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dimethyl ester for use in food contact materials**

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Safety assessment of the substance 1,2,3,4-tetrahydronaphthalene-2,6-dicarboxylic acid, dimethyl ester for use in food contact materials

EFSA Panel on Food Contact Materials, Enzymes, Flavourings and Processing Aids (CEF), Vittorio Silano, Claudia Bolognesi, Jean-Pierre Cravedi, Karl-Heinz Engel, Paul Fowler, Roland Franz, Konrad Grob, Rainer Gürtler, Trine Husøy, Sirpa Kärenlampi, Wim Mennes, Maria Rosaria Milana, André Penninks, Andrew Smith, Maria de Fátima Tavares Poças, Christina Tlustos, Detlef Wölfle, Holger Zorn, Corina-Aurelia Zugravu, Martine Kolf-Clauw, Eugenia Lampi, Kettil Svensson, Eric Barthélémy and Laurence Castle

Abstract

This scientific opinion of the EFSA Panel on Food Contact Materials, Enzymes, Flavourings and Processing aids (CEF Panel) deals with the safety assessment of 1,2,3,4-tetrahydronaphthalene-2,6-dicarboxylic acid, dimethyl ester (TDCM) for use as a co-monomer to manufacture polyester layers. The polyester layer is not intended to be in direct contact with food. The finished multilayer articles are intended for packaging aqueous, acidic and low alcoholic foodstuffs. Contact conditions include sterilisation followed by long-term storage at room temperature. No thermal degradation of TDCM is expected during the manufacture of the middle polyester layer and of the multilayer articles. Total mass transfer of the substance from a polyester monolayer was calculated to be up to 0.032 mg/kg food. Based on three *in vitro* genotoxicity tests, the CEF Panel considered that the substance does not raise concern for genotoxicity. When tested behind a polypropylene layer, migrating TDCM-related oligomers, their oxidation products and other related reaction products were identified. The major components were TDCM dimers. When tested behind a cyclo-olefin polymer layer, none of the TDCM-related substances were found to migrate. Based on the lack of genotoxicity of the co-monomer, the ester nature of the oligomers and on (quantitative) structure–activity relationship ((Q)SAR) analysis, the CEF Panel considered that there is no indication of genotoxicity for the oligomers, their oxidation products and other TDCM-related reaction products. The CEF Panel concluded that the substance is not of safety concern for the consumer if used as a co-monomer for the manufacture of a polyester layer intended to be used as an inner (non-food contact) layer of a multilayer material for contact with foods simulated by simulants A, B, C, D1 (as set in Regulation (EU) 10/2011). The migration of the sum of the substance and the dimers (cyclic and open chain) should not exceed 0.05 mg/kg food.

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Keywords: 1,2,3,4-tetrahydronaphthalene-2, 6-dicarboxylic acid, dimethyl ester (TDCM), CAS No 23985-75-3, FCM substance No 1066, monomer, polyester, food contact materials, safety assessment

Requestor: Food Standards Agency, United Kingdom

Question number: EFSA-Q-2015-00242

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Panel members: Claudia Bolognesi, Laurence Castle, Jean-Pierre Cravedi, Karl-Heinz Engel, Paul Fowler, Roland Franz, Konrad Grob, Rainer Gürtler, Trine Husøy, Sirpa Kärenlampi, Wim Mennes, Maria Rosaria Milana, André Penninks, Vittorio Silano, Andrew Smith, Maria de Fátima Tavares Poças, Christina Tlustos, Detlef Wölfle, Holger Zorn and Corina-Aurelia Zugravu.

Note: 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. The following information has been provided under the confidentiality framework and has been redacted awaiting the decision of the Commission: the maximum percentage of the substance intended to be used in the formulation of the polyester layer and the mode of function of the polyester layer.

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Table of contents

Abstract.....	1
1. Introduction.....	4
1.1. Background and Terms of Reference as provided by the requestor.....	4
2. Data and methodologies.....	4
2.1. Data.....	4
2.2. Methodologies.....	4
3. Assessment.....	5
3.1. Non-toxicological data.....	5
3.2. Toxicological data.....	6
4. Conclusions.....	6
Documentation provided to EFSA.....	7
References.....	7
Abbreviations.....	7

1. Introduction

1.1. Background and Terms of Reference as provided by the requestor

Before a substance is authorised to be used in food contact materials (FCM) and included in a positive list, EFSA's opinion on its safety is required. This procedure has been established in Articles 8, 9 and 10 of 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 the European Food Safety Authority (EFSA) for their evaluation.

In this case, EFSA received an application from the Food Standards Agency, the United Kingdom, requesting the evaluation of the substance called 'dimethyl-1,2,3,4-tetrahydronaphthalene-2,6-dicarboxylate' then renamed by the CEF Panel '1,2,3,4-tetrahydronaphthalene-2,6-dicarboxylic acid, dimethyl ester', with the CAS number 23985-75-3, and the FCM substance No 1066. The dossier was submitted on behalf of Mitsubishi Gas Chemical Company, Inc.

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.

2. Data and methodologies

2.1. Data

The applicant has submitted a dossier in support of their application for the authorisation of the substance '2,6-naphthalenedicarboxylic acid, 1,2,3,4-tetrahydro-, 2,6-dimethyl ester', to be used in FCMs. Data submitted and used for the evaluation are:

Non-toxicological data and information

- Data on identity
- Data on physical and chemical properties
- Data on intended use and authorisation
- Data on residual content of the substance
- Worst case calculated migration of the substance
- Data on identification and migration of oligomers and reaction products.

Toxicological data

- Bacterial gene mutation test
- *In vitro* mammalian cell gene mutation test
- *In vitro* mammalian cell micronucleus test
- (Q)SAR on the oxidised oligomers.

2.2. Methodologies

The assessment was conducted in line with the principles laid down in Regulation (EC) No 1935/2004 on materials and articles intended to come into contact with food. This Regulation underlines that applicants may consult the Guidelines of the Scientific Committee on Food (SCF) for the presentation of an application for safety assessment of a substance to be used in FCM prior to its authorisation (European Commission, 2001), including the corresponding data requirements. The dossier that the applicant submitted for evaluation was in line with the SCF guidelines (European Commission, 2001).

The methodology is based on the characterisation of the substance(s) that is subject of the request for safety assessment prior to authorisation, its impurities and reaction and degradation products, the evaluation of the exposure to those substances through migration, and the definition of minimum sets of toxicity data required for safety assessment.

To establish the safety from ingestion of migrating substances, the toxicological data indicating the potential hazard and the likely human exposure data need to be combined. Exposure is estimated from studies on migration into food or food simulants and considering that a person may consume daily up to 1 kg of food in contact with the relevant FCM.

As a general rule, the greater the exposure through migration, the more toxicological data is required for the safety assessment of a substance. Currently, there are three tiers with different thresholds triggering the need for more toxicological information as follows:

- In case of high migration (i.e. 5–60 mg/kg food), an extensive data set is needed.
- In case of migration between 0.05 and 5 mg/kg food, a reduced data set may suffice.
- In case of low migration (i.e. < 0.05 mg/kg food), only a limited data set is needed.

More detailed information on the required data is available in the SCF guidelines (European Commission, 2001).

The assessment was conducted in line with the principles described in the EFSA Guidance on transparency in the scientific aspects of risk assessment (EFSA, 2009) and considering the relevant existing guidance from the EFSA Scientific Committee.

3. Assessment

The substance, 1,2,3,4-tetrahydronaphthalene-2,6-dicarboxylic acid, dimethyl ester (called by the applicant 'TDCM'), is intended to be used as co-monomer [REDACTED] for the manufacture of polyester layers. The polyester layer made with the substance is not intended to be in direct contact with food, but behind a layer of cyclo-olefin polymer (COP) or cyclo-olefin copolymer (COC). The polyester middle layer containing the substance aims to limit the ingress of oxygen [REDACTED] and so protect the food. The finished multilayer articles are intended for packaging aqueous, acidic and low alcoholic foodstuffs, such as fruit juices, alcoholic drinks (beer), sodas, coffee and tea. Contact conditions include sterilisation (30 min at 121°C) followed by long-term storage (more than 6 months) at room temperature.

3.1. Non-toxicological data

Chemical formula: $C_{14}H_{16}O_4$ (Figure 1)

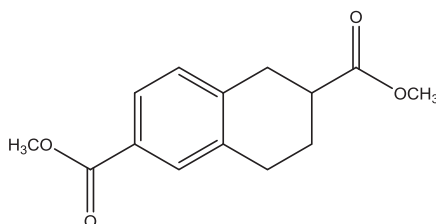


Figure 1: Chemical structure of 1,2,3,4-tetrahydronaphthalene-2,6-dicarboxylic acid, dimethyl ester (TDCM)

The molecular weight of the substance is 248.3 Da, the boiling point at atmospheric pressure 263°C. Purity is above 99.5%. The substance is freely soluble in isopropanol. Considering its structure, it is expected to have high solubility also in other polar organic solvents, but to be poorly soluble in non-polar organic solvents and in water.

The substance is thermally stable up to above 300°C. Therefore, no thermal degradation of TDCM is expected during the manufacture of the middle polyester layer and of the multilayer articles intended to be processed at up to 275°C and 290°C, respectively. TDCM may undergo hydrolysis under acidic conditions.

Overall migration was determined gravimetrically by filling simulants into a multilayer container made with cyclo-olefin polymer inner and outer layers and the middle polyester layer manufactured with the maximum intended use level of TDCM. Migration was tested into 3% acetic acid, 10% ethanol and 50% ethanol (each with conditions of 30 min at 121°C + 10 days at 60°C) and into 95% ethanol (2 h at 100°C + 10 days at 60°C). The highest overall migration, 0.6 mg/dm², was measured under the acidic contact conditions. Overall migration from a multilayer container made with the same middle polyester layer but now sandwiched between two polypropylene layers (food contact layer thickness 100–200 µm) was up to 4 mg/dm² into 95% ethanol (same simulants and contact conditions except 20% instead of 10% ethanol and 2 h at 100°C instead of 30 min at 121°C for 50% ethanol).

Specific migration of TDCM was not determined; instead a worst-case migration was calculated based on total mass transfer of the residual amount measured in a monolayer polyester resin

manufactured with the maximum intended use level of the substance. Total mass transfer calculated for a monolayer of 0.025 cm thickness with a density of 1.25 g/cm³ was up to 0.032 mg/6 dm².

The migration of oligomers and reaction products related to the TDCM-based layer and below 1,000 Da was investigated by liquid chromatography–mass spectrometry (LC/MS) on multilayer samples identical to those used for overall migration. The same simulants and contact conditions were used. When tested from a multilayer container made with polypropylene inner and outer layers, TDCM-related linear and cyclic dimers, their oxidation products and other TDCM-related reaction products were identified in 3% acetic acid, 20% ethanol, 50% ethanol and 95% ethanol. The major components were cyclic and open-chain TDCM dimers. When multilayer containers made with the cyclo-olefin polymer inner and outer layers were tested, no TDCM-related oligomers and reaction products were detected at a limit of detection estimated to be below 0.01 mg/kg food.

3.2. Toxicological data

Genotoxicity of the substance

The substance was tested for genotoxicity in three adequately performed *in vitro* tests in the presence and absence of metabolic activation up to the solubility limit.

In a bacterial mutation test using *Salmonella* Typhimurium strains TA 1535, TA 1537, TA 98, TA 100 and *Escherichia coli* strain WP2 *uvrA*, no increase in the number of revertant colonies was observed compared to the vehicle control. In addition the substance was not mutagenic at the thymidine-kinase (TK)-locus of mouse lymphoma L5178Y cells. When tested with the micronucleus assay using human lymphocyte cultures in two separate experiments, the substance did not induce statistically significant increases in the number of binucleated cells containing micronuclei.

Therefore, the CEF Panel considered that the substance does not raise concern for genotoxicity.

Genotoxicity of the substance-related oligomers and their oxidation products

The substance-related oligomers are predominantly TDCM dimers with other oligomers and oxidised oligomer derivatives in smaller amounts. As non-oxidised oligomers are esters, the Panel considered that there is no concern with respect to genotoxicity on the basis of data on the TDCM co-monomer.

The genotoxic potential of oxidation products of TDCM dimers was evaluated with (quantitative) structure–activity relationship ((Q)SAR) analysis using three *in silico* tools (US EPA T.E.S.T. v4.2, VegaNIC v1.1.3 and OECD Toolbox v3.4.0.17) based on databases on gene mutation (bacterial mutation test) and chromosomal damage (chromosomal aberration test and micronucleus assay). All possible isomers of monohydroxylated-, dihydroxylated- and keto-oxidised dimers were evaluated in the (Q)SAR analysis. No alert for genotoxicity was identified for oxidised TDCM dimers. The other oxidised TDCM-related reaction products contain the same structural fragments which were considered in the (Q)SAR analyses of the oxidised TDCM dimers. Therefore, the CEF Panel concluded that there is no alert for genotoxicity also for those reaction products. Considering the low migration potential for all of these oxidised substances in relation to the predominant dimers at the proposed migration limit of 0.05 mg/kg food, no additional data on their genotoxicity potential were requested.

Therefore, the CEF Panel considered that there is no indication of genotoxicity for the substance-related oligomers and their oxidation products.

4. Conclusions

Having considered the above-mentioned data, the CEF Panel concluded that the substance 1,2,3,4-tetrahydronaphthalene-2,6-dicarboxylic acid, dimethyl ester does not raise safety concerns for the consumer if it is used as a co-monomer for the manufacture of a polyester layer intended to be used as an inner (non-food contact) layer of a multilayer material for contact with foods simulated by simulants A, B, C, D1 (as set in Regulation (EU) 10/2011¹). The migration of the sum of the substance and the dimers (cyclic and open chain) should not exceed 0.05 mg/kg food.

¹ Commission Regulation (EU) No 10/2011 of 14 January 2011 on plastic materials and articles intended to come into contact with food. Text with EEA relevance. OJ L 12, 15.1.2011, p. 1–89.

Documentation provided to EFSA

- 1) Initial dossier. April 2014. Submitted on behalf of Mitsubishi Gas Chemical Company, Inc.
- 2) Additional data. June 2016. Submitted on behalf of Mitsubishi Gas Chemical Company, Inc.
- 3) Additional information. January 2017. Submitted on behalf of Mitsubishi Gas Chemical Company, Inc.

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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. Available online: http://ec.europa.eu/food/fs/sc/scf/out82_en.pdf

Abbreviations

CEF	Panel on food Contact Materials, Enzymes, Flavourings and Processing Aids
COC	cyclo-olefin polymer
COP	cyclo-olefin copolymer
FCM	food contact materials
LC/MS	liquid chromatography–mass spectrometry
OECD	Organisation for Economic Co-operation and Development
(Q)SAR	(quantitative) structure–activity relationship
SCF	Scientific Committee on Foods
TDCM	1,2,3,4-tetrahydronaphthalene-2,6-dicarboxylic acid dimethyl ester
TK	thymidine-kinase
US EPA	United States Environmental Protection Agency