

SCIENTIFIC OPINION

Scientific Opinion on 26th list of substances for food contact materials^{1,2}

EFSA Scientific Opinion of the Panel on food contact materials, enzymes, flavourings and processing aids (CEF)³

European Food Safety Authority (EFSA), Parma, Italy

ABSTRACT

This scientific opinion of EFSA deals with the risk assessment of the following monomers:

1. 3,4-Diacetoxy-1-butene, CAS No. 18085-02-4, REF. No. 15180 for which the CEF Panel concluded that there is no safety concern for the consumer if the substance is used as a comonomer for the manufacture of ethylene vinyl alcohol copolymers (EVOH) and the migration of the substance together with its hydrolysis product, 3,4-dihydroxy-1-butene, is up to 0.05 mg/kg food.
2. 3-Methyl-1,5-pentanediol, CAS No. 4457-71-0, REF. No. 22074 for which the CEF Panel concluded that there is no safety concern for the consumer if the substance is used in materials in contact with food at a surface to mass ratio up to 0.5 dm²/kg (e.g. sealing gaskets) and its migration is up to 0.05 mg/kg.

The opinion of the Panel for each substance was based on data in the dossiers provided by industry.

1 On request from the Food Standards Agency, UK, Question No EFSA-Q-2008-020, and from the Ministerie van Volksgezondheid, Welzijn en Sport, the Netherlands, Question No EFSA-Q-2007-077, adopted on 24 September 2009.

2 In chapter 2, page 7, under the heading “2. 3-Methyl-1,5-pentanediol”, EFSA corrected the name and the CAS number which were previously those of the substance 3,4-diacetoxy-1-butene. The changes do not affect the conclusion of the opinion. To avoid confusion, the original version of the opinion has been removed from the website.

3 Panel members: Arturo Anadón, David Bell, Mona-Lise Binderup, Wilfried Bursch, Laurence Castle, Riccardo Crebelli, Karl-Heinz Engel, Roland Franz, Nathalie Gontard, Thomas Haertlé, Trine Husøy, Klaus-Dieter Jany, Catherine Leclercq, Jean-Claude Lhuguenot, Wim Mennes, Maria Rosaria Milana, Karla Pfaff, Kjetil Svensson, Fidel Toldrá, Rosemary Waring, Detlef Wölfle. One member of the Panel, M.-L. Binderup declared an interest for the substance REF. No. 15180 as she prepared the evaluation report of the substance under contract of her Institute DTU with EFSA. This was considered as a conflict of interest because she could not act at the same time as a representative of the contractor and a member of the Panel with voting rights. She was allowed to stay in the room to answer questions specifically addressed to her but did not participate in the discussion of the opinion. Correspondence: cef@efsa.europa.eu

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KEY WORDS

Ref. No. 15180, CAS number 18085-02-4, 3,4-Diacetoxy-1-butene; Ref. No. 22074, CAS number 4457-71-0, 3-Methyl-1,5-pentanediol.

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 requests from competent Member States Authorities for safety evaluation of substances following corresponding applications from the industry. The safety evaluation of the substances is based on data submitted by the industry following 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 (http://ec.europa.eu/food/fs/sc/scf/out82_en.pdf).

The requests received and the outcome of the safety evaluations are summarised below:

1. Food Standards Agency, UK, request for evaluation of the monomer 3,4-diacetoxy-1-butene with a CAS number 18085-02-4 and a European Commission reference number (REF. No.) 15180, for use as a comonomer in small percentages for the production of ethylene vinyl alcohol copolymer (EVOH). Dossier submitted by the company Nippon Gohsei, Tokyo, Japan.

The Panel concluded that the use of the substance as a comonomer in EVOH copolymers does not pose a risk to human health provided that the migration of the substance (including the hydrolysis product 3,4-dihydroxy-1-butene) into the food does not exceed 0.05 mg/kg food. The safety evaluation of the substance concerns only its use as a co-monomer for EVOH copolymers. The Panel noted that for enforcement purposes only an analytical method for the residual content of the substance in the polymer was provided.

2. Ministerie van Volksgezondheid, Welzijn en Sport, the Netherlands, request for evaluation of the monomer 3-methyl-1,5-pentanediol with a CAS number 4457-71-0 and a REF. No. 22074, for use as a comonomer for the production of polyurethane sealing gaskets for metal closures intended to be in contact with all types of foodstuffs packed in glass jars and bottles. Dossier submitted by the company Japan Crown Cork Co. Ltd., Yokohama, Japan.

The Panel concluded that the use of the substance does not pose a risk to human health provided that the migration of the substance into the food does not exceed 0.05 mg/kg food. The substance should be used in materials in contact with food at a surface to mass ratio up to 0.5 dm²/kg (e.g. sealing gaskets).

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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 food⁴.

According to this procedure the industry submitted applications to the Member States competent Authorities which in their turn transmitted the applications to the EFSA.

Within this general task the Scientific Panel on food contact materials, enzymes, flavourings and processing aids evaluated the following two substances:

1. 3,4-Diacetoxy-1-butene, CAS No. 18085-02-4, REF. No. 15180. On a request from the Food Standards Agency, UK and registered in EFSA as Question No EFSA-Q-2008-00020. Dossier submitted by the company Nippon Gohsei, Tokyo, Japan.
2. 3-Methyl-1,5-pentanediol, CAS No. 4457-71-0, REF. No. 22074. On a request from the Ministerie van Volksgezondheid, Welzijn en Sport, the Netherlands and registered in EFSA as Question No EFSA-Q-2008-00077. Dossier submitted by the company Japan Crown Cork Co. Ltd., Yokohama, Japan.

TERMS OF REFERENCE AS PROVIDED BY THE LEGISLATION

The EFSA is required by Article 10 of Regulation (EC) No. 1935/2004 of the European Parliament and of the Council on materials and articles intended to come into contact with food to carry out risk assessments on the risks originating from the migration of substances from food contact materials into food and deliver a scientific opinion on:

1. new substances intended to be used in food contact materials before their authorisation and inclusion in a positive list;
2. substances which are already authorised in the framework of Regulation (EC) No. 1935/2004 but need to be re-evaluated.

ACKNOWLEDGEMENTS⁵

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⁴ This Regulation replaces Directive 89/109/EEC of 21 December 1988, OJ L 40, 11.2.1989, P.38.

⁵ M.-L. Binderup declared an interest for the substance REF. No. 15180, as she prepared the evaluation report of the substance under contract of her Institute DTU with EFSA. She presented the evaluation results and another member of the WG was appointed as rapporteur to present the report to the Panel.

ASSESSMENT

Within this general task the Scientific Panel on food contact materials, enzymes, flavourings and processing aids evaluated the following substances used in food contact materials.

The substances examined are listed in ascending order of their REF. Nos. Since in the past the evaluation of substances used in food contact materials was undertaken by the Scientific Committee on Food (SCF), the same system of classification into a “SCF list” is retained for uniformity purposes. The definitions of the various SCF lists and the abbreviations used are given in the APPENDIX A.

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 (http://ec.europa.eu/food/fs/sc/scf/out82_en.pdf).

1. 3,4-DIACETOXY-1-BUTENE

The European Food Safety Authority was asked by the Food Standards Agency, UK, to evaluate the safety of the monomer 3,4-diacetoxy-1-butene with a CAS number 18085-02-4 and a REF. No. 15180. The request has been registered in the EFSA’s register of received questions under the number EFSA-Q-2008-00020. The dossier was submitted by the company Nippon Gohsei, Tokyo, Japan.

1.1. General information

According to the petitioner, the substance 3,4-diacetoxy-1-butene is used as a comonomer in small percentages for the production of ethylene vinyl alcohol copolymer (EVOH).

Final products containing the copolymer are intended to be used with all types of foodstuffs under conditions of long term storage at room temperature. Applications also include multilayer materials where the copolymer layer will not be in direct contact with food. The maximum thickness of the copolymer layer is 0.025 mm.

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

1.2. Data available in the dossier used for this evaluation

The following data were provided by the petitioner and according to the SCF guidelines and the EFSA Note for Guidance (http://www.efsa.europa.eu/EFSA/efsa_locale-1178620753812_1211902600895.htm)

Non-toxicity data:

- Data on identity
- Data on physical and chemical properties
- Data on intended use and authorisation
- Data on worst case migration of residual content

- Data on residual content of the substance and its hydrolysis product

Toxicity data:

- Bacteria gene mutation test
- *In vitro* mammalian cell gene mutation test
- *In vitro* mammalian chromosome aberration test
- *In vivo* bone marrow micronucleus test
- *In vivo* hepatocytes UDS test
- 28-day oral toxicity study in rats

1.3. Evaluation

1.3.1. Non-toxicological data

During the alkaline hydrolysis step used in the manufacture of the copolymer EVOH, any residual 3,4-diacetoxy-1-butene is largely hydrolysed to 3,4-dihydroxy-1-butene.

The migration of the substance, its hydrolysis product and the fraction with MW < 1000 Da was estimated for two typical EVOH polymers by measuring residual content and assuming 100% migration. The worst case thickness of 0.025 mm was used to calculate migration. The residual levels of the substance and its hydrolysis product were up to 0.32 and 7.0 mg/kg copolymer respectively. Their worst-case migration was calculated as 0.6 µg/kg food and 12.6 µg/kg food respectively.

The fraction with MW < 1000 Da of the two polymer samples tested was 0.15% and 0.22% and consisted of oligomers, lubricant (additive) and residual acetic acid. The worst case migration of this low MW fraction was calculated as 2.8 and 4.0 mg/kg food respectively. Only a small fraction of this mass will be derived from the starting substance.

1.3.2. Toxicological data

The substance did not show mutagenic potential in bacteria. It was tested positive in mouse lymphoma cells *in vitro* where indications of induction of both gene mutations and chromosome aberrations were obtained. It also induced chromosome aberrations in CHO cells *in vitro*. *In vivo*, oral administration of the substance did not induce DNA repair in a rat liver UDS assay, nor clastogenic/aneugenic effects in mouse bone marrow micronucleus tests. Even though treatments were not toxic to target cells, they elicited signs of general toxicity, indicating systemic exposure. Based on these data, the Panel concluded that the substance does not raise concern for genotoxicity.

The substance was tested in a 28-day oral toxicity study in rats from 75 to 750 mg/kg bw/day. Effects were observed on pancreas, liver and kidney at doses above 75 mg/kg bw/day.

The Panel considered that the hydrolysis product is also covered by the genotoxicity and toxicity testing of the substance.

Considering the oligomeric fraction, as a consequence of the addition polymerisation process and the subsequent hydrolysis step, the reactive elements of the starting substance, namely the C=C double bond and the ester groups are eliminated. The FTIR spectrum of the low molecular weight fraction is consistent with this conclusion and shows no evidence of double-bonds. Consequently, the oligomeric fraction is of no safety concern.

1.4. Conclusions – recommendations

The CEF Panel after having considered the above-mentioned data proposes that the substance 3,4-diacetoxy-1-butene be classified in the SCF_List 3 with a restriction of 0.05 mg/kg food (including the hydrolysis product 3,4-dihydroxy-1-butene) and only for use as a comonomer for EVOH copolymers. The Panel noted that for enforcement purposes only an analytical method for the residual content of the substance in the polymer was provided.

1.5. Documentation provided to EFSA

- Dossier referenced: NI10974/2. Month: January 2008. Submitted on behalf of Nippon Gohsei, Tokyo, Japan.
- Dossier referenced: NI10974-02 Month: March 2009. Submitted on behalf of Nippon Gohsei, Tokyo, Japan.

2. 3-METHYL-1,5-PENTANEDIOL

The European Food Safety Authority was asked by the Ministerie van Volksgezondheid, Welzijn en Sport, the Netherlands to evaluate the safety of the monomer 3-methyl-1,5-pentanediol with a CAS number 4457-71-0 and a REF. No. 22074. The request has been registered in the EFSA's register of received questions under the number EFSA-Q-2008-00077. The dossier was submitted by the company Japan Crown Cork Co. Ltd., Yokohama, Japan.

2.1. General information

According to the petitioner, the substance 3-methyl-1,5-pentanediol is intended to be used as a comonomer along with other alcohols and aliphatic isocyanates for the production of polyurethane sealing gaskets for metal closures intended to be in contact with all types of foodstuffs packed in glass jars and bottles. The conditions of use include pasteurization or sterilisation followed by storage at ambient temperature.

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

2.2. Data available in the dossier used for this evaluation

The following data were provided by the petitioner and according to the SCF guidelines and the EFSA Note for Guidance (http://www.efsa.europa.eu/EFSA/efsa_locale-1178620753812_1211902600895.htm)

Non-toxicity data:

- Data on identity
- Data on physical and chemical properties
- Data on the intended use and authorisation of the substance
- Data on migration of the substance
- Data on oligomers and reaction products

Toxicity data:

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

2.3. Evaluation

2.3.1. Non-toxicological data

3-Methyl-1,5-pentanediol (MPD) is hydrophilic. Overall migration and specific migration were tested for an aliphatic polyurethane sample made using the maximum use level of 9% MPD. The food simulants used were 3% acetic acid, 10% ethanol, olive oil and iso-octane which are appropriate taking into account both the nature of the polymer and the substance. The test conditions mimicked high temperature treatment followed by long storage. A surface to mass ratio of 0.5 dm² polyurethane lid/kg food was considered.

The specific migration of MPD was highest in acetic acid at 29 µg/kg food. The overall migration was up to 2 mg/kg into 10% ethanol and up to 6 mg/kg into iso-octane as well as into olive oil.

Analysis of the oligomers and reaction products was carried out. The components with molecular mass below 1000 Da are cyclic oligomers which were identified as having urethane, ester and ether linkages. The cyclic ethers derived only from the polyol used in the polyurethane formulation. Approximately 20% of the cyclic oligomers contained the MPD unit and the remaining 80% were comprised of only other comonomers. Migration of the cyclic oligomers containing the MPD unit with molecular mass below 1000 Da was estimated to be 0.35 mg/kg in isooctane, 0.41 mg/kg in olive oil and 0.36 mg/kg in 10% ethanol.

2.3.2. Toxicological data

The structures of the cyclic oligomers containing MPD were characterized by ester or amide bonds with no steric hindrance in the ring. Accordingly, these bonds are expected to be cleaved rapidly in the gastro-intestinal tract. The corresponding hydrolysis products would be adipic acid (authorised without any restriction; EC, 2002), 1,3-butanediol (authorised without any restriction; EC, 2002), hexamethylene diamine (authorised with a specific migration limit of 2.4 mg/kg food; EC, 2002) and MPD, the substance under evaluation.

3-Methyl-1,5-pentanediol did not induce mutagenicity in bacteria and in mammalian cells and did not induce chromosome aberrations in mammalian cells. Therefore it is considered as non-genotoxic.

2.4. Conclusions

The CEF Panel after having considered the above-mentioned data proposes that the substance 3-methyl-1,5-pentanediol be classified in the SCF_List 3 with a restriction of 0.05 mg/kg food and only to be used in materials in contact with food at a surface to mass ratio up to 0.5 dm²/kg (e.g. sealing gaskets)

2.5. Documentation provided to EFSA

- Dossier referenced: AR 07-0191/SIT-dia. Month: March 2007. Submitted on behalf of Japan Crown Cork Co. Ltd., Yokohama, Japan.
- Dossier referenced: AR 08-0207191/SIT. Month: March 2008. Submitted on behalf of Japan Crown Cork Co. Ltd., Yokohama, Japan.
- Dossier referenced: AR-09-0412/SIT-schm Month: June 2009. Submitted on behalf of Japan Crown Cork Co. Ltd., Yokohama, Japan.

2.6. References

- EC (European Commission), 2002. Commission Directive 2002/72/EC, relating to plastic materials and articles intended to come into contact with foodstuffs; http://europa.eu.int/comm/food/food/chemicalsafety/foodcontact/2002-72_en.pdf

APPENDICES

APPENDIX A

DEFINITION OF THE SCF LISTS

The classification into a SCF_List is a tool used for tackling authorisation dossiers and do not prejudice the management decisions that will be taken on the basis of the scientific opinions of the CEF Panel and in the framework of the applicable legislation

List 0 Substances, e.g. foods, which may be used in the production of plastic materials and articles, e.g. food ingredients and certain substances known from the intermediate metabolism in man and for which an ADI need not be established for this purpose.

List 1 Substances, e.g. food additives, for which an ADI (=Acceptable Daily Intake), a t-ADI (=temporary ADI), a MTDI (=Maximum Tolerable Daily Intake), a PMTDI (=Provisional Maximum Tolerable Daily Intake), a PTWI (=Provisional Tolerable Weekly Intake) or the classification "acceptable" has been established by this Committee or by JECFA.

List 2 Substances for which this Committee has established a TDI or a t-TDI.

List 3 Substances for which an ADI or a TDI could not be established, but where the present use could be accepted.

Some of these substances are self-limiting because of their organoleptic properties or are volatile and therefore unlikely to be present in the finished product. For other substances with very low migration, a TDI has not been set but the maximum level to be used in any packaging material or a specific limit of migration is stated. This is because the available toxicological data would give a TDI, which allows that a specific limit of migration or a composition limit could be fixed at levels very much higher than the maximum likely intakes arising from present uses of the additive.

Depending on the available toxicological studies a restriction of migration into food of 0.05 mg/kg of food (3 mutagenicity studies only) or 5 mg/kg of food (3 mutagenicity studies plus 90-day oral toxicity study and data to demonstrate the absence of potential for bio-accumulation in man) may be allocated.

List 4 (for monomers)

4A Substances for which an ADI or TDI could not be established, but which could be used if the substance migrating into foods or in food simulants is not detectable by an agreed sensitive method.

4B Substances for which an ADI or TDI could not be established, but which could be used if the levels of monomer residues in materials and articles intended to come into contact with foodstuffs are reduced as much as possible.

List 4 (for additives)

Substances for which an ADI or TDI could not be established, but which could be used if the substance migrating into foods or in food simulants is not detectable by an agreed sensitive method.

List 5 Substances that should not be used.

List 6 Substances for which there exist suspicions about their toxicity and for which data are lacking or are insufficient.

The allocation of substances to this list is mainly based upon similarity of structure with that of chemical substances already evaluated or known to have functional groups that indicate carcinogenic or other severe toxic properties.

6A Substances suspected to have carcinogenic properties. These substances should not be detectable in foods or in food simulants by an appropriate sensitive method for each substance.

6B Substances suspected to have toxic properties (other than carcinogenic). Restrictions may be indicated.

List 7 Substances for which some toxicological data exist, but for which an ADI or a TDI could not be established. The required additional information should be furnished.

List 8 Substances for which no or only scanty and inadequate data were available.

List 9 Substances and groups of substances which could not be evaluated due to lack of specifications (substances) or to lack of adequate description (groups of substances).

Groups of substances should be replaced, where possible, by individual substances actually in use. Polymers for which the data on identity specified in "SCF Guidelines" are not available.

List W "Waiting list". Substances not yet included in the Community lists, as they should be considered "new" substances, i.e. substances never approved at national level. These substances cannot be included in the Community lists, lacking the data requested by the Committee.

APPENDIX B

TERMS USED RELEVANT TO MIGRATION:

Overall migration: The sum of the amounts of volatile and non volatile substances, except water, released from a food contact material or article into food or food simulant

Specific migration: The amount of a specific substance released from a food contact material or article into food or food stimulant

ABBREVIATIONS

bw	Body weight
CAS	Chemical abstracts service
CEF	Scientific Panel on “food contact materials, enzymes, flavourings and processing aids”
CHO	Chinese hamster ovary
Da	Dalton
DNA	Deoxyribonucleic acid
EC	European Commission
EFSA	European Food Safety Authority
EVOH	Ethylene vinyl alcohol
FCM	Food contact material(s)
FTIR	Fourier transform infrared spectroscopy
MW	Molecular weight
MPD	3-Methyl-1,5-pentanediol
REF No	Reference Number
SCF	Scientific Committee on Food
UDS	Unscheduled DNA synthesis