SCIENTIFIC OPINION

Scientific Opinion on the safety assessment of the substance, N,N'-bis(2,2,6,6-tetramethyl-4-piperidinyl) isophthalamide, CAS No 42774-15-2, for use in food contact materials

EFSA Panel on Food Contact Materials, Enzymes, Flavourings and Processing aids (CEF)

European Food Safety Authority (EFSA), Parma, Italy

The full opinion will be published in accordance with Article 10(6) of Regulation (EC) No 1935/2004 once the decision on confidentiality, in line with Article 20(3) of the Regulation, will be received from the European Commission. Data on purity and migration as well as toxicological data have been provided under the established confidentiality agreements and they are redacted awaiting the decision of the Commission.

ABSTRACT

This scientific opinion of the EFSA Panel on Food Contact Materials, Enzymes, Flavourings and Processing Aids (CEF) deals with the risk assessment of N,N'-bis(2,2,6,6-tetramethyl-4-piperidinyl) isophthalamide, CAS No 42774-15-2, FCM No 1051, for use as an additive in poly(ethylene terephthalate) (PET), in polyamide (PA) inner layer in multilayers, and in the ethylene vinyl alcohol (EVOH) layer in polypropylene (PP)/EVOH/PP and polyethylene (PE)/EVOH/PE laminates. Migration tests for the substance were performed in food simulants: acetic acid 3 %, ethanol solutions (10, 20 and 50 %) and olive oil, at time/temperature testing conditions representing the intended use. The results show migration less than 5 mg/kg. Comparison between the chromatograms of solvent extracts of films of PA, PET and two multilayer structures of PP and PE containing EVOH, each with and without the substance as reference films, do not show significant differences. Based on negative results from five in vitro genotoxicity tests, the Panel concluded that the substance does not raise a concern related to genotoxicity. Based on the negative results from the toxicological studies an overall 'No Observed Adverse Effect Level' NOAEL is set to 0 mg/kg bw.. Based on a consideration of the structure of the molecule along with the low log Pow value of 1.12, the substance does not give rise to concern for accumulation in man. The CEF Panel concluded that the substance N,N'-Bis(2,2,6,6-tetramethyl-4-piperidinyl) isophthalamide is not a safety concern for the consumer if used as an additive in plastics and its migration does not exceed 5 mg/kg food.

1 On request from the Bundesamt für Verbraucherschutz und Lebensmittelsicherheit, Germany, Question No EFSA-Q-2013-00887, adopted on 25 September 2014.
2 Panel members: Claudia Bolognesi, Laurence Castle, Jean-Pierre Cravedi, Karl-Heinz Engel, Paul Fowler, Roland Franz, Konrad Grob, Rainer Gürtler, Trine Husøy, Wim Mennes, Maria Rosaria Milana, André Penninks, Vittorio Silano, Andrew Smith, Maria de Fátima Tavares Poças, Christina Tlustos, Fidel Toldrá, Detlef Wölfle and Holger Zorn. One member of the Panel did not participate in the discussion on the subject referred to above because of potential conflicts of interest identified in accordance with the EFSA policy on declarations of interests. Correspondence: fip@efsa.europa.eu
3 Acknowledgement: The Panel wishes to thank the members of the Working Group on Food Contact Materials: Mona-Lise Binderup, Laurence Castle, Riccardo Crebelli, Alessandro Di Domenico, Nathalie Gontard, Ragna Bogen Hetland, Martine Kolf-Clauw, Eugenia Lampi, Maria Rosaria Milana, Maria de Fátima Tavares Poças, Philippe Saillard, Kettil Svensson and Detlef Wölfle for the preparatory work on this scientific opinion.


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KEY WORDS
N,N’-Bis(2,2,6,6-tetramethyl-4-piperidinyl) isophthalamide, CAS 42774-15-2, FCM No 1051, food contact materials, safety assessment, evaluation
SUMMARY

Within the general task of evaluating substances intended for use in materials in contact with food, according to the Regulation (EC) No 1935/2004 of the European Parliament and of the Council of 27 October 2004 on materials and articles intended to come into contact with foodstuffs, the CEF Panel received a request from the Bundesamt für Verbraucherschutz und Lebensmittelsicherheit, Germany for safety assessment of the substance N,N'-bis(2,2,6,6-tetramethyl-4-piperidinyl) isophthalamide following a corresponding application submitted on behalf of Clariant Produkte (Deutschland) GmbH.

The safety evaluation of N,N'-bis(2,2,6,6-tetramethyl-4-piperidinyl) isophthalamide with CAS No 42774-15-2, and the FCM No 1051 was requested for use as an additive in poly(ethylene terephthalate)(PET), in polyamide(PA) inner layer in multilayers, and in the ethylene vinyl alcohol (EVOH) layer in polypropylene (PP)/EVOH/PP and polyethylene (PE)/EVOH/PE laminates at intended use levels up to 1 % in PET; 0.15 % - 0.2 % in PA and 0.5 % in EVOH. The additive acts as a process stabilizer in PET, as a processing stabilizer, antioxidant and light stabilizer in PA, and as an oxygen barrier enhancer in EVOH. Final materials and articles are intended to be used in contact with all types of foodstuffs. Contact conditions include sterilization followed by long term storage for PA and EVOH laminates; and hot filling and pasteurization above 66 °C followed by long time storage, for PET.

Migration tests for the substance were performed in food simulants: acetic acid 3 %, ethanol solutions (10, 20 and 50 %) and olive oil, at time/temperature testing conditions representing the foreseen use. Samples of monolayer of PA and PET films and samples of typical multi-layer structures, with an EVOH inner layer and polyolefin (PP or PE) outer layers, were used in the migration tests, with the substance added at the maximum intended level or higher.

Migration of the substance in the above conditions was below 0.5 mg/kg in all cases, except for the PA film sample for which a value higher than 5 mg/kg was observed. Migration of the substance from PA film was mg/kg into olive oil and up to mg/kg into the other simulants used. However, according to the applicant, PA is more typically used as an inner layer of multilayer structures due to its need for moisture protection and lack of sealability, and such multilayer structures can limit the migration to below 5 mg/kg. Migration from the PET film was non-detectable into olive oil at a limit of detection (LOD) of 0.004 mg/kg and was up to mg/kg into the other simulants used. Migration from the EVOH laminates was mg/kg into olive oil and up to mg/kg into the other simulants used.

Comparison between the chromatograms of solvent extracts of films of PA, PET and two multilayer structures of PP and PE containing EVOH, both with and without the substance as reference films, did not show significant differences.

Based on negative results from five in vitro genotoxicity tests, the Panel concluded that the substance does not raise a concern related to genotoxicity. Two subacute 28 days oral toxicity studies, a subchronic 90-day oral toxicity study and a one generation reproductive toxicity study of the substance were performed. Based on the at the highest dose levels in the subchronic and subacute studies an overall NOAEL is set to mg/kg bw. The Panel concluded that based on this NOAEL and the absence of accumulation in man the substance does not give rise to a safety concern up to a migration level of 5 mg/kg food.

The CEF Panel concluded that the substance N,N'-bis(2,2,6,6-tetramethyl-4-piperidinyl) isophthalamide is not a safety concern for the consumer if used as an additive in plastics and the migration of the substance does not exceed 5 mg/kg food.
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BACKGROUND AS PROVIDED BY THE LEGISLATION

Before a substance is authorised to be used in food contact materials, and is included in a positive list, EFSA’s opinion on its safety is required. This procedure has been established in Articles 8 and 9 of the Regulation (EC) No 1935/2004 of the European Parliament and of the Council of 27 October 2004 on materials and articles intended to come into contact with food.

According to this procedure the industry submits applications to the Member States competent Authorities which transmit the applications to EFSA for their evaluation. The application is supported by a technical dossier submitted by the industry following the scientific committee for food (SCF) guidelines for the “presentation of an application for safety assessment of a substance to be used in food contact materials prior to its authorisation” (EC, 2001).

In this case, EFSA received an application from the Bundesamt für Verbraucherschutz und Lebensmittelsicherheit, Germany, requesting the evaluation of the additive N,N’-bis(2,2,6,6-tetramethyl-4-piperidinyl) isophthalamide with the CAS number 42774-15-2, the European Commission FCM substance No 1051.

TERMS OF REFERENCE AS PROVIDED BY THE LEGISLATION

According to Regulation (EC) No 1935/2004 of the European Parliament and of the Council on materials and articles intended to come into contact with food, EFSA is asked to carry out an assessment of the risks related to the intended use of the substance and to deliver a scientific opinion.

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ASSESSMENT

1. Introduction

The European Food Safety Authority was asked by the Bundesamt für Verbraucherschutz und Lebensmittelsicherheit, Germany, to evaluate the safety of \(N,N'-\text{bis}(2,2,6,6\text{-tetramethyl-4-piperidinyl})\) isophthalamide with a CAS number 42774-15-2, and FCM substance No 1051. The request has been registered in the EFSA’s register of questions under the number EFSA-Q-2013-00887. The dossier was submitted on behalf of Clariant Produkte (Deutschland) GmbH.

2. General information

According to the applicant, the substance \(N,N'-\text{bis}(2,2,6,6\text{-tetramethyl-4-piperidinyl})\)isophthalamide, CAS No 42774-15-2, is intended to be used as an additive in PET, in PA inner layer in multilayers, and in the EVOH layer in PP/EVOH/PP and PE/EVOH/PE laminates. The substance is intended to be used up to 1 % in PET; up to 0.15 % - 0.2 % in PA and up to 0.5 % in EVOH. The additive acts as a process stabilizer in PET, as a processing stabilizer, antioxidant and light stabilizer in PA, and as an oxygen barrier enhancer in EVOH.

Final materials and articles are intended to be used in contact with all types of foodstuffs. Contact conditions include sterilization followed by long term storage for PA and EVOH laminates; and hot filling and pasteurization above 66 °C followed by long time storage, for PET.

The substance has not been evaluated by SCF or EFSA in the past.

3. Data available in the dossier used for this evaluation

The studies submitted for evaluation followed the SCF guidelines for the presentation of an application for safety assessment of a substance to be used in food contact materials prior to its authorisation (EC, 2001).

**Non-toxicity data:**
- Data on identity
- Data on physical and chemical properties
- Data on intended use and authorisation
- Data on migration of the substance
- Data on residual content of the substance
- Data on identification, quantification and migration of reaction products

**Toxicity data:**
- Two Bacterial gene mutation tests
- \(In\ \text{vitro}\) mammalian cell gene mutation test
- Two \(In\ \text{vitro}\) mammalian chromosome aberration tests
- Two 28-day oral toxicity studies
- A 90-day oral toxicity study
- A one generation reproductive toxicity study
4. **Evaluation**

4.1. **Non-toxicological data**

Chemical formula: $C_{26}H_{42}N_4O_2$

![Chemical structure of N,N'-bis(2,2,6,6-tetramethyl-4-piperidinyl) isophthalamide](image)

**Figure 1:** Chemical structure of N,N'-bis(2,2,6,6-tetramethyl-4-piperidinyl) isophthalamide

The substance N,N'-bis(2,2,6,6-tetramethyl-4-piperidinyl) isophthalamide, CAS No 42774-15-2, has a molecular weight of 442.7 Da, a log Po/w of 1.12 and a water solubility of 0.139 g/L at 30 °C, and a purity of %.

The substance is thermally stable up to 352 °C which is higher than maximum temperature of 320 °C foreseen for processing of the different polymers.

Migration tests for the substance were performed in food simulants: acetic acid 3 %, ethanol solutions (10, 20 and 50 %) and olive oil, at time/temperature testing conditions representing the foreseen use conditions. Samples of monolayer of PA and PET films and samples of typical multi-layer structures, with an EVOH inner layer and polyolefin (PP or PE) outer layers, were used in the migration tests, with the substance added at the maximum intended level or higher.

Migration of the substance in the above conditions was below 0.5 mg/kg in all cases, except for the PA film sample for which a value higher than 5 mg/kg was observed. Migration of the substance from PA film was mg/kg into olive oil and up to mg/kg into the other simulants used. However these results were obtained for a monolayer PA film, whereas according to the applicant PA is intended to be used as an inner layer of multilayer structures due to its need for moisture protection and lack of sealability, and such multilayer structures can limit the migration to below 5 mg/kg. Migration from the PET film was non-detectable into olive oil at a LOD of 0.004 mg/kg and was up to mg/kg into the other simulants used. Migration from the EVOH laminates was mg/kg into olive oil and up to mg/kg into the other simulants used.

Films of PA, PET and two multilayer structures of PP and PE containing EVOH, were extracted using dichloromethane (DCM) and 95 % ethanol and the extracts were analysed by GC-FID and GC-MS. Corresponding films but without the substance added were used as a reference. No differences between the chromatograms were found at an LOD of 3 µg/dm² for PA or 8 µg/dm² for the multilayer structures. For the PET film, two additional peaks were detected. One of these peaks was identified and it was also present in the reference film although at lower concentration. The second peak was not possible to identify since it did not give a mass spectrum. Based on this compositional analysis the potential for migration was estimated by migration modelling. It was being below 1 µg/kg.

4.2. **Toxicological data**

The substance was tested in five *in vitro* genotoxicity tests with and without metabolic activation. In two bacterial gene mutation assays using respectively, the substance did not induce gene mutations when tested up to µg/plate.

In a test for gene mutation activity at the, no mutations were induced when the substance was tested up to the maximum recommended
concentration of ). The substance did not induce chromosomal aberrations in a test using l. Based on the results of these *in vitro* tests, the Panel considered that the substance does not raise a concern related to genotoxicity.

In a subchronic oral toxicity study the substance was administered to . Some statistically significant changes of parameters were noted in at the highest dose.

As supporting information to the repeated dose toxicity two subacute oral toxicity studies with were submitted.

In a 28 day oral toxicity study the substance was administered to . There were no clear adverse effects except at the highest dose.

In another subacute 28 day study

In a one generation reproductive toxicity study groups of . The substance did not affect . Consequently the parental and offspring *No Observed Adverse Effect Level* (NOAEL) was at  mg/kg body weight per day or higher in this study.

Based on a consideration of the structure of the molecule along with the low log Pow value (1.12) the substance does not give rise to concern for accumulation in man.

Based on the at the highest dose levels in the subchronic and subacute studies an overall NOAEL is set to  mg/kg bw. The Panel concluded that based on this NOAEL and the absence of accumulation in man the substance does not give rise to a safety concern up to a migration level of 5 mg/kg food.

**CONCLUSIONS**

The CEF Panel having considered the above-mentioned data concluded that the substance N,N'-bis(2,2,6,6-tetramethyl-4-piperidinyl) isophthalamide is not a safety concern for the consumer if used as an additive in plastics and the migration of the substance does not exceed 5 mg/kg food.

**DOCUMENTATION PROVIDED TO EFSA**


2. Additional data for dossier “Nylostab S-EED”. May 2014. Submitted on behalf of Clariant Produkte (Deutschland) GmbH.
REFERENCES

EC (European Commission), (2001). Guidelines of the Scientific Committee on Food for the presentation of an application for safety assessment of a substance to be used in food contact materials prior its authorisation; http://ec.europa.eu/food/fs/sc/scf/out82_en.pdf.
### ABBREVIATIONS

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
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<tbody>
<tr>
<td>CAS</td>
<td>Chemical Abstracts Service</td>
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<tr>
<td>CEF</td>
<td>EFSA Panel on food contact materials, enzymes, flavourings and processing aids</td>
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<tr>
<td>DCM</td>
<td>Dichloromethane</td>
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<tr>
<td>EC</td>
<td>European Commission</td>
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<tr>
<td>EFSA</td>
<td>European food safety authority</td>
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<tr>
<td>EVOH</td>
<td>Ethylene vinyl alcohol</td>
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<tr>
<td>FCM</td>
<td>Food contact materials</td>
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<tr>
<td>GC-FID</td>
<td>Gas chromatography - flame ionization detector</td>
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<tr>
<td>GC-MS</td>
<td>Gas chromatography - mass spectrometer</td>
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<tr>
<td>LOD</td>
<td>Limit of detection</td>
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<tr>
<td>NOAEL</td>
<td>No observed adverse effect level</td>
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<tr>
<td>PA</td>
<td>Polyamide</td>
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<tr>
<td>PE</td>
<td>Polyethylene</td>
</tr>
<tr>
<td>PET</td>
<td>Poly(ethylene terephthalate)</td>
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<tr>
<td>PP</td>
<td>Polypropylene</td>
</tr>
<tr>
<td>SCF</td>
<td>Scientific committee for food</td>
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