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Safety assessment of the substance dimethyl carbonate for use in food contact materials

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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 dimethyl carbonate used as monomer for making a polycarbonate prepolymer with 1,6-hexanediol and then reacted with 4,4′-methylenediphenyldiisocyanate (MDI) and diols, such as polypropylene glycol and 1,4-butanediol, to form a thermoplastic polyurethane containing 29% of the polycarbonate prepolymer. This polymer is intended for repeated use articles with short-term contact ($\leq$ 30 min) at room temperature for types of food, simulated by 10% ethanol and 3% acetic acid. In the third migration test performed at 40°C during 30 min, overall migration was below 2 mg/dm^2. Complete migration of the residual dimethyl carbonate would have amounted to less than 1.5 μg/kg food. The migration of two cyclic hexanediol carbonate oligomers was below 50 μg/kg food when determined by the third migration test; that of all others was below 1 μg/kg food. Three *in vitro* genotoxicity studies performed in accordance with OECD Guidelines and covering the three endpoints gene mutation, structural and numerical aberrations were provided and were considered negative by the CEF Panel. The oligomers detected by the migration tests are formed from dimethyl carbonate and 1,6-hexanediol (FCM ref No 1067) do not give rise to concern for genotoxicity. The CEF Panel concluded that the use of dimethyl carbonate does not raise safety concern in the application described above. It is aware that dimethyl carbonate may be used for other polycarbonates and/or under other conditions. These are likely to result in different migrates which need to be evaluated by the business operators. In such cases, the migration of dimethyl carbonate and the total polycarbonate oligomers below 1,000 Da is of no safety concern, if each of them does not exceed 0.05 mg/kg food.

Keywords: dimethyl carbonate, CAS number 616-38-6, FCM materials No 1067, Food contact materials, Safety assessment

Requestor: Bundesamt für Verbraucherschutz und Lebensmittelsicherheit, Germany

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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 is 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 the Regulation (EC) No 1935/2004[1] 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 evaluation.

In this case, EFSA received an application from the Bundesamt für Verbraucherschutz und Lebensmittelsicherheit, Germany, requesting the evaluation of the substance dimethyl carbonate for use as monomer in FCMs, with the CAS number 616-38-6 and the FCM substance No 1067.

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 dimethyl carbonate as monomer to be used in FCM.

Data submitted and used for the evaluation are:

Non-toxicological data and information

- Chemical identity
- Description of manufacturing process of the substance
- Physical and chemical properties
- Intended use
- Existing authorisation(s)
- Migration of the substance
- Residual content of the substance
- Oligomers
- Identification, quantification and migration of reaction products and impurities

Toxicological data

- Bacterial gene mutation test
- *In vitro* mammalian cell gene mutation test
- *In vitro* mammalian chromosome aberration test

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 that is the 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 migrated substances, the toxicological data indicating the potential hazard and the likely human exposure data need to be combined. Exposure is estimated from

[1] 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 and repealing Directives 80/590/EEC and 89/109/EEC. OJ L 338, 13.11.2004, p. 4–17.

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 toxicological information as following:

a) In case of high migration (i.e. 5–60 mg/kg food), an extensive data set is needed;
b) In case of migration between 0.05 and 5 mg/kg food, a reduced data set may suffice;
c) 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 guidance from the EFSA Scientific Committee.

3. Assessment

According to the applicant, dimethyl carbonate was reacted with 1,6-hexanediol to 1,6-hexanediol-polycarbonate. This prepolymer was then reacted with 4,4′-methylenediphenyldiisocyanate (MDI) and diols, such as polypropylene glycol and 1,4-butanediol, to form a thermoplastic polyurethane (TPU). The TPU is intended for repeated use articles used at ambient temperature for short times (≤ 30 min) and in contact with foods for which 3% acetic acid and 10% ethanol are specified as simulants (EU Reg. No 10/2011).[2]

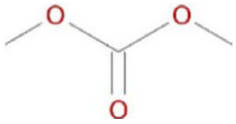
The applicant limited the scope of use of the substance to this formulation. No data are available to indicate if this formulation can be considered to be a representative example or a 'worse case' compared to other potential uses.

The use of dimethyl carbonate has not been evaluated by EFSA or the SCF for food contact materials in the past.

3.1. Non-toxicological data

Chemical formula: $C_3H_6O_3$

Chemical structure:



Molecular weight = 90 Da

Dimethyl carbonate is a liquid with a boiling point of 90°C. The substance used by the applicant had a purity of 99%, with methanol and water being the principal impurities. It was made from propylene oxide and CO_2; the resulting propylene carbonate was reacted with methanol in combination with sodium methoxide as a catalyst to produce dimethyl carbonate and propylene glycol. There are, however, also other methods of synthesis. Solubility in water at 20°C exceeds 100 g/L; the log $P_{o/w}$ was calculated as 0.23.

The substance was used to make a prepolymer with 1,6-hexanediol in a molar ratio close to 1:1, which was then reacted with MDI, polypropylene glycol and 1,4-butanediol to the corresponding TPU. The prepolymer made up about 30% of the TPU.

Overall, migration from this TPU sample (sheets of 1 cm thickness) into 3% acetic acid and 10% ethanol under repeated use conditions, during 30 min at 40°C, was below 2 mg/dm^2 in the third migration test.

The specific migration of dimethyl carbonate was not measured. The residual content in the polycarbonate prepolymer was below the detection limit of 0.2 mg/kg prepolymer. Assuming a proportion of 50% prepolymer in the polyurethane, 6 dm^2/kg food contact surface and a thickness of the article of 0.25 mm from which all residual dimethyl carbonate migrates into food, the calculated migration was less than 1.5 μg/kg food.

[2] Commission Regulation (EU) No 10/2011 of 14 January 2011 on plastic materials and articles intended to come into contact with food. Available online: http://eur-lex.europa.eu/legal-content/EN/TXT/HTML/?uri=CELEX:32011R0010&from=EN

In the third migration test, the concentrations of cyclic oligomeric hexanediol carbonates with n = 2 (MW = 288 Da) and n = 3 (MW = 432 Da) from the TPU in 3% acetic acid amounted to 33 and 6 μg/kg, respectively, that in 10% ethanol to 42 and 15 μg/kg, respectively. The migration of the oligomer n = 4 (MW = 576 Da) was below the limit of quantification of 0.7 μg/kg. The migration of other oligomeric reaction products incorporating the substance that had been identified in a 95% ethanol extract was below the detection limit. Other substances were found to migrate, but did not originate from the polycarbonate prepolymer and, therefore, were not considered.

3.2. Toxicological data

Dimethyl carbonate was tested for genotoxicity in three adequately performed *in vitro* tests, according to OECD guidelines, in the presence and absence of metabolic activation up to the recommended maximum test concentrations.

The substance (purity 99.9%) dissolved in dimethyl sulfoxide (DMSO), was tested for mutagenicity using the pre-incubation assay in *Salmonella* Typhimurium strains TA98, TA100, TA1535, TA1537 and *Escherichia coli* WP2uvrA, at concentrations up to 5,000 μg/plate. No significant increases in the frequency of revertant colonies were recorded for any of the bacterial strains, with any concentration of the test compound.

In an *in vitro* gene mutation assay carried out in mammalian cells (Chinese hamster V79 HPRT locus), the substance (purity not reported), dissolved in water up to a concentration of 10 mM, did not reveal any mutagenic response.

The substance (purity not reported) tested for chromosomal aberrations in human lymphocytes up to the concentration of 10 mM (in water) did not show any induction of chromosomal damage.

Based on the results of these three tests, the substance does not give rise to concern for genotoxicity.

The oligomers detected by the migration tests are formed from dimethyl carbonate and 1,6-hexanediol (FCM ref No. 18700) and based on the knowledge of their structures, they do not give rise to concern for genotoxicity.

4. Conclusions

Based on the above-mentioned data, the EFSA Panel on Food Contact Materials, Enzymes, Flavourings and Processing Aids (CEF Panel) concluded that there is no safety concern for the use of dimethyl carbonate described by the applicant, when:

- used with 1,6-hexanediol in the manufacture of polycarbonate prepolymers
- this prepolymer is used at up to 30% to make a thermoplastic polyurethane with MDI and diols, such as polypropylene glycol and 1,4-butanediol
- applied in repeated use articles intended for contact with foods for which 3% acetic acid and 10% ethanol are specified as simulants and under contact conditions covered by simulation during 30 min at 40°C

The CEF Panel is aware that dimethyl carbonate may be used for other polycarbonates and/or under other conditions. These are likely to result in different migrates which need to be evaluated by the business operators. In such cases, the migration of dimethyl carbonate and total polycarbonate oligomers below 1,000 Da is of no safety concern, if each of them does not exceed 0.05 mg/kg food.

Documentation provided to EFSA

1) Dossier "Dimethyl carbonate" for use as monomer in plastics. December 2015. Submitted by WTConsulting GmbH on behalf of Covestro Deutschland AG.
2) Additional data for dossier "Dimethyl carbonate". April 2016. Submitted by WTConsulting GmbH on behalf of Covestro Deutschland AG.
3) Additional data for dossier "Dimethyl carbonate". July 2016. Submitted by WTConsulting GmbH on behalf of Covestro Deutschland AG.
4) Additional data for dossier "Dimethyl carbonate". April 2017. Submitted by WTConsulting GmbH on behalf of Covestro Deutschland AG.

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EFSA (European Food Safety Authority) Scientific Committee, 2009. Guidance of the Scientific Committee on transparency in the scientific aspects of risk assessments carried out by EFSA. Part 2: general principles. EFSA Journal 2009;7(5):1051, 22 pp. https://doi.org/10.2903/j.efsa.2009.1051

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Abbreviations

CAS	Chemical Abstracts Service
CEF Panel	EFSA Panel on Food Contact Materials, Enzymes, Flavourings and Processing Aids
Da	Dalton
DMSO	dimethyl sulfoxide
FCM	food contact materials
MDI	4,4′-methylenediphenyldiisocyanate
$P_{o/w}$	octanol/water partition coefficient
SCF	Scientific Committee on Food
TPU	thermoplastic polyurethane