prohibits the use of zirconium in aerosol cosmetics under 21 CFR 700.16. In addition, FDA has established specifications for lead, arsenic, and mercury in most color additives. A few more heavy metal specifications have been established for certain color additives.

Japan

Ministry of Health, Labour and Welfare stipulates in General provisions of Standards for Cosmetics⁵ that ingredients of cosmetics, including any impurities contained therein, shall not contain anything that may cause infection or that otherwise makes the use of the cosmetics a potential health hazard.

Standards of Cosmetics regulate ingredients which must not be formulated in cosmetics, and ingredients such as UV filters, preservatives, etc, of which inclusion is limited.

Regulations which stipulate the level of traces do not exist in Japan at present. Under the cosmetic licensing system, each cosmetic ingredient had specification in the past. For examples, The Japanese Standards of Cosmetic Ingredients (JSCI)⁶ give the level of lead for Zinc Oxide as less than 40ppm, Titanium Dioxides less than 50ppm, and Silicic Anhydride less than 30ppm as heavy metals. There was a period when

⁵ Standard for Cosmetics; Ministry of Health and Welfare Notification No.331 of 2000

⁶ The Japanese Standards of Cosmetic Ingredients : 1st edition published in 1967, 2nd in 1982, 1st supplement in 1985, and 2nd supplement in 1991

submission of these specifications was required at the time of application for permission of a cosmetic product.

Since the revision of cosmetic licensing system in 2001, those who are responsible for marketing of cosmetics are required to follow Standards of Cosmetics as for regulated ingredients, and to guarantee quality and safety of the rest of ingredients on their own responsibility.

Canada

The Canadian Food and Drugs Act (F&DA) stipulates that "No person shall sell any cosmetic that:

- (a) has in or on it any substance that may cause injury to the health of the user when the cosmetic is used,[...];
- (b) consists in whole or in part of any filthy or decomposed substance or of any foreign matter; or
- (c) was manufactured, prepared, preserved, packaged or stored under unsanitary conditions."

Substances known to cause injury or that are not appropriate for use in cosmetics are reflected on Health Canada's Cosmetic Ingredient Hotlist. Substances found on the Cosmetic Ingredient Hotlist may find their way into finished cosmetic products at trace levels. These trace levels may be acceptable if they do not pose a hazard to human health and are technically unavoidable..

In December 2008, Health Canada released a Draft Guidance on Heavy Metal Impurities in Cosmetics that outlines impurity limits in cosmetics for lead (10 ppm), arsenic (3 ppm), cadmium (3 ppm), mercury (3 ppm), and antimony (5 ppm).

The European Union

The European Cosmetics Directive (76/768) and the new Cosmetics Products Regulation (1223/2009) allow the non intended presence of small quantities of a prohibited substance, stemming from impurities of natural or synthetic ingredients, the manufacturing process, storage, migration from packaging, which is technically unavoidable in good manufacturing practice, provided that such presence does not cause damage to human health when the product containing the trace is applied under normal or reasonably foreseeable conditions of use.

More specifically, the new Cosmetics Products Regulation states in the preamble (Whereas 37) that "In order to ensure product safety, prohibited substances should be acceptable at trace levels only if they are technologically inevitable with correct

manufacturing processes and provided that the product is safe". Furthermore, Annex I to the same regulation lists the following information concerning impurities and traces amongst the minimum content of the cosmetic product safety report:

- The purity of the substance and mixtures.
- In the case of traces of prohibited substances, evidence for their technical unavoidability.
- The relevant characteristics of packaging material, in particular purity and stability.

For most traces, which can be found in the cosmetic products, there are currently no regulatory concentration limits available. The safety of the non-intended trace levels in the finished product is the responsibility of the manufacturer or of the person under whose responsibility the product is placed on the market".
