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SCIENTIFIC OPINION

Scientific Opinion on the evaluation of the substances currently on the list in the annex to Commission Directive 96/3/EC as acceptable previous cargoes for edible fats and oils – Part III of III[1]

EFSA Panel on Contaminants in the Food Chain (CONTAM)[2, 3]

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ABSTRACT

Shipping of edible fats and oils into Europe is permitted in bulk tanks, in which substances, included in a positive list, had been previously transported. The European Commission requested EFSA to evaluate the list of substances in the Annex to Commission Directive 96/3/EC as acceptable previous cargoes for edible fats and oils, taking into account its review of the Scientific Committee on Food criteria for acceptable previous cargoes and criteria proposed by the Codex Committee for Fats and Oils. This is the third and last scientific opinion of the EFSA Panel on Contaminants in the Food Chain (CONTAM Panel) on this topic, in which sixteen of these substances or groups of substances have been evaluated. The CONTAM Panel concluded that sodium silicate (water glass) solution, iso-octanol, iso-nonanol, iso-decanol, 1,3-propanediol, isobutyl acetate, sec-butyl acetate, tert-butyl acetate, n-butyl acetate, propylene tetramer, paraffin wax, candelilla wax, white mineral oils and glycerol would not be of health concern as previous cargoes. The CONTAM Panel concluded that carnauba wax was not acceptable as a previous cargo because of its insolubility in water and high melting point, which raise concerns regarding the efficiency of tank cleaning. There was insufficient information available on the composition of montan wax for the CONTAM Panel to conclude that it would be of no health concern when used as previous cargo and hence it does not meet the criteria for acceptability as previous cargo. The CONTAM Panel made several recommendations regarding the way in which the substances are described in the Annex to Commission Directive 96/3/EC, to correct inaccuracies and to better reflect current transport practices.

KEY WORDS

acceptable previous cargo, edible fats and oils, sea transport, criteria for acceptability of previous cargoes

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SUMMARY

The worldwide trade of edible fats and oils in bulk requires their transport by road, railroad, inland waterways and sea. The carriage by sea of edible fats and oils into Europe is also permitted in bulk tanks that have previously been used to transport substances included in a positive list of acceptable previous cargoes. The EFSA Panel on Contaminants in the Food Chain (CONTAM Panel) reviewed the Scientific Committee on Food (SCF) criteria for acceptable previous cargoes and criteria proposed by the Codex Committee for Fats and Oils in 2009. In addition, the CONTAM Panel identified the importance of taking into account possible impurities and reaction products with edible fats and oils of the chemicals shipped as previous cargoes, as these might be more toxic than the chemical itself. Since usually no specifications of the impurities are available for the often rather crude substances shipped in bulk, those potentially present were determined primarily by assessing information on the source or starting substances, making worse case assumptions in each case. In November 2009, the CONTAM Panel published an opinion on a limited number of substances that had been proposed at Codex level for addition to the list of Codex acceptable previous cargoes, which were evaluated against the criteria in the previously mentioned opinion of the CONTAM Panel.

Following a request from the European Commission, the CONTAM Panel was asked to deliver a scientific opinion on the evaluation of the substances listed in the Annex to Commission Directive 96/3/EC as acceptable previous cargoes for edible fats and oils. This was to ensure that substances currently on the list of acceptable previous cargoes had been evaluated against the same criteria as recently agreed by EFSA.

This is the third and last scientific opinion of the CONTAM Panel on the evaluation of the substances listed in the Annex to Commission Directive 96/3/EC. The CONTAM Panel considered that sodium silicate (water glass) solution, 1,3-propanediol, isobutylacetate, sec-butyl acetate, tert-butyl acetate, n-butyl acetate, propylene tetramer, paraffin wax, candelilla wax, white mineral oils and glycerol when used as previous cargoes would not raise any concerns regarding their acute or chronic toxicity, genotoxicity, carcinogenicity or reproductive toxicity. In addition there were no concerns regarding possible allergenicity or adjuvant effects from such transport. In the case of iso-octanol, iso-nonanol and iso-decanol, because of data gaps in the respective toxicological profiles, the CONTAM Panel used 'read-across' from the assessment profile of oxo-alcohols C9-C13 category and concluded that the iso-alcohols under consideration are of low toxicity following acute and chronic exposure, they are not genotoxic or allergenic and therefore they are of no toxicological concern when used as previous cargoes.

The CONTAM Panel noted that four of these substances are authorized for use in food either as flavouring (isobutyl acetate, sec-butyl acetate, n-butyl acetate) or glazing (candelilla wax) agents. For two substances, acceptable daily intakes of 'not specified' or 'not limited' have been established by the Joint FAO/WHO Expert Committee on Food Additives (JECFA) or SCF because of low toxicological concern. These are sodium silicate (water glass) solution and glycerol. n-Butyl acetate has an ADI established by the SCF greater than 0.1 mg/kg body weight (b.w.) per day. In the case of sec-butyl acetate, it is a Cramer Class I substance for which exposures below a threshold of toxicological concern of 1 800 μg/person per day (30 μg/kg b.w. per day) would not be expected to be of safety concern, and the available information does not indicate any toxicological concern at the exposure levels that might occur from transport as a previous cargo. The remaining substances (iso-octanol, iso-nonanol and iso-decanol, 1,3-propanediol, tert-butyl acetate, propylene tetramer) are of relatively low toxicity and the margin of exposure that would occur comparing the maximum assumed carryover from their transport as previous cargo and the respective no-observed-adverse-effect level would indicate no concern for human health.

For all these substances no reaction products with fats and oil of toxicological concern were identified or anticipated. The CONTAM Panel noted that the only impurities of potential concern are aromatic hydrocarbons, which may be present in paraffin wax and white mineral oils. While in the case of white mineral oils they are controlled to very low levels, in the case of paraffin waxes the CONTAM Panel

concluded that this entry should be restricted to paraffin waxes that have been treated to remove aromatic hydrocarbons and which otherwise meet relevant standards to be considered as 'food grade'.

Regarding mineral oil hydrocarbons the CONTAM Panel notes that some aliphatic hydrocarbons bioaccumulate in the body, such as branched and cyclic species in the mass range of 16 - 35 carbon atoms. However, since exposure to mineral oil hydrocarbons via contamination of edible fats and oils from previous cargoes occurs only rarely and mostly at levels lower than those observed anyway in edible oils, it will contribute little to overall exposure.

In the case of montan wax, there was insufficient information available on the composition and toxicological profile of this substance for the CONTAM Panel to conclude that it does not contain components that would be of concern to human health when used as previous cargo. The CONTAM Panel therefore concludes that it does not meet the criteria for acceptability as a previous cargo for edible fats and oils.

Although the CONTAM Panel considered that there would be no health concerns arising from the use of carnauba wax as a previous cargo, using normal assumptions regarding worst case carryover, the Panel concluded that it does not meet the criteria for its acceptability as previous cargo because of its insolubility in water and high melting point and hence doubts concerning the efficiency of tank cleaning.

In addition, the CONTAM Panel noted a number of inaccuracies in the chemical identification and inconsistencies in the chemical specification of substances with respect to current transport practices, in the Annex to Commission Directive 96/3/EC. The CONTAM Panel therefore made a number of recommendations regarding the way in which the substances are described in this Annex, to correct such inaccuracies and inconsistencies.

The CONTAM Panel also made recommendations on the information that should be provided by interested parties when new substances are to be evaluated as previous cargoes.

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BACKGROUND AS PROVIDED BY THE EUROPEAN COMMISSION

General hygiene requirements relating to transport of food applicable to all food business operators laid down in Regulation (EC) No 852/2004[4] (Annex II, Chapter IV) state, amongst others, that "receptacles in vehicles and/or containers are not to be used for transporting anything other than foodstuffs where this may result in contamination."

Information showed that the application of this principle to the bulk transport was not practical and imposed an unduly onerous burden on food business when applied to bulk transport in sea-going vessels of liquid fats and oils and of raw sugar. This led to the adoption of two derogations[5,6] providing equivalent protection to public health.

Equivalent protection to public health is guaranteed on technical (e.g. tank design) and procedural (e.g. intermediate cleaning) conditions, on record keeping (e.g. on effectiveness of cleaning and on the nature of the previous cargoes) and, in the case of bulk transport of liquid fats and oils in sea-going vessels, on a list of acceptable previous cargoes. The presence of substances on the list of acceptable previous cargoes for fats and oils in the Annex to Commission Directive 96/3/EC is based on three opinions of the former Scientific Committee on Food (SCF).[7,8,9]

On 26 May 2009, the Panel on Contaminants in the Food Chain (CONTAM Panel) issued a scientific opinion on the criteria for acceptable previous cargoes for edible fats and oils. In this opinion, the CONTAM Panel reviewed the 5 criteria for the assessment of acceptability as previous cargoes for edible fats and oils previously used by the SCF and evaluated the appropriateness of four criteria developed for the same purpose by the Codex Committee for Fats and Oils (CCFO).

The CONTAM Panel noted that by application of CCFO criterion 2 some substances will turn out to be unacceptable as previous cargoes. This could include substances with ADI (or TDI) < 0.1 mg/kg b.w. or substances with genotoxic activity. The Panel considers that the exclusion of such substances as previous cargoes is appropriate.

The criteria in this Scientific Opinion were subsequently applied in the CONTAM Scientific Opinion on the evaluation of substances as acceptable previous cargoes for edible fats and oils, adopted on 29 November 2009. In this opinion, a limited number of substances that had been proposed at Codex level for addition to the list of acceptable previous cargoes were evaluated against the criteria in the previously mentioned Scientific Opinion.

In order to assure that the substances currently on the list of acceptable previous cargoes are evaluated against the same criteria, an additional Scientific Opinion covering an evaluation of the substances currently on the list of acceptable previous cargoes against the criteria used in the Opinion on the

[4] Regulation (EC) No 852/2004 of the European Parliament and of the Council of 29 April 2004 on the hygiene of foodstuffs (OJ L 139, 30.4.2004, p. 1).

[5] Commission Directive 96/3/EC of 26 January 1996 granting a derogation from certain provisions of Council Directive 93/43/EEC on the hygiene of foodstuffs as regards the transport of bulk liquid oils and fats by sea (OJ L 21, 27.01.1996, p. 42).

[6] Commission Directive 98/28/EC of 29 April 1998 granting a derogation from certain provisions of Directive 93/43/EEC on the hygiene of foodstuffs as regards the transport by sea of bulk raw sugar (OJ L 140, 12.05.1998, p. 10).

[7] SCF, 1996. Scientific Committee on Food. Opinion on the potential risk to human health arising from the transport in ships' tanks of oils and fats from substances proposed as acceptable previous cargoes, expressed on 20 September 1996 - Fortieth Series (1997) Catalogue No: GT 07 97652-EN-DE-FR). http://ec.europa.eu/food/fs/sc/scf/reports/scf_reports_40.pdf

[8] SCF, 2003. Updated opinion of the Scientific Committee on Food on the potential risk to human health arising from the transport in ships' tanks of oils and fats from substances proposed as acceptable previous cargoes, expressed on 4 April 2003. Health and Consumer Protection Directorate-General, European Commission, Brussels. http://ec.europa.eu/food/fs/sc/scf/out189_en.pdf

[9] SCF, 1997. Scientific Committee on Food. Amendment of its previous opinion of 20 September (SCF 1996). Opinion on Methyl esters of fatty acids in previous cargoes, expressed on 12-13 June 1997. Minutes of the 107th Meeting of the Scientific Committee for Food http://ec.europa.eu/food/fs/sc/oldcomm7/out13_en.html

evaluation of substances as acceptable previous cargoes for edible fats and oils carried out by EFSA would be needed.

TERMS OF REFERENCE AS PROVIDED BY THE EUROPEAN COMMISSION

In accordance with Art 29 (1) of Regulation (EC) No 178/2002, the European Commission asks the European Food Safety Authority for a scientific opinion on the evaluation of the substances currently on the list in the Annex to Commission Directive 1996/3/EC as acceptable previous cargoes for edible fats and oils. The evaluation should be based on the SCF criteria and the criteria proposed by the CCFO as reviewed by the Panel on Contaminants in Food Chain in 2009[10] for acceptable previous cargoes for edible fats and oils.

[10] http://www.efsa.europa.eu/en/scdocs/scdoc/1110.htm

ASSESSMENT

1. Introduction

General hygiene requirements relating to transport of food applicable to all food business operators are laid down in Annex II, Chapter IV of Regulation (EC) No 852/2004[11] and state, amongst others, that 'receptacles in vehicles and/or containers are not to be used for transporting anything other than foodstuffs where this may result in contamination'. However, the application of this principle to bulk transport is not practical and imposes an unduly onerous burden on food businesses when applied to bulk transport in sea-going vessels of liquid fats and oils. Commission Directive 96/3/EC[5] permits sea transport of fats and oils in bulk tanks, which have previously been used to transport substances included in a positive list of acceptable previous cargoes.

The majority of the global trade in oils and fats is done under contracts of the Federation of Oils, Seeds and Fats Associations (FOSFA), a professional international contract-issuing and arbitral body concerned exclusively with the world trade in oilseeds, oils and fats, which provides a wide range of standards covering different methods of transportation and different terms of trade. FOSFA does not require dedicated containers and allows transport in tanks that have previously been used to transport substances from an approved positive list. A FOSFA list of banned previous cargoes also exists (FOSFA, 2008).

In 1996, the Scientific Committee on Food (SCF) assessed the risk to human health arising from potential contamination of fats and oils shipped in tanks, which may have been used to transport the substances as given in the Annex to Commission Directive 96/3/EC[5] (SCF, 1997a). A number of substances were evaluated and a set of criteria for acceptable previous cargoes (SCF criteria) was proposed. In 2003, the SCF issued an update of its previous opinion in the light of new toxicological information, where available (SCF, 2003).

Based on the evaluations carried out by the SCF in 1996 and 2003, the list of substances acceptable as previous cargoes set out in the Annex to Commission Directive 96/3/EC[5] was amended by Commission Decision 2004/4/EC.[12] However, the substances in the list were only considered to be acceptable as long as the legal provisions were applied, especially regarding the cleaning and condition of the tanks and accurate documented evidence relating to the nature of the three previous cargoes, and to the efficacy of the cleaning process between cargoes, to be kept by the captain of the vessel.

The Codex Alimentarius Commission (CAC) also sets international food standards to protect the health of consumers and ensure fair practices in the food trade. Under the Codex system, the Codex Committee for Fats and Oils (CCFO) has been established to elaborate standards for fats and oils of animal, vegetable and marine origin, including margarine and olive oil. It has adopted the Recommended International Code of Practice for the Storage and Transport of Edible Fats and Oils in Bulk, which includes a Draft Codex List of Acceptable Previous Cargoes and a Proposed Draft List of Acceptable Previous Cargoes. In addition, a set of criteria (CCFO criteria) has been developed to determine the acceptability of substances as previous cargoes, based on the criteria proposed by the Food and Agriculture Organization of the United Nations (FAO) and the World Health Organization (WHO) (FAO/WHO) Joint Technical Meeting (FAO/WHO, 2007). Both the draft lists of acceptable previous cargoes and the criteria were adopted by the CAC (Geneva, 4-9 July 2011) (FAO/WHO, 2011).

[11] Regulation (EC) No 854/2004 of the European Parliament and of the Council of 29 April 2004 laying down specific rules for the organisation of official controls on products of animal origin intended for human consumption. OJ L 139, 30.4.2004, p. 206-320.

[12] Commission Directive 2004/4/EC of 15 January 2004 amending Directive 96/3/EC granting a derogation from certain provisions of Council Directive 93/43/EEC on the hygiene of foodstuffs as regards the transport of bulk liquid oils and fats by sea. OJ L 15, 22.1.2004, p. 25-30.

In 2009, the European Commission requested the European Food Safety Authority (EFSA) to review the SCF criteria for acceptable previous cargoes for edible fats and oils, in the light of the CCFO criteria (CCFO, 2009). The EFSA Panel on Contaminants in the Food Chain (CONTAM Panel) issued an opinion in May 2009 and concluded that the criteria for evaluation of acceptable previous cargoes as proposed by the CCFO were not in conflict with any of the five criteria developed by the SCF (EFSA, 2009a). Most of the SCF criteria were either explicitly or implicitly covered by the CCFO criteria. The last SCF criterion, dealing with the availability of analytical methods is not explicitly addressed in the CCFO criteria and the CONTAM Panel considered that this criterion is still important, though rather in the sense that the development of a corresponding method is considered to be feasible rather than the immediate availability of such a method (as most substances used as previous cargoes are not routinely analyzed in fats and oils). The Panel also considered relevant the inclusion of criteria covering possible allergenicity and the potential for reaction of compounds with oils and fats.

The criteria in the Scientific Opinion of 2009 were subsequently applied by the CONTAM Panel for the evaluation of the acceptability as previous cargoes of the substances included in the Codex Proposed Draft List of Acceptable Previous Cargoes (EFSA, 2009b).

The European Commission asked EFSA for a scientific opinion on the evaluation of the substances currently on the list in the Annex to Commission Directive 96/3/EC as acceptable previous cargoes for edible fats and oils. The evaluation should be based on the review of the criteria performed by the CONTAM Panel in 2009, in order to ensure that the substances currently on the list are evaluated against the same criteria.

The outcome of the evaluation of the substances is presented in three scientific opinions, for practical purposes. A first opinion was published in December 2011 reporting the evaluation of 13 substances in the list (EFSA, 2011). A second opinion reporting the evaluation of 35 substances (or groups of) in the list was published in May 2012 (EFSA, 2012a). In this third and last output, the evaluation of 16 substances (or groups of) listed in Table 1 is described. The entries in Table 1 are as listed in the Annex to Commission Directive 96/3/EC.[5] In reviewing these substances, the CONTAM Panel concluded that modifications to some of these entries would improve accuracy and these are discussed in the Opinion (see Table 4).

Substances transported in bulk as previous cargoes are often rather crude and usually no specific information is available on the impurities present. Hence, for many substances, the CONTAM Panel had to determine which impurities might be present primarily by assessment of the source or starting material and likely method of preparation of the substance to be transported. Chemicals transported as previous cargoes may vary in composition, depending on the starting materials and the method of preparation, details for which were obtained, in part, from information obtained from FOSFA. The CONTAM Panel based its evaluations on worst case assumptions on these aspects.

Table 1: Substances on the list in the Annex to Commission Directive 96/3/EC as acceptable previous cargoes for edible fats and oils and re-evaluated in the present opinion.

Substance (synonyms)	CAS Number
Sodium silicate (water glass)	1344-09-8
iso-Octanol (isooctyl alcohol)	26952-21-6
iso-Nonanol (isononyl alcohol)	27458-94-2
iso-Decanol (isodecyl alcohol)	25339-17-7
1,3-Propylene glycol (trimethylene glycol; 1.3-propanediol)	504-63-2
iso-Butyl acetate	110-19-0
sec-Butyl acetate	105-46-4
tert-Butyl acetate	540-88-5
n-Butyl acetate	123-86-4
Propylene tetramer	6842-15-5
Montan wax	8002-53-7
Paraffin wax	8002-74-2 / 63231-60-7
Carnauba wax — (Brazil wax)	8015-86-9
Candelilla wax	8006-44-8
White mineral oils	8042-47-5
Glycerine (glycerol; glycerin)	56-81-5

2. Previous risk assessments

2.1. Scientific Committee on Food (SCF)

In 1996, the SCF issued an opinion on the potential risk to human health arising from the transport of fats and oils in ships' tanks from substances proposed as acceptable previous cargoes (SCF, 1997a). The Committee was asked to examine the substances given in the Annex to Commission Directive 96/3/EC[5] and other substances that may be proposed for addition to the list. The SCF was asked to take into account the information provided by industry concerning (i) the likelihood and potential levels of contamination in the light of the information regarding cleaning procedures, dilution and limits of detection of analytical methods and (ii) the additional processing of fats and oils. The SCF focused its attention on the evaluation of the toxicological properties of the substances without considering other aspects such as the ecotoxicological characteristics, the microbial status or nutritional relevance. The Committee's view on the acceptability of the substances in the list of acceptable previous cargoes from Commission Directive 96/3/EC[5] was based on the criteria shown in Table 2.

Table 2: Criteria for the inclusion of substances in the list of acceptable previous cargoes according to the SCF (SCF, 1997a, 2003).

	SCF Criteria[(a)]
1.	No toxicological concerns, particularly with regard to their genotoxic and carcinogenic potential, for which a threshold is difficult to establish.
2.	Efficacy of procedures used to clean ships' tanks between cargoes
3.	Dilution factor in relation to the potential amount of residue of the previous cargo and any impurity which the previous cargo might have contained and the quantity of oil or fat transported.
4.	Subsequent application of refining processes and solubility relevant to the occurrence of possible contaminating residues.
5.	Availability of analytical methods to verify the presence of trace amounts of residues or the absence of contamination of oils and fats.

(a): The SCF criteria have no numbering in the original reference. In the present opinion they have been included for an easier referral throughout the document.

The substances in the list were only considered to be acceptable as long as the provisions of the Hygiene of Foodstuffs Directive 93/43/EEC,[13] later replaced by Regulation (EC) 852/2004,[14] were applied, and especially regarding the cleaning and condition of the tanks, as well as the requirement included in Commission Directive 96/3/EC,[5] where accurately documented evidence relating to the three previous cargoes, and the efficacy of the cleaning process between cargoes, should be kept by the captain of the vessel.

Some of the substances evaluated were accepted as previous cargoes by the SCF because they are food or food components. A number of other substances were considered acceptable from a toxicological point of view.

For others, although the available toxicological information was insufficient to enable a full evaluation, the SCF was able to accept a number of compounds provisionally on the basis of their unlikely genotoxic potential, their easy removal by tank cleaning procedures, and the very low residues expected as a result of these factors and their likely dilution in a subsequent cargo of edible fats or oils (e.g. iso-decanol, iso-nonanol, iso-octanol, montan and paraffin wax, white mineral oils and methyl tertiary butyl ether (MTBE)).

Ten substances were considered as not acceptable due to inadequate toxicological and/or technical data (2,3-butanediol, 1,3-propylene glycol, methyl esters of fatty acids (laurate, palmitate, stearate, and oleate) and nonane) or because their genotoxic and carcinogenic potential were a reason for concern (iso-butanol, cyclohexanol and cyclohexanone).

Later, the SCF was requested to update the list of substances from its previous opinion in the light of new toxicological information, if available (SCF, 2003). Priority was given to those substances provisionally accepted as previous cargoes. As in its previous opinion, the SCF focused on the potential toxicological concerns, without considering other aspects. Neither the specifications of the transported fats and oils nor the purity of the previous cargo were taken into account. The criteria used for re-evaluation were the same as those described in its opinion from 1996 (Table 2). The re-evaluation led to the full acceptance of some substances previously considered as not acceptable (e.g. methyl esters of the following fatty acids: laureate, palmitate, stearate and oleate) or provisionally acceptable (e.g. MTBE) in view of the new toxicological information. Others were still considered to be not acceptable as previous cargoes since the new information did not allow for a re-evaluation of their carcinogenicity or genotoxicity (e.g. 2,3-butanediol, isobutanol, cyclohexanol and cyclohexanone). Finally, some were considered to be still only provisionally acceptable, as there was insufficient new information on their toxicity to allow re-evaluation (iso-decanol, iso-nonanol, iso-octanol, montan and paraffin wax and white mineral oils).

Details of the SCF conclusions are given in the corresponding Section for each substance under evaluation.

2.2. European Food Safety Authority (EFSA)

At the request of the European Commission, the EFSA reviewed the criteria for acceptable previous cargoes for edible fats and oils set by the SCF (Table 2). In doing so, the CONTAM Panel assessed the appropriateness of the four CCFO criteria (Table 3), one by one, by comparing them with those set by the SCF for acceptable previous cargoes for edible fats and oils in 1996.

[13] Council Directive 93/43/EEC on the hygiene of foodstuffs of 14 June 1993. OJ L 175, 19.7.1993, p. 1-11.
[14] Regulation (EC) No 852/2004 of the European Parliament and of the Council of 29 April 2004 on the hygiene of foodstuffs. OJ L 139, 30.4.2004, p. 1.

Table 3: Criteria proposed for immediate previous cargoes by the CCFO during their 21st meeting (CCFO, 2009) and adopted by the CAC (FAO/WHO, 2011).

	CCFO Criteria (adopted at Step 5)
1.	The substance is transported/stored in an appropriately designed system; with adequate cleaning routines, including the verification of the efficacy of cleaning between cargoes, followed by effective inspection and recording procedures.
2.	Residues of the substance in the subsequent cargo of fat or oil should not result in adverse human health effects. The ADI (or TDI) of the substance should be greater than or equal to 0.1 mg/kg b.w./day. Substances for which there is no numerical ADI (or TDI) should be evaluated on a case by case basis.
3.	The substance should not be or contain a known food allergen, unless the identified food allergen can be adequately removed by subsequent processing of the fat or oil for its intended use.
4.	Most substances do not react with edible fats and oils under normal shipping and storage conditions. However, if the substance does react with edible fats and oils, any known reaction products must comply with criteria 2 and 3.

ADI: acceptable daily intake; b.w.: body weight; CAC: Codex Alimentarius Commission; CCFO: Codex Committee for Fats and Oils; TDI: tolerable daily intake.

Criterion 2 was based on the fact that it could be estimated, as a worst case, that the residue of the substance remaining in the tanks after cleaning could give rise to a maximum of 100 mg residue/kg of fat or oil (FAO/WHO, 2007). Average consumption of fats and oils, based on the WHO-GEMS/Food Consumption Cluster diets is 25 g/day for a single type of fat or oil. Using a factor of 2.5 to take account of high consumers, an ADI of 0.1 mg/kg body weight (b.w.) per day would be the minimum requirement to ensure sufficient protection of all consumers, including children and high-intake consumers.

The CONTAM Panel concluded that the criteria for evaluation of acceptable previous cargoes for edible fats and oils as proposed by the CCFO are not in conflict with any of the five criteria developed by the SCF. SCF criteria 1 to 4 are either explicitly or implicitly covered by the CCFO criteria. SCF criterion 5 dealing with the availability of analytical methods is not explicitly addressed in the CCFO criteria. The CONTAM Panel considers that SCF criterion 5 is still important. The CCFO criteria also cover food allergens and the potential for compounds to react with edible fats and oils. The CONTAM Panel considers these additions relevant.

In addition, the CONTAM Panel made the following remarks:

- The CCFO criteria specifically apply to the immediate previous cargo. The CCFO criterion 1, which addresses among other issues, documentation procedures, does not specify for how many previous cargoes records should be kept. This might be particularly important in the event that earlier previous cargoes comprise substances for which an acceptable daily intake (ADI) (or tolerable daily intake (TDI)) has not been established. The CONTAM Panel was of the opinion that records of the three previous cargoes should be kept, in accordance with the Codex Recommended International Code of Practice for the Storage and Transport of Edible Fats and Oils in Bulk.

- With respect to CCFO criterion 2, the CONTAM Panel agreed with the proposed threshold of an ADI (or TDI) of ≥ 0.1 mg/kg b.w. For substances for which there is no numerical ADI (or TDI) a case by case evaluation is needed. The Panel also considered the situation of second and third previous cargoes and concluded that for non-genotoxic substances their transport as second and third previous cargoes is not of concern, taking into account their very limited carry over. However, the CONTAM Panel noted that genotoxic substances would not be acceptable as previous cargoes. Also in relation to CCFO criterion 2, the CONTAM Panel noted that as consequence of the above some substances will turn out to be unacceptable as

previous cargoes. This could include substances with an ADI (or TDI) < 0.1 mg/kg b.w. or substances with genotoxic activity. The Panel was of the opinion that the exclusion of such substances as previous cargoes is appropriate.

- CCFO criterion 3 is sufficient to cover 'known food allergens'. However, the CONTAM Panel considered that the scope of the CCFO criterion is too narrow, and should apply to all known allergens, not just to known food allergens, given the fact that the same cargo may be sold for cosmetic use.

- The CONTAM Panel endorsed CCFO criterion 4 without any further remarks.

3. Evaluation of the substances currently on the list in the annex to Commission Directive 96/3/EC as acceptable previous cargoes for edible fats and oils

The CONTAM Panel has evaluated the acceptability of the substances listed in Table 1 (as amended, see Table 4) as previous cargoes for edible fats and oils. The evaluation is based on its review of the criteria for acceptable previous cargoes as described in Section 2.2. (EFSA, 2009a) and the experience gained in its subsequent evaluation of 13 substances as previous cargoes which highlighted the importance of addressing any impurities that might be present (EFSA, 2009b):

- The substance is transported/stored in an appropriately designed system; with adequate cleaning routines, including the verification of the efficacy of cleaning between cargoes, followed by effective inspection and recording procedures. The CONTAM Panel was of the opinion that records of the three previous cargoes should be kept, in accordance with the Codex Recommended International Code of Practice for the Storage and Transport of Edible Fats and Oils in Bulk. The CONTAM Panel noted that the choices made with respect to design of the transport system and the cleaning methods are the responsibility of those managing the transport of previous cargoes. It was the nature and amount of substances that might be carried over into a subsequent cargo of edible fats and oils that was taken into account by the CONTAM Panel in its evaluation of previous cargoes.

- Residues of the substance in the subsequent cargo of fat or oil should not result in adverse human health effects. The ADI (or TDI) of the substance should be greater than or equal to 0.1 mg/kg b.w. per day. Substances for which there is no numerical ADI (or TDI) should be evaluated on a case by case basis. For non-genotoxic substances their transport as second and third previous cargoes is not of concern, taking into account their very limited carry over. However, genotoxic substances would not be acceptable as previous cargoes.

- The substance should not be or contain a known allergen, unless the identified allergen can be adequately removed by subsequent processing of the fat or oil for its intended use. This criterion covers all allergens, not only food allergens.

- If the substance reacts with edible fats and oils, any known reaction products must comply with the above two criteria. Reactions may be promoted by the acidity from free fatty acids (crude oils) and may occur over many months; they do not need to result in high yields to be potentially relevant. Transesterifications are known to occur under such conditions (Biedermann et al., 2008). Prominent reactive functions of lipids are hydroxyl groups on the alkyl chain of fatty acids or non-esterified positions of the glycerol moiety and epoxides from epoxidized fatty acids (Fankhauser-Noti et al., 2006).

- The development of analytical methods of sufficient sensitivity to verify the presence of trace amounts of residues or the absence of contamination of fats and oils should be feasible, e.g. for control authorities. Such methods are seldom routinely available, since most substances used as previous cargoes are not commonly analyzed in fats and oils. The CONTAM Panel therefore evaluated the feasibility of developing such methodology as part of its assessment of

each substance. In those cases where, due to the nature or composition of the substance (or group of) to be evaluated as previous cargo, the feasibility of developing suitable analytical methods was considered questionable, this was indicated when discussing the substance (or group of) in the respective chapter and was used as an argument for the rejection of a substance as previous cargo.

- It is unrealistic to assume that chemical analysis would regularly be applied to check the suitability of a material used as previous cargo or the efficiency of a cleaning procedure for a substance. Therefore the substances were evaluated under worst case assumptions with regard to cleaning efficiency and material composition (in particular the potential presence of toxic impurities or the formation of reaction products with edible fats and oils).

- Potentially relevant impurities in the previous cargo should be taken into account since they may be toxicologically more important than the substance itself. As most products exist in different grades, a reasonable worst-case product within the specification provided was assumed, the concentration of the impurity estimated from available literature and evaluated in the same way as a listed substance. Impurities are often specified for fine chemicals and highly purified products. However, these are unlikely to be shipped in bulk. Those more commonly encountered are likely to be of intermediate to low purity grade and no specific information about impurities is publicly available (methods of synthesis are usually confidential). Due to this lack of information, the source and most probable way (or ways) of synthesis of the substance was investigated to determine potentially relevant impurities, such as unreacted starting substances or products of side reactions.

The current evaluation of the substances as acceptable previous cargoes is based on available studies/information from literature searches carried out, up to the time of the evaluation, on public databases, e.g. PubMed, International Uniform Chemical Information Database (IUCLID), European Chemicals Agency (ECHA), evaluations made by national and international bodies, e.g. WHO and Organisation for Economic Co-operation and Development (OECD) and on information requested from FOSFA.

The safety of the substances as identified chemically in the Annex (Table 1, with any clarifications necessary as indicated in Table 4) was evaluated first. If the substance was considered acceptable as a previous cargo from a toxicological point of view, it was further evaluated in accordance with the additional criteria listed above (EFSA, 2009a,b).

As part of the evaluation of safety for human health, responses of the immune system have been considered. This is necessary for allergens, but it is also relevant for substances which are not allergens themselves but can promote allergy, so-called adjuvants. Adjuvant activity has been shown e.g. for various natural lipids such as pollen-associated oxylipins (Traidl-Hoffmann et al., 2009), for plant lectins (reviewed by Lavelle et al., 2001), for saponins from a variety of plants (Lacaille-Dubois, 2005; Sun et al., 2009), and for inulin and certain other carbohydrates (Petrovsky and Cooper, 2011). It has been determined on a case-to-case basis whether any documented adjuvant activity is sufficiently strong to be of concern in the context of transport as a previous cargo.

3.1. SODIUM SILICATE (water glass) (CAS No 1344-09-8)

Sodium silicate, also called water glass, is traded as a solid (powder) or as a viscous liquid when dissolved in water. In reality, solid sodium silicate is a metasilicate of oligomeric structure containing on average 3-5 silicate moieties. Sodium silicate solutions are strongly basic and barely soluble in edible fats and oils.

Sodium silicate is prepared by heating sodium carbonate with silicium dioxide (quartz sand).

Sodium silicate has many different uses. Large amounts are used in the building industry as an additive to special cements (e.g. to improve tightness of concrete), but also for ceramics, as a binder for mineral dyes, for bleaching pulp, repairing cars, etc.

3.1.1. Previous evaluations

The SCF evaluated sodium silicate (water glass) in 1996 as a previous cargo for edible fats and oils and considered this substance acceptable in view of the fact that it was approved as a food additive by the European Union (E550) (Annex 1 of Directive 95/2/EC[15]), with an ADI 'not specified' (SCF, 1997a). In the 2003 SCF evaluation of acceptable previous cargoes, sodium silicate was not further evaluated as it was already considered acceptable (SCF, 2003).

In 1974, an ADI 'not limited' was also assigned by the Joint FAO/WHO Expert Committee on Food Additives (JECFA) to sodium silicate (JECFA, 1974).

In 2004, OECD reviewed the toxicological data of soluble silicates including sodium silicate and concluded that soluble silicates possess properties indicating a hazard for human health (irritancy/corrosivity) but, provided that adequate risk reduction measures are in place (classification and labelling), they were currently considered of low priority for further work (OECD, 2004a).

3.1.2. Current evaluation

Sodium silicate is a solid at normal temperature and pressure, with a melting point above 800 °C. Hence, in this form it is not a suitable cargo for the type of tanker used to transport edible fats and oils by sea. When used as a previous cargo to edible fats and oils it has to be transported as a solution, to enable effective transfer and tank cleaning (see Documentation provided to EFSA).

3.1.2.1. Expected impurities

Sodium silicate is often made starting from crude minerals, and for many applications purity is not critical. It will contain other alkali or earth alkali ions and also other anions. These tend to be easily removed from the tank by washing with water. Hence, these substances are unlikely to be of any concern at the levels that would occur in edible fats and oils when sodium silicate is transported as the previous cargo.

3.1.2.2. Reactivity and reaction products

Sodium silicate solution is strongly basic. When mixed into fats and oils at low amounts (below 100 mg/kg), it will interact immediately with free fatty acids in the oil and be neutralised. The resulting salts of organic acids are not reactive. This is also why it does not cause saponification when mixed with fats and oils at the concentrations expected when used as a previous cargo.

3.1.2.3. Toxicological profile

Absorption, distribution, metabolism and excretion

Silicon is an essential trace element that participates in important metabolic processes including bone, cartilage and connective tissue formation. The silicon is present almost entirely as free soluble monosilicic acid (Carlisle, 1986, as cited in OECD, 2004a). No reliable toxicokinetic, metabolic or mechanistic studies are available for soluble silicates. Since concentrated silicate solutions are only stable at pH >11.5 and lowering the pH leads to the formation of an insoluble silica gel, after ingestion gel formation is expected to occur due to the hydrochloric acid of the stomach. The degree of gel formation will depend on the amount of ingested silicate solution and the neutralising and buffering capacity of the gastrointestinal tract. Gastrointestinal absorption of insoluble silica will be insignificant as compared to that of soluble anions. Absorbed soluble silicates are excreted via urine and to a lesser

[15] European Parliament and Council Directive No 95/2/EC of 20 February 1995 on food additives other than colours and sweeteners. OJ L 61, 18. 3. 1995, p. 1.

extent via the faeces. Markedly increased and rapid urinary excretion of silica was observed when soluble sodium silicates were administered by various routes to different animal species (OECD, 2004a). The excretion rate of sodium silicate administered to rats via stomach tube (Benke and Osborn, 1979, as cited in OECD, 2004a) was independent of the doses applied, indicating that the limiting factor is the rate of production of soluble or absorbable silicon in the gastrointestinal tract.

Acute toxicity

Exposure to silicate solutions involves not only exposure to silica in the form of its various silicate anions but also to alkalinity. Both distribution of the various silicate anion species and alkalinity depend on the silica to alkali-oxide ratio and the concentration of a given solution.

Sodium and potassium silicates can be irritating or corrosive to the skin of animals as well as of humans, depending on their molar ratio and concentration. Any effects on the skin decrease with increasing molar ratio, superimposed by increasing irritancy with increasing concentrations (OECD, 2004a).

The oral toxicity of sodium silicate in rats decreased at increasing molar ratio SiO_2:Na_2O. The LD_{50} ranged from 500 mg/kg b.w. for molar ratio 0.5 to 8 650 mg/kg b.w. for 3.38, thus showing the inverse correlation between molar ratio and toxicity (Schleyer and Blumberg, 1982 and references therein, as cited in OECD, 2004a). Clinical signs observed near to or exceeding the LD_{50} values (Saiwai et al., 1980, as cited in OECD, 2004a) consisted of apathy, staggering gait, dyspnoea, piloerection, abdominal discomfort, and unconsciousness. Autopsy revealed acute gastro-enteritis, vascular congestion, mottled livers, changes in pH of body fluids, shock, chemical irritation and/or corrosion of the viscera. In another study in rats the acute oral LD_{50} was 1 960 mg/kg in groups receiving the 2.0 molar ratio and 2 710 mg/kg in groups receiving the 2.4 ratio sodium silicate (Rhone-Poulenc, 1971, as cited in Elmore, 2005). Although it is not possible to attribute unequivocally any observed toxicity of a silicate solution to either silicate, alkalinity or a combination of both, the observed toxicological signs are indicative of effects due to high alkalinity.

Subacute, subchronic and chronic toxicity studies

Soluble silicates have been tested in drinking water in a number of repeated dose studies. Sodium silicate had a no-observed-adverse-effect level (NOAEL) of 159 mg/kg b.w. per day (highest tested dose) in rats exposed for 180 days (Smith et al., 1973, as cited in OECD, 2004a). The NOAEL for sodium metasilicate in rats exposed for 3 months was 227 and 237 mg/kg b.w. per day for males and females, respectively (Ito et al., 1975, as cited in OECD, 2004a). When rats were administered sodium metasilicate pentahydrate in the diet at 1 259 mg/kg b.w. per day for 8 weeks no effects on body or organ weights were observed but plasma calcium and magnesium and liver zinc were significantly reduced (Kayongo-Male and Jia, 1999, as cited in OECD, 2004a).

Genotoxicity

In vitro, soluble silicates did not induce gene mutations in a series of in vitro bacterial assays including *Salmonella typhimurium* Ames test (Saiwai et al., 1980; Ito et al., 1986, as cited in OECD, 2004a). An aqueous sodium silicate solution (36 % active ingredient) induced no chromosomal aberrations in V79 cells, either in the absence or in the presence of metabolic activation (Schulz, 2006, as cited in OECD, 2004a, amended in 2006). *In vivo*, sodium metasilicate did not induce chromosomal aberrations in bone marrow cells of mice (Saiwai et al., 1980, as cited in OECD, 2004a). Although the reliability of these studies cannot be fully evaluated, the lack of structural alerts and these negative results indicate that sodium silicate is unlikely to present any genotoxic potential.

Carcinogenicity

There were no carcinogenicity studies available.

Developmental and reproductive toxicity

The available data on toxicity to reproduction are limited and do not allow any firm conclusions to be drawn. In a developmental toxicity study with mice, sodium metasilicate in aqueous solution was administered at doses of 12.5, 50 or 200 mg/kg b.w. per day from day 0 until day 17/18 of gestation by gavage. No treatment-related effects were observed either in mothers or in pups (Saiwai et al., 1980, as cited in OECD, 2004a).

3.1.2.4. Allergenicity

There is a single report on immediate type allergic contact reactions in a worker exposed to 20 % aqueous sodium silicate (Tanaka et al., 1982). A mouse study on allergy-prone BALB/c mice reported an allergic reaction at high concentrations (4-6 % sodium metasilicate), but no effects on cell proliferation in the auricular lymph nodes were observed at concentrations up to 6 % (Karrow et al., 2002, as cited in OECD, 2004a). Available data give no indication that sodium silicate is an allergen or an adjuvant at concentrations expected from its use as a previous cargo.

3.1.3. Conclusions

Current shipping practices mean that when sodium silicate is transported prior to edible fats and oils, the design of the tanker will be such that sodium silicate has to be transported as a solution. Hence, the CONTAM Panel recommends that the entry for the substance in the Annex to Commission Directive 96/3/EC be amended to 'Sodium silicate (water glass) solution (CAS No 1344-09-8)'.

Toxicological effects of sodium silicate following acute and repeat dosing are mostly due to high alkalinity. However, following ingestion it will be diluted and buffered by the neutralising capacity of the gastrointestinal tract. Thus the CONTAM Panel considered that the levels that would occur following oral ingestion of fats and oils transported subsequent to sodium silicate as a previous cargo would not give rise to any toxicological concern. Although there are no carcinogenicity studies available sodium silicate did not show any genotoxic activity in a variety of *in vitro* and *in vivo* assays thus indicating no genotoxic potential. Available data give no indication that sodium silicate is an allergen or an adjuvant at concentrations expected from its use as a previous cargo. Exposure to sodium silicates can be irritating or corrosive to the skin, however the potential levels arising in fats and oils following its transport as previous cargo would be of no concern. There are no reactions of concern with edible fats and oils, nor are any anticipated impurities likely to be present at levels of toxicological concern.

The CONTAM Panel therefore concludes that sodium silicate solution meets the criteria for acceptability as a previous cargo for edible fats and oils.

3.2. ISO-OCTANOL (isooctyl alcohol) (CAS No 26952-21-6), ISO-NONANOL (isononyl alcohol) (CAS No 27458-94-2) and ISO-DECANOL (isodecyl alcohol) (CAS No 25339-17-7)

Iso-octanol, iso-nonanol and iso-decanol are grouped as a family of saturated alcohols. They consist of complex mixtures of straight chain and branched alcohols and are usually not completely separated from each other, e.g. iso-nonanol may contain some iso-octanol as well as some iso-decanol.

Iso-octanol, iso-nonanol and iso-decanol are slightly viscous, high boiling liquids, less dense than water and insoluble in water.

These iso-alcohols are also called oxo-alcohols, as they are produced by hydroformylation (also called 'oxo' process); this process involves reaction of an olefin with carbon monoxide and hydrogen to produce an aldehyde that then undergoes hydrogenation to an alcohol. The olefins are obtained by condensation of propylene and butenes with phosphoric acid at 200 °C under pressure to give a mixture of branched olefins. A recent development in the oxo technology uses a modified rhodium catalyst in order to enable working with a broader range of olefins.

These iso-alcohols are traded as mixtures of isomers.

Iso-octanol, iso-nonanol and iso-decanol are used as intermediates for the production of plasticizers, such as diisononyl- and diisodecyl phthalate (DINP and DIDP) or corresponding adipates, as ingredient in synthetic lubricants, agents in uranium refining, specialty solvents and antifoaming agents in textile processing. Iso-octanol is also used as an intermediate for non-ionic detergents and surfactants, synthetic drying oils, cutting and lubricating oils, hydraulic fluids, resin solvents, emulsifiers and antifoaming agents.

3.2.1. Previous evaluations

The SCF evaluated iso-decanol, iso-nonanol and iso-octanol as previous cargoes in 1996 and they were included in the list of Annex 2 of its Opinion as substances provisionally acceptable because of a lack of toxicological data and uncertainty as to their composition. It was also noted that they can be easily removed if vegetable oil is refined (SCF, 1997a).

In 2003 the SCF re-evaluated a series of provisionally accepted previous cargoes, including iso-decanol, iso-nonanol and iso-octanol, on the basis of further information provided by FOSFA. However, the information available was considered inadequate or needed additional clarification. Therefore, the SCF decided to maintain its previous opinion unchanged (SCF, 2003).

In 2006, OECD published an initial assessment report on the environmental fate and human health effects of oxo-alcohols (C9 to C13) including a mixture of alcohols C8-C10-iso, iso-nonanol and iso-decanol (OECD, 2006). A detailed assessment of the available toxicological database was carried out. It was concluded that the chemicals of this category are of a low order of toxicity, do not posses mutagenic activity, there is no evidence of carcinogenic potential or adverse effects on fertility and reproduction and therefore they are of low priority for further work.

3.2.2. Current evaluation

3.2.2.1. Expected impurities

Iso-octanol, iso-nonanol and iso-decanol are mixtures in themselves and mostly of technical quality. The starting substances are volatile and their byproducts would easily be removed when not integrated into the product. The residual amounts of intermediate alkenes and aldehydes would not be of concern at the levels present in products used as previous cargoes. Hydroformylation is not expected to result in byproducts of concern.

3.2.2.2. Reactivity and reaction products

Iso-octanol, iso-nonanol and iso-decanol may react with lipids by interesterification, but this does not result in any products of concern.

3.2.2.3. Toxicological profile

<u>Absorption, distribution, metabolism and excretion</u>

The C8-C10 oxo-alcohols are readily absorbed from the gastrointestinal tract and are rapidly eliminated from the blood. The main metabolic pathway involves initial oxidation to the corresponding aldehyde, catalysed primarily by cytosolic alcohol dehydrogenases (ADH), with a lesser contribution from P450 and other oxidases. The aldehydes are then converted to the respective carboxylic acids, by aldehyde dehydrogenases (ALDH). The carboxylic acids are subsequently metabolized to carbon dioxide via mitochondrial beta-oxidation pathways and the tricarboxylic acid cycle, in the same way as dietary fatty acids (OECD, 2006). This stepwise removal of C2 units is more efficient for linear acids than for the corresponding branched acids. The latter can also be metabolised by microsomal ω- or ω–1 oxidation followed by β-oxidation, which is relatively efficient for such compounds (Verhoeven et al., 1998). For unsaturated carboxylic acids, cleavage of C2-units continues

until a double bond is reached. These double bonds will be in the cis-configuration, and can be isomerised to the trans-configuration by enoyl-CoA isomerase. β-Oxidation then continues with the trans-isomer (JECFA, 1999). The alcohols (both parent substances and their primary metabolites) or their oxidation products can be conjugated with sulphate or glucuronic acid, catalysed by sulphotransferases and UDP-glucuronosyltransferases respectively, the extent of these reactions increasing with the degree and complexity of branching (Williams, 1959; Bevan, 2001; OECD, 2006).

The CONTAM Panel undertook a limited exercise on the prediction of the main metabolites of two examples of oxo-alcohols, representing the potential for most branching amongst the compounds likely to be present in the technical mixtures being assessed as previous cargoes (See Figure 1a and 1b).

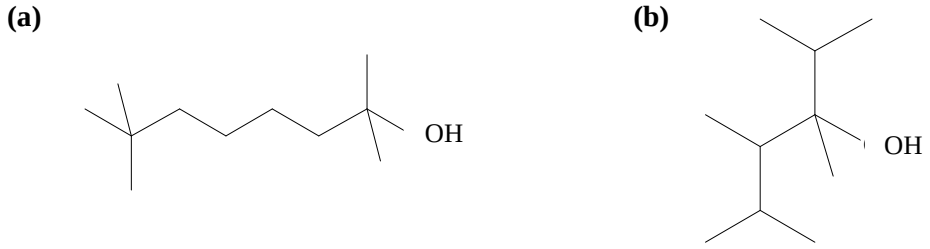

Figure 1: Two examples of oxo-alcohols representing the potential for most branching amongst the compounds likely to be present in the technical mixtures being assessed as previous cargoes.

Using the METEOR software 13.0.0 (Lhasa Ltd), plausible metabolic transformations of the compounds depicted in Figure 1a and Figure 1b included terminal methyl oxidation, primary alcohol oxidation and glucuronide conjugation of the resulting carboxylic acids. These pathways were supported by reference to several known examples in each case (Wim Mennes, 2012, personal communication).

The CONTAM Panel concluded that the potential for retention or bioaccumulation for the parent alcohols and their biotransformation products is likely to be limited.

Acute toxicity

In the OECD assessment (2006) it was concluded that the sub-category of oxo-alcohols C9 to C13 is practically non-toxic with oral LD_{50}s ranging from > 2 000 to 5 400 mg/kg b.w. Acute oral LD_{50}s of 6 500 and 3 950 mg/kg b.w. were reported in rats orally administered iso-decanol (Nishimura et al., 1994), and iso-nonanol (Anonymous 1986a, as cited in ECHA, online) respectively. Oral LD_{50}s of 1 480 and 1 670 mg/kg b.w. were reported in rats and mice respectively, upon oral administration of iso-octanol.[16,17] Dermal LD_{50}s ranged from > 2 600 to 5 010 mg/kg b.w. and inhalation exposures conducted at saturated vapour pressures generally produced no deaths (OECD, 2006). Members of this category were moderately irritating to the skin and irritating to the eyes of rabbits and, in addition, the alcohols C9-C11-iso, C9 rich, produced moderate upper airway sensory irritation in male mice exposed to vapours. There is no indication of skin sensitizing potential for the oxo-alcohols C9-C13 category (OECD, 2006).

Subacute, subchronic and chronic toxicity studies

In a 14-day study in rats, designed to evaluate potential effects on liver and testes, iso-decanol and iso-nonanol given by gavage produced minimal or no effects on the liver, and no testicular effects at doses of 168 and 144 mg/kg b.w. per day, respectively (Rhodes et al., 1984; OECD, 2006). No oral repeated dose toxicity studies were identified for iso-octanol. In general, the available data suggest that

[16] ChemID Plus, online. Available at: http://chem.sis.nlm.nih.gov/chemidplus/chemidheavy.jsp
[17] RTECS, online. Available at: http://www.cdc.gov/niosh/rtecs/

the members of the oxo-alcohols C9-C13 category present low order of subchronic toxicity (OECD, 2006).

Genotoxicity

Bacterial mutagenicity studies (using *Salmonella typhimurium* as well as *Escherichia coli*) for four members of the oxo-alcohols C9-C13 category showed a consistent lack of mutagenic activity (OECD, 2006). In particular, iso-nonanol (Anonymous 1986d, as cited in ECHA online) and iso-octanol (Henkel KgaA, 1982a; HLS, 1996k, both as cited in OECD, 2006) were negative in the Ames test with and without metabolic activation. Iso-decanol was also tested in an *in vitro* chromosomal aberration assay with V79 Chinese hamster lung fibroblasts, and no mutagenic effects were noted with or without metabolic activation (OECD, 2006). In addition to these *in vitro* results, two category members and the analogue linear alcohol 1-dodecanol were negative in an *in vivo* mouse bone marrow micronucleus test (OECD, 2006) thus indicating that the members of the oxo-alcohols C9-C13 category are unlikely to present any genotoxic potential either *in vitro* or *in vivo*.

Carcinogenicity

No carcinogenicity studies have been conducted on oxo-alcohols C9-C13 category members. The potential for initiation, promotion or co-carcinogenicity has been investigated for several aliphatic alcohols including the analogue linear alcohol 1-dodecanol. Even taking into account the limitations and low reliability of these experiments, the data show that none of the aliphatic alcohols tested have a potential to induce local skin tumours upon repeated dermal application at or above the maximum tolerated (irritant) dose (Sicé, 1966; Bingham and Falk, 1969; Van Duuren and Goldschmidt, 1976, as cited in OECD, 2006).

In other assays, oxo-alcohols C10-C12 members were repeatedly injected into the peritoneal cavity or implanted in the bladder of mice. Although there are limitations to these studies, no induction of tumours was observed (Bryan and Springberg, 1966; Stoner et al., 1973, both as cited in OECD, 2006) and in one study (Ando et al., 1972, as cited in OECD, 2006) a prolongation of survival time was reported.

Based on the lack of genotoxic effects both *in vitro* and *in vivo* and on the absence of any structural alerts, members of the oxo-alcohols C9-C13 category are unlikely to possess genotoxic carcinogenic potential.

Developmental and reproductive toxicity

In a comparative developmental toxicity study with rats, iso-decanol (a mixture of different isomers) was administered by gavage at doses of 0, 1, 5 and 10 mmol/kg (0, 158, 790, and 1 580 mg/kg b.w. per day) during gestation day (GD) 6 to 15. Iso-decanol elicited maternal toxicity at 10 mmol/kg and caused a low incidence of retardations and rare malformations at that dose level. Body weight, uterus weight, and fetal weights were all significantly lower than controls in the highest dose group. Overt maternal mortality (4/10) was observed only in this dose group thus accounting for the effects observed. Some maternal signs of toxicity, but no fetal effects, were observed at 5 mmol/kg. The NOAELs for maternal and fetal effects were 1 mmol/kg and 5 mmol/kg, respectively (Hellwig and Jäckh, 1997).

In another study maternal toxicity, including decreased feed intake and body weight gain and abnormal clinical signs, was observed at 790 mg/kg b.w. given by gavage to rats from gestation day 6 to 15. No embryo-fetal toxicity was observed (Eastman Kodak Co., 2009).

No effects to parents or offspring were observed in a combined repeated dose developmental/reproductive toxicity study with the analogue 1-dodecanol at doses up to 2 000 mg/kg

b.w. per day (OECD, 2006) thus supporting the conclusion that members of the oxo-alcohols C9-C13 category are not reprotoxic.

3.2.2.4. Allergenicity

Available data give no indication that iso-decanol, iso-nonanol or iso-octanol are allergens or adjuvants.

3.2.3. Conclusion

Iso-octanol, iso-nonanol and iso-decanol were classified by the SCF in its more recent re-evaluation (SCF, 2003) as provisionally acceptable as previous cargoes because the information available was considered inadequate or limited. The CONTAM Panel used a 'read across' approach (OECD, 2006) to fill data gaps on the toxicological profile of iso-octanol, iso-nonanol and iso-decanol. They are of a low order of toxicity following acute and repeated exposures upon oral, dermal or inhalational exposure. The lack of effects found in the limited studies available suggests that they are not genotoxic. They are not allergenic and there are no reactions of concern with edible fats and oils, nor are any anticipated impurities likely to be present at levels of toxicological concern.

The CONTAM Panel therefore concludes that iso-decanol, iso-nonanol or iso-octanol meet the criteria for acceptability as previous cargoes for edible fats and oils.

3.3. 1,3-PROPYLENE GLYCOL (trimethylene glycol; 1.3-propanediol) (CAS No 504-63-2)

The term 'propylene glycol' is misleading: when used without specification of the position of the hydroxyl groups, 1,2-propylene glycol is meant, which is produced in far larger quantities than the 1,3-analogue. For this reason, '1,3-propanediol' is the preferred name of the substance considered here. 1,2-Propylene glycol was evaluated for its acceptability as a previous cargo for edible fats and oils by the CONTAM Panel in 2011 and it was concluded that it met the criteria for acceptability (EFSA, 2011).

1,3-Propanediol is a flammable, colourless, stable liquid. 1,3-Propanediol is produced commercially from acrolein (addition of water in acidic medium followed by hydrogenation), by hydroformylation of ethylene oxide or biochemical fermentation from glycerol (a by-product of the biodiesel chain) or by starch fermentation. 1,3-Propanediol is then separated and purified by several means, including ultrafiltration and/or distillation.

Between 75 and 90 % of 1,3-propanediol is used in a polymerization process to manufacture polytrimethylene terephthalate (PTT). 1,3-Propanediol may also be a component of de-icing fluids, engine coolants, heat transfer fluids, chemical intermediates, personal care products, or process solvents.

3.3.1. Previous evaluations

In the SCF's 1996 opinion on acceptable previous cargoes (SCF, 1997a), 1,3-propanediol was considered not acceptable as a previous cargo because of inadequate toxicological data on a substance that is structurally of concern.

In 1998, the SCF considered 1,3-propanediol for use as a co-monomer in polyesters. On the basis of new mutagenicity and developmental toxicity studies, the SCF concluded that the use of 1,3-propanediol was acceptable and should be classified in SCF List 3 (defined as substances for which an ADI or a TDI could not be established, but where the present use could be accepted) with a restriction of not more than 0.05 mg/kg in food (SCF, 1998).

In 2003 the SCF, on the basis of new information from a sub-chronic toxicity study showing low oral toxicity of 1,3-propanediol and provided that residues would be low after tank cleaning, considered that 1,3-propanediol was acceptable as a previous cargo (SCF, 2003).

3.3.2. Current evaluation

3.3.2.1. Expected impurities

After production, 1,3-propanediol is purified by distillation. As the boiling point is far above that of acrolein (211-217 °C *versus* 53 °C), an efficient separation and removal of acrolein is expected.

3.3.2.2. Reactivity and reaction products

1,3-Propanediol slowly reacts with lipids by transesterification, but no products of concern are expected when it is transported as a previous cargo.

3.3.2.3. Toxicological profile

Absorption, distribution, metabolism and excretion

Pollitt et al. (1987) proposed that 1,3-propanediol can be metabolized to 3-hydroxypropionaldehyde and then to 3-hydroxypropionic acid or to malonaldehyde. Malonaldehyde is expected to be a short-lived metabolic intermediate which can be further converted to malonic semialdehyde and then to malonic acid (Gingell et al., 2000).

Acute toxicity

1,3-Propanediol was administered to rats by gavage at doses ranging between 9.0 and 18.7 mL/kg b.w. (Spanjers and Til, 1979, as cited in ACC 1,3-Propanediol Panel, 2007). Sluggishness, ataxia and sedation were the only signs observed within a few hours. The LD_{50} was 14.9 mL/kg b.w., corresponding to 15.8 g/kg b.w. In another experiment with rats administered by gavage the LD_{50} was 10 mL/kg b.w. corresponding to 10.5 g/kg b.w. (Coombs and Clark, 1977, as cited in ACC 1,3-Propanediol Panel, 2007).

Subacute, subchronic and chronic toxicity studies

1,3-Propanediol was orally administered to rats by gavage at doses up to 1 000 mg/kg b.w. per day for 13 weeks (Gingell et al., 2000). All animals survived and showed no evidence of any systemic toxicity. In particular, no effects on haematology or serum chemistry parameters were reported, spermatogenic end-points were unaffected and no apparent pathological or functional effects were observed in the liver. The NOAEL for this study was therefore 1 000 mg/kg b.w. per day, the highest dose tested (Kirkpatrick, 1999, as cited in ACC 1,3-Propanediol Panel, 2007; Gingell et al., 2000). A NOAEL of 1 000 mg/kg b.w. per day (highest dose tested) was also identified in a 2-week oral toxicity study with rats (Mertens, 1997, as cited in ACC 1,3-Propanediol Panel, 2007).

Genotoxicity

1,3-Propanediol was negative in the Ames test (Degussa, 1994a, as cited in SCF, 2003; Wollny, 1994a, as cited in ACC 1,3-Propanediol Panel, 2007) and in a gene mutation assay in cultured mammalian cells (Degussa,1994b, as cited in SCF, 2003; Wollny, 1994b, as cited in ACC 1,3-Propanediol Panel, 2007). Contrasting data were reported for clastogenic effects in mammalian cells in culture (Degussa, 1994c, as cited in SCF, 2003;Volkner, 1994, as cited in ACC 1,3-Propanediol Panel, 2007; Gudi and Brown, 2001, as cited in ACC 1,3-Propanediol Panel, 2007).

In 1984 one study was published (Summerfield and Tappel, 1984) indicating that administration of 1,3-propanediol at 500 mg/kg in the diet of rats for up to 15 weeks caused DNA-protein and interstrand DNA cross-links, as detected by high-performance liquid chromatography, in liver and, to a limited extent, in testis. This was associated with the fact that liver but not testis can metabolize 1,3-propanediol to malondialdehyde, a cross-linking agent. In a well conducted mouse micronucleus study (Krauser, 1995, as cited in ACC 1,3-Propanediol Panel, 2007), male and female mice received a single oral dose of 1,3-propanediol (at 1 000, 1 470 or 2 150 mg/kg b.w.) and were euthanized at

24 and 48 hours after treatment. The assay was conducted on two separate occasions. All animals, in both assays, survived to scheduled termination and no treatment-related toxic signs were observed. In the initial assay, 1,3-propanediol was not considered to induce chromosome mutations in mice by damage to chromosomes or the mitotic apparatus, but a statistically significant increase in micronucleated polychromatic erythrocytes (PCEs) was observed at 48 hours in the sexes combined, as compared to the negative control (23/1000 cf 11/1000, $P < 0.05$). Hence, it was not possible to exclude a weak clastogenic effect. However, in the second assay, there was no increase in the number of micronucleated PCEs following exposure to 1,3-propanediol. In conclusion, based on the overall weight of evidence, 1,3-propanediol does not have genotoxic potential.

Carcinogenicity

No data are available on the carcinogenicity of 1,3-propanediol.

Developmental and reproductive toxicity

In 90-day oral toxicity studies with rats there were no effects of 1,3-propanediol at any dose up to 1 000 mg/kg per day on reproductive organs or on spermatogenic endpoints (Kirkpatrick, 1999, as cited in ACC 1,3-Propanediol, 2007; Gingell et al., 2000).

In a developmental toxicity study with rats, 1,3-propanediol orally administered at doses up to 1 000 mg/kg b.w. per day (Mitterer, 1992) did not induce any treatment-related adverse effect. The NOAEL for maternal and fetal toxicity was therefore 1 000 mg/kg b.w., the highest dose tested (ACC 1,3-Propanediol Panel, 2007).

3.3.2.4. Allergenicity

In the guinea pig maximization test and in the guinea pig Landsteiner/Draize test, 1,3-propanediol did not act as a sensitizer (Coombs and Clark, 1977; Til and Keizer, 1979, both as cited in ACC 1,3-Propanediol Panel, 2007). In a study with human volunteers, 1,3-propanediol did not produce adverse skin responses in any of the study participants (Anonymous, 2006b, as cited in ECHA, online).

Available data give no indication that 1,3-propanediol is an allergen or an adjuvant.

3.3.3. Conclusions

The term ‘propylene glycol’ is misleading: when used without specification of the position of the hydroxyl groups, 1,2-propylene glycol is meant, which is produced in far larger quantities than the 1,3-analogue. For this reason, ‘1,3-propanediol’ is the preferred name of the substance considered here. The CONTAM Panel therefore recommends that the entry for the substance in the Annex to Commission Directive 96/3/EC is amended to ‘1,3-propanediol (1,3-propylene glycol; trimethylene glycol) (CAS No 504-63-2)’.

1,3-Propanediol is of low systemic toxicity when administered by the oral route. There are no carcinogenicity data but the available evidence indicates that 1,3-propanediol does not have any genotoxic potential. 1,3-Propanediol is not an allergen. There are no reactions of concern with edible fats and oils, nor are any anticipated impurities likely to be present at levels of toxicological concern.

Therefore, the CONTAM Panel concludes that 1,3-propanediol meets the criteria for acceptability as a previous cargo for edible fats and oils.

3.4. ISO-BUTYL ACETATE (CAS No 110-19-0)

Chemically, the term iso-butyl refers to a number of branched butyl groups (including 1-methyl propyl, also called sec-butyl, and 1,1-dimethyl ethyl, also called tert-butyl). Isobutyl is a trivial name

standing for 2-methyl propyl. For this reason 'isobutyl acetate' is the preferred name, i.e. without the hyphen. The IUPAC name of isobutyl acetate is 2-methylpropyl acetate.

Isobutyl acetate is used as a solvent for coatings, thinners, sealants, adhesives, printing inks, caulks, leather treatment, cleaners, cosmetics (nail polishes), and as a process solvent in numerous applications. It is also used in perfumes and as a flavouring agent in various foods and non-alcoholic beverages.

It is produced from the esterification of isobutanol with acetic acid in the presence of a strong acid (usually sulphuric acid).

All of the butyl acetate isomers have been found to occur naturally in a range of fruits, such as bananas (Macku and Jennings, 1987; Bisesi, 1994, as cited in WHO, 2005) and nectarines (Takeoka et al., 1988, as cited in WHO, 2005).

3.4.1. Previous evaluations

The SCF evaluated isobutyl acetate in 1996 as a previous cargo for edible fats and oils and considered this substance was acceptable on the basis that it was 'generally used as a flavouring in food on FEMA and GRAS lists' (SCF, 1997a). In the 2003 SCF evaluation of acceptable previous cargoes, isobutyl acetate was not further evaluated as it was already considered acceptable (SCF, 2003).

Isobutyl acetate was given Generally Recognized as Safe (GRAS) status by the Flavor and Extract Manufacturers Association of the US (FEMA) in 1965.

In a monograph on fragrance raw materials, published in 1978, Opdyke states that the Council of Europe listed isobutyl acetate as an acceptable flavouring substance, with an ADI of 1.0 mg/kg b.w. (Opdyke, 1978).

The SCF (1992a) considered isobutyl acetate acceptable as a flavouring substance for use in food, on the basis of an evaluation by the Expert Committee on Flavourings of the Council of Europe. The Expert Committee classified it as category A, which may be used in foodstuffs, and established practical upper levels of 150 mg/kg in food and 10 mg/kg in beverages (CoE, 1992).

JECFA (1998) evaluated isobutyl acetate as a flavouring agent and concluded that there was 'no safety concern at current levels of intake', estimated to be 1 200-1 300 µg/person per day. This was because isobutyl acetate is a Cramer class I substance, and it can be predicted to be metabolised to innocuous products. Hence, exposures below a threshold of toxicological concern (TTC) of 1 800 µg/person per day (30 µg/kg b.w. per day) would not be expected to be of safety concern.

OECD (2003) concluded that isobutyl acetate was currently of low priority for further work.

WHO (2005) published a Concise International Chemical Assessment of isobutyl acetate, in which it was concluded that there was insufficient information, including an absence of data on potential carcinogenicity, to enable derivation of tolerable intakes or concentrations.

Isobutyl acetate is approved under US Food and Drug Administration (FDA), Title 21 US CFR citations for food additives permitted for direct addition to food for human consumption (FDA, 2011a).

3.4.2. Current evaluation

3.4.2.1. Expected impurities

Technical grades of butyl acetates contain butyl alcohol as an impurity (Syracuse Research Corp., 1979, as cited in WHO, 2005). This would not be of toxicological concern.

3.4.2.2. Reactivity and reaction products

Isobutyl acetate may be hydrolysed to isobutanol and acetic acid or transesterified with lipids. Neither these nor any other reaction products of concern are expected when isobutyl acetate is transported as a previous cargo.

3.4.2.3. Toxicological profile

Absorption, distribution, metabolism and excretion

There is little specific information on the absorption and disposition of isobutyl acetate. Given its physicochemical characteristics (log P_{ow} 2.3; molecular weight 116.2) it is likely to be readily absorbed from the gastrointestinal tract and distributed throughout the body. Isobutyl acetate partitions somewhat more into tissues than blood, with tissue/blood ratios of 2-5 for most tissues, but approx 20 for fat (Kaneko et al., 1994). Metabolism is by hydrolysis to acetic acid and isobutanol, most likely by carboxylesterases, which are found in a variety of tissues, including liver and gastrointestinal tract (Longland et al., 1977; Dahl et al., 1987). As the hydrolysis rate of n- and isobutyl acetate are similar (Dahl et al., 1987), it is likely that isobutyl acetate, by analogy with n-butyl acetate, will have a very short half-life in rats, as will its hydrolysis products, in the order of minutes (Teeguarden, 2005, as cited in ECHA online). Acetic acid is oxidised via the citric acid cycle to carbon dioxide and water. Isobutanol is rapidly metabolised by alcohol dehydrogenase (mainly class 1) to isobutyraldehyde and then by aldehyde dehydrogenase to isobutyric acid. These are further oxidised to carbon dioxide (JECFA, 1999; WHO, 2005). Small amounts of isobutanol may be excreted unchanged or conjugated with glucuronic acid (WHO/IPCS, 1987; OECD, 2004b).

Acute toxicity

Isobutyl acetate is of low acute oral toxicity, with LD_{50} values in rats and rabbits of the order of several grams per kg b.w. (Smyth et al., 1962; Munch, 1972, as cited in OECD, 2007).

The irritant properties of isobutyl acetate to the skin have not been well characterised. In an early study (1962) it was reported not to be irritating to skin following uncovered application, whereas in a later study (1978), with limited information available, it was reported to be irritating when applied under occlusion. Isobutyl acetate caused only minor, reversible irritation to the eyes in a well conducted study.[18] Isobutyl acetate was tested as a 2 % preparation in petrolatum in human volunteers, in a 48-h closed-patch test. It was not irritating to skin in this test (Opdyke, 1978). This substance has not been classified as irritating to either skin or to eyes in the ECHA database.[19]

Subacute, subchronic and chronic toxicity studies

No data are available on the repeat dose toxicity of isobutyl acetate.

The toxicity of its major metabolite, isobutanol, has been investigated by the oral and inhalation route. Groups of 30 Crj: CD(SD) rats of both sexes received isobutanol (purity not stated) by oral gavage daily at doses of 0, 100, 316 and 1 000 mg/kg b.w. per day for 90 days. Effects were seen only at the highest dose. There was an early reduction in body weight in males and in food consumption in both sexes. Clinical signs, including hypoactivity, ataxia and salivation, were observed in males and females for the first few weeks. Serum potassium was reduced by 11-15 % at week 4 or 5. No histopathological changes were observed. The NOAEL was 316 mg/kg b.w. per day (OECD, 2007).

[18] European Chemicals Agency (ECHA). Isobutyl acetate. CAS No 110-19-0. Available at: http://apps.echa.europa.eu/registered/data/dossiers/DISS-9d8c29e4-9219-2519-e044-00144f67d249/AGGR-ec680302-4ca3-4ee8-a91e-723cf0590511_DISS-9d8c29e4-9219-2519-e044-00144f67d249.html#section_1.1

[19] European Chemicals Agency (ECHA). Summary Of Classification and Labelling. Available at: http://clp-inventory.echa.europa.eu/SummaryOfClassAndLabelling.aspx?SubstanceID=24499&HarmOnly=no?fc=true&lang=en; accessed 17/05/2012

In an inhalation study, groups of 10 or 20 male and female Sprague-Dawley (SD) rats were exposed (whole body) to isobutanol (purity > 99 %) at concentrations of up to 2 500 ppm (ca. 7 700 mg/m³) (ca. 2 200 mg/kg b.w. per day) for 13 weeks, for 6 h per day, 5 days per week. At the highest concentration, there were slight increases in total erythrocyte count, haemoglobin, and haematocrit in females. There were no other toxicologically relevant treatment-related effects (Li et al., 1999).

In a study of a structural analogue, isobutyl isobutyrate (purity ≥ 98 %) was administered by oral gavage at doses of 0, 10, 100, and 1 000 mg/kg b.w. per day to groups of 15 Wistar rats/sex daily for 18 weeks. No treatment-related effects of toxicological significance were observed in any dose group. The NOAEL was 1 000 mg/kg b.w. per day, the highest dose tested.[18]

Genotoxicity

Isobutyl acetate was negative in an Ames/Salmonella test with *Salmonella typhimurium* strains TA98, TA100, TA1535, TA1537 and TA1538, either with or without metabolic activation by hepatic post-mitochondrial supernatant (S9 preparation) (OECD, 2007).

Isobutanol, a major metabolite, had no effect on the frequency of micronuclei and there was no evidence of clastogenicity or 'impairment of chromosome distribution' in bone marrow of mice administered doses of up to 2 000 mg/kg b.w. by oral gavage (OECD, 2007).

Carcinogenicity

No studies on the potential carcinogenicity of isobutyl acetate were identified.

Developmental and reproductive toxicity

No studies on the reproductive or developmental toxicity of isobutyl acetate could be identified.

Studies on the major metabolite, isobutanol, following inhalation exposure, are available. In a 2-generation study of possible effects on reproduction, groups of 30 male and 30 female, Crl:CD(SD)IGS BR rats were exposed (whole body) to isobutanol (purity > 99 %) at concentrations of 500 ppm, 1 008 ppm and 2 522 ppm (approx 0, 1 515, 3 030 or 7 575 mg/m^3) for 6 h/day, 7 days/week, for 10 weeks prior to mating. Females were exposed during gestation and lactation (from postnatal day 5). F1 pups were exposed directly from the day of weaning, on postnatal day 29, for 10 weeks prior to mating. No treatment-related effects were observed on parents or offspring at any exposure level. The no-observed-adverse-effect concentration (NOAEC) was 7 600 mg/m^3 (ca. 3 100 mg/kg b.w. per day), the highest concentration tested (WHO, 2005; OECD, 2007).

In developmental toxicity studies, groups of pregnant Wistar rats (25 per dose group) and Himalayan rabbits (15 per group) were exposed by inhalation (whole body) to concentrations of 0, 500, 2 500 and 10 000 mg/m^3 isobutanol for 6 hours per day during gestation (rats: GD6-GD15; rabbits: GD7-GD19). Body weight gain was slightly reduced in rabbits exposed to the highest concentration. No treatment-related effects were observed in rat dams. There was no evidence for either developmental or fetotoxic effects in either species. The NOAEC for developmental toxicity was 10 000 mg/m^3 (ca. 4 100 and 900 mg/kg b.w. per day for rats and rabbits, respectively), the highest concentration tested, in both rats and rabbits (OECD, 2007).

3.4.2.4. Allergenicity

A maximization test was carried out on 28 volunteers with 2 % isobutyl acetate in petrolatum. No dermal sensitization was observed (Epstein, 1976, as cited in OECD, 2003). Isobutyl acetate did not cause sensitization in the guinea pig maximization test (OECD TG 406) (Huels, 1988, as cited in OECD, 2003 and WHO, 2005).

Available data give no indication that isobutyl acetate is an allergen or an adjuvant.

3.4.3. Conclusions

The CONTAM Panel notes that the name iso-butyl acetate is rarely used to refer to this substance. It is more normally referred to as isobutyl acetate. The preferred IUPAC name is 2-methylpropyl acetate. The CONTAM Panel therefore recommends that the entry for the substance in the Annex to Commission Directive 96/3/EC[5] to be amended to 'Isobutyl acetate (2-methylpropyl acetate) (CAS No 110-19-0)'.

The toxicity of acetate, one of the major metabolites of isobutyl acetate, was addressed in a previous Opinion of the CONTAM Panel, when it was considered that there would be no health concerns following the maximum potential carryover into edible fats and oils when it is transported as a previous cargo (EFSA, 2012a).

In its evaluation of previous cargoes in 1996, the SCF concluded that isobutanol, the other major metabolite, was 'not acceptable', because 'limited toxicological data indicates a suspicion of carcinogenic concerns.' In a re-evaluation in 2003, the SCF maintained its previous opinion that this substance was not acceptable as a previous cargo because the Committee was aware of a number of issues that still needed clarification. The CONTAM Panel considered isobutanol as a previous cargo for edible fats and oils in 2009, and concluded that it was acceptable, based on the low level of toxicity observed in a more recent chronic toxicity study, as well as its volatility and ease of tank cleaning (EFSA, 2009b).

Although the toxicological database for isobutyl acetate is limited, available data on this substance and on its hydrolysis products, acetic acid and isobutanol, suggest that isobutyl acetate is of relatively low systemic toxicity. It is not genotoxic or allergenic. There are no reaction products or impurities expected to be of toxicological concern.

The CONTAM Panel therefore concludes that isobutyl acetate meets the criteria for acceptability as a previous cargo for edible fats and oils.

3.5. SEC-BUTYL ACETATE (CAS No 105-46-4)

sec-Butyl acetate, s-butyl acetate, 2-butanol acetate or 1-methylpropyl acetate is a racemic mixture. It is a solvent commonly used in lacquers and enamels.

The first method of production of sec-butyl acetate was the esterification of sec-butanol and acetic anhydride. sec-Butyl acetate is now prepared by direct esterification of acetic acid with secondary butyl alcohol at 100-110 °C in the presence of H_2SO_4 in a continuous process. sec-Butyl acetate is purified by distillation.

3.5.1. Previous evaluations

The SCF evaluated sec-butyl acetate in 1996 as a previous cargo for edible fats and oils and considered this substance was acceptable, with the explanation 'Limited toxicological data but no indication of a hazard. Easily removed by tank cleaning.' (SCF, 1997a). In the 2003 SCF evaluation of acceptable previous cargoes, sec-butyl acetate was not further evaluated as it was already considered acceptable (SCF, 2003).

WHO (2005) concluded that there was insufficient information on sec-butyl acetate to enable a tolerable intake to be established.

EFSA (2008a) evaluated sec-butyl acetate as a flavouring agent and concluded that it was a Cramer class I substance, and that it can be predicted to be metabolised to innocuous products. Hence, exposures below a TTC of 1 800 µg/person per day (30 µg/kg b.w. per day) would not be expected to be of safety concern.

3.5.2. Current evaluation

3.5.2.1. Expected impurities

sec-Butyl acetate is synthesised from substances which are not expected to contain impurities of concern. Also, the esterification step is not expected to result in impurities of concern.

3.5.2.2. Reactivity and reaction products

sec-Butyl acetate may be hydrolysed to sec-butanol and acetic acid or transesterified with lipids. Neither these nor any other reaction products are expected to be of concern when sec-butyl acetate is transported as a previous cargo.

3.5.2.3. Toxicological profile

There is very little specific information on the toxicity of sec-butyl acetate.

Absorption, distribution, metabolism and excretion

There is little specific information on the absorption and disposition of sec-butyl acetate. Given its physicochemical characteristics (log P_{ow} 1.51; molecular weight 116.2) it is likely to be readily absorbed from the gastrointestinal tract and distributed throughout the body. Metabolism is by hydrolysis to acetic acid and sec-butanol, most likely by carboxylesterases, which are found in a variety of tissues, including liver and gastrointestinal tract (Longland et al., 1977; Dahl et al., 1987). As the hydrolysis rates of n- and sec-butyl acetate are similar (Dahl et al., 1987), it is likely that sec-butyl acetate, by analogy with n-butyl acetate, will have a very short half-life in rats, as will its hydrolysis products, in the order of minutes (Teeguarden et al., 2005, as cited in ECHA online). Acetic acid is oxidised via the citric acid cycle to carbon dioxide and water. sec-Butanol is rapidly metabolised by alcohol dehydrogenase (mainly class 1) to 2-butanone (methyl ethyl ketone), which is then either excreted unchanged in breath and urine or further metabolised to 3-hydroxy-2-butanone and 2,3-butanediol (WHO, 2005). There is evidence that sec-butyl acetate can also be hydroxylated by at least one form of P450 to yield an unstable hemiketal (2-hydroxy-2-acetoxybutane), which is cleaved non-hydrolytically to 2-butanone (Peng et al., 1995; WHO, 2005).

The toxicity of methyl ethyl ketone (MEK) was reviewed in a previous opinion of the CONTAM Panel (EFSA, 2012a), when it was considered to meet the criteria for acceptability as a previous cargo for edible fats and oils.

Acute toxicity

sec-Butyl acetate is of low acute toxicity, with an oral LD_{50} value in rats of 3 200-6 400 mg/kg b.w. (WHO, 2005).

Some information sheets suggest that sec-butyl acetate is mildly irritating to the eyes, but no specific information is provided (e.g. ICSC, 1994). In their review of 2005, WHO was unable to identify any data on the irritation or sensitization potential of sec-butyl acetate. sec-Butyl acetate has not been classified in the ECHA database for irritation to skin or eyes.[20]

Subacute, subchronic and chronic toxicity studies

No data were identified on the repeat dose toxicity of sec-butyl acetate. Nor could any data be found for the effects of the major metabolite, sec-butanol.

[20] European Chemicals Agency (ECHA). Summary of Classification and Labelling. Available at: http://clp-inventory.echa.europa.eu/SummaryOfClassAndLabelling.aspx?SubstanceID=120101&HarmOnly=no?DisclaimerAgr=Agree&Index=105-46-4&ExecuteSearch=true&fc=true&lang=en (accessed 17/05/2012)

Genotoxicity

No information on the genotoxicity of sec-butyl acetate could be identified.

The major metabolite sec-butanol has been tested for genotoxicity in a number of organisms *in vitro*. It did not cause mutations in *Salmonella typhimurium* strains TA98, TA100, TA1535, TA1537 and TA1538, *Escherichia coli* WP2uvrA/pKM101, not did it cause gene conversion in yeast (*Saccharomyces cerevisiae* JD1), either with or without metabolic activation by hepatic postmitochondrial supernatant (S9 preparation) from Aroclor 1254-treated rats (Brooks et al., 1988, as cited in WHO, 2005).

Carcinogenicity

No information could be found on the carcinogenicity of either sec-butyl acetate or of its major metabolite, sec-butanol.

Developmental and reproductive toxicity

No studies on the developmental or reproductive toxicity of sec-butyl acetate could be identified. The reproductive toxicity of its major metabolite, sec-butanol, has been evaluated in a two-generation study in rats. Groups of 30 male and 30 female Wistar rats received sec-butanol in their drinking water at concentrations of 0, 0.3, 1 and 3 % (equivalent to 0, 450, 1 500 and 4 500 mg/kg b.w. per day). The highest dose was reduced to 2 % (3 000 mg/kg b.w. per day) in the second generation, because of toxicity. In a developmental phase of the study, fetuses were examined on gestation day 20. Exposure to sec-butanol at 3 000 mg/kg b.w. per day resulted in a significant reduction in fetal weight and retardation of skeletal maturation. There were no skeletal or visceral malformations. There were no effects on fertility. The NOAEL for developmental toxicity was 1 500 mg/kg b.w. per day (Gallo et al., 1977, as cited in WHO, 2005).

The developmental toxicity of sec-butanol has been investigated in rats following exposure by inhalation. Groups of 15 pregnant SD rats were exposed to sec-butanol by inhalation for 7 h/day from gestation day 1-19, at concentrations of 0, 3 500, 5 000 and 7 000 ppm (i.e. 0, 11 000, 15 000 or 22 000 mg/m^3). There was a reduction in body weight gain in dams in all groups exposed to sec-butanol. At the highest concentration, there was a reduction in the number of live fetuses and an increase in the number of resorptions. Fetal body weight was reduced at ≥15 000 mg/m^3. There was no increase in the incidence of malformations. The NOAEC for developmental toxicity was 11 000 mg/m^3 (ca. 5 200 mg/kg b.w. per day) (Nelson et al., 1989, as cited in WHO, 2005).

3.5.2.4. Allergenicity

Available data give no indication that sec-butyl acetate is an allergen or an adjuvant.

3.5.3. Conclusion

There are no data on repeated-dose toxicity of sec-butyl acetate. It is a Cramer class I substance, with a TTC of 1 800 µg/person per day. It is rapidly metabolised to acetate and sec-butanol, which can be further metabolised to MEK. The CONTAM Panel has previously evaluated acetic acid and MEK for their suitability as previous cargoes for edible fats and oils and concluded that they meet the criteria for acceptability (EFSA, 2012a). Sec-Butanol is not genotoxic. The information available on sec-butanol does not indicate any toxicological concern at the exposure levels that might occur from the transport of sec-butyl acetate as a previous cargo to edible fats and oils. sec-Butyl acetate is not allergenic. There are no reaction products or impurities of toxicological concern.

The CONTAM Panel therefore concludes that sec-butyl acetate meets the criteria for acceptability as a previous cargo for edible fats and oils.

3.6. TERT-BUTYL ACETATE (CAS No 540-88-5)

Tert-butyl acetate or t-butyl acetate is used as a solvent in the production of lacquers, enamels, inks, adhesives, thinners and industrial cleaners.

Tert-butyl acetate is synthesised by reaction of acetic acid with isobutylene.

3.6.1. Previous evaluations

The SCF evaluated tert-butyl acetate in 1996 as a previous cargo for edible fats and oils and considered this substance was acceptable, with the explanation 'Limited toxicological data but no indication of a hazard. Easily removed by tank cleaning.' (SCF, 1997a). In the 2003 SCF evaluation of acceptable previous cargoes, tert-butyl acetate was not further evaluated as it was already considered acceptable (SCF, 2003).

WHO (2005) concluded that there was insufficient information on tert-butyl acetate to enable a tolerable intake to be established.

3.6.2. Current evaluation

3.6.2.1. Expected impurities

Available information does not suggest that there are any impurities of concern in tert-butyl acetate.

3.6.2.2. Reactivity and reaction products

tert-Butyl acetate may be hydrolysed to tert-butanol and acetic acid or transesterified with lipids. Neither these nor any other reaction products are expected to be of concern when tert-butyl acetate is transported as a previous cargo.

3.6.2.3. Toxicological profile

Absorption, distribution, metabolism and excretion

There is little specific information on the absorption and disposition of tert-butyl acetate. Given its physicochemical characteristics (log P_{ow} 1.64; molecular weight 116.2) it is likely to be readily absorbed from the gastrointestinal tract and distributed throughout the body. Elimination becomes saturated at high exposure levels in experimental animals. Saturation of elimination of the major metabolite, tert-butanol, persists for longer than for that of the parent compound (WHO, 2005). Metabolism is by hydrolysis to acetic acid and tert-butanol, most likely by carboxylesterases, which are found in a variety of tissues, including liver and gastrointestinal tract (Longland et al., 1977; Dahl et al., 1987). The hydrolysis rate is somewhat slower than that of n-butyl acetate, most likely a consequence of steric hindrance (Dahl et al., 1987). Hydrolysis by rat or human blood *ex vivo* was up to two orders of magnitude slower than that of n-butyl acetate (WHO, 2005). A second major route of metabolism involves hydroxylation of the tertiary-butyl moiety to yield 2-hydroxymethylisopropyl acetate. Hydroxylation of the tert-butyl side chain appears to predominate at lower exposures whilst hydrolysis predominates at higher exposures. Oxidation of the acetate side chain can also occur to a minor extent (Cruzan and Kirkpatrick, 2006). tert-Butanol is not a substrate for alcohol dehydrogenase and is metabolised only slowly, either by glucuronide conjugation of the hydroxyl group, with excretion in the urine, or oxidation of one or more of the alkyl substituents, which can be catalysed by P450 enzymes. The oxidation products include acetone, which is excreted in the urine and expired air, either unchanged or following metabolism to carbon dioxide (Cederbaum et al., 1983; WHO/IPCS, 1987). Acetic acid is oxidised via the citric acid cycle to carbon dioxide and water.

Acute toxicity

tert-Butyl acetate is of low acute toxicity by the oral route, with reported LD_{50} values in rats from 3 300-4 500 mg/kg b.w. (WHO, 2005).

tert-Butyl acetate is slightly irritating to the skin and slightly irritating to the eyes. The effects are readily reversible. tert-Butyl acetate has not been classified in the ECHA database for irritation to skin or eyes.

Subacute, subchronic and chronic toxicity studies

Groups of 30 male and 30 female CD-1 mice were exposed by inhalation (whole-body) to tert-butyl acetate (> 99 % purity) at target concentrations of 0, 100, 400 and 1 600 ppm (actual concentrations were 0, 101, 400 and 1 698 ppm) for 6 h/day, 7 days/week for 90 days. Mid- and high-dose animals showed transient clinical signs, hyperactivity, excessive grooming, impaired equilibrium and laboured respiration (at 1 600 ppm). Both males and females in the high-dose group showed a slight increase in liver weights. Circulating T4 levels were statistically significantly reduced in the 1 600 ppm group males. The NOAEC in this study was 100 ppm (ca. 240 mg/kg b.w. per day).[21]

Groups of 10 male and 10 female SD rats were exposed by inhalation (whole-body) to tert-butyl acetate (> 99 % purity) at target concentrations of 0, 100, 400 and 1 600 ppm (actual concentrations were 0, 101, 400 and 1 600 ppm) for 6 h/day, 7 days/week for 13 weeks. Absolute and relative adrenal gland and liver weights were increased in both sexes at the highest dose. Relative kidney weights were increased in a dose-dependent manner in all treated groups of males, and was slightly increased in high-dose females. Renal histopathology revealed an increased incidence of hyaline droplets (primarily alpha-2u-globulin accumulation), 100 % at the lowest dose and tubular basophilia (increasing with dose) in males of all treated groups. No such effects were seen in females.[21] The NOAEC was 400 ppm (ca. 780 mg/kg b.w. per day), on the basis that the renal effects observed in males were a consequence of accumulation of alpha-2u-globulin, and therefore not relevant to humans. Exposure of rats to tert-butanol, a major metabolite of tert-butyl acetate, via the drinking water also resulted in a male-specific increase in the incidence of hyaline droplets in the kidney (NTP, 1995).

The chronic toxicity of tert-butanol administered in drinking water has been investigated in rats and mice (NTP, 1995). Groups of 60 male and 60 female B6C3F1 mice received drinking water with concentrations of tert-butanol of 0, 5.0, 10 and 20 mg/ml, corresponding to received doses of 0, 540, 1 040 and 2 070 mg/kg b.w. in males and 0, 510, 1 020 and 2 110 mg/kg b.w. in females, for 2 years. Survival in the high-dose group was reduced. Final body weight of high-dose females was significantly lower than in controls. The incidence of follicular cell hyperplasia of the thyroid gland was statistically significantly increased in all male dose groups, but there was little dependency on dose (5/60 [13 %] in controls; 18/59 [26 %] at 5 mg/mL; 15/59 [25 %] at 10 mg/mL; 18/57 [32 %] at 20 mg/mL). The incidence of this lesion was statistically significantly and dose-dependently increased in mid- and high-dose females. The incidence of chronic inflammation of the bladder was statistically significantly increased in high dose males and females, and there was also an increase in the incidence of transitional epithelial hyperplasia in the high-dose males. The NOAEL is this study was 510 mg/kg b.w. per day, based on an increased incidence of follicular cell hyperplasia of the thyroid gland in females at the LOAEL, and assuming that the changes observed in low-dose males were spurious, as reflected by the absence of any difference in incidence between the low- and mid-dose groups.

Groups of 60 male and 60 female Fischer F334/N rats received drinking water with concentrations of tert-butanol in males of 0, 1.25, 2.5 and 5.0 mg/mL, corresponding to received doses of 0, 90, 200 and 420 mg/kg b.w. and in females of 0, 2.5, 5.0 and 10 mg/mL, corresponding to received doses of 0,

[21] European Chemicals Agency (ECHA). tert-Butyl acetate. CAS No 540-88-5. Available at: http://apps.echa.europa.eu/registered/data/dossiers/DISS-9d9b886e-dba3-571e-e044-00144f67d249/DISS-9d9b886e-dba3-571e-e044-00144f67d249_DISS-9d9b886e-dba3-571e-e044-00144f67d249.html

180, 330 and 650 mg/kg b.w., for 2 years. Ten rats per group were evaluated after 15 months. Final body weights were reduced in high-dose males and females, as was survival. Urine volume was reduced in mid- and high-dose females after 15 months. At the interim time point (15 months), relative kidney weights were increased in mid- and high-dose males and in all female dose groups. At 2 years, in males there was increased mineralisation of the kidney and renal tubule hyperplasia, which was statistically significant in the high-dose group. The severity and incidence of nephropathy and the incidence of transitional cell hyperplasia in the kidney were increased at the high dose in both males and females (NTP, 1995). The NOAEL for this study was 200 mg/kg b.w. per day in males and 330 mg/kg b.w. per day in females, if one considers that effects seen at lower doses in males were due to accumulation of alpha-2u-globulin and hence not relevant to humans.

Genotoxicity

tert-Butyl acetate was negative in tests for mutagenicity with *Salmonella typhimurium* strains TA98, TA100, TA102, TA1535, and TA1537 and with *E. coli* WP2uvrA/pKM101, with and without metabolic activation by hepatic postmitochondrial supernatant (S9 preparation) from Aroclor 1254-treated rats (McGregor et al., 2005). tert-Butyl acetate was negative in a test for induction of chromosomal aberrations in isolated human lymphocytes at concentrations up to 10 mM, with and without metabolic activation by hepatic postmitochondrial supernatant (S9 preparation) from Aroclor 1254-treated rats (WHO, 2005). Groups of male and female SD rats were exposed to tert-butyl acetate, at concentrations of 480, 1 900 and 7 700 mg/m^3 for 6 hours and then killed 24 h or 48 h later. There was no statistically significant effect on the frequency of micronucleated immature erythrocytes (WHO, 2005).

Carcinogenicity

tert-Butyl acetate has not been tested for its potential carcinogenicity.

One of its major metabolites, tert-butanol has been evaluated for carcinogenicity in rats and mice (NTP, 1995). Details of these studies have been described above. In mice exposed to tert-butanol for 2 years, the only tissue in which there was any increase in the incidence of tumours, compared to the controls, was the thyroid gland of females, in which there was an increase in the incidence of follicular cell adenomas in the high-dose group, 2 110 mg/kg b.w. per day. In rats exposed to tert-butanol for 2 years, there was no effect of treatment on tumour incidence in females, and in males the only tissue in which there was an increase in the incidence of tumours compared to the controls was the kidney. There was some indication for an increase in the incidence of renal tubular adenomas, although this reached statistical significance only in the mid-dose group, 200 mg/kg b.w. per day. There was also some evidence for a marginal increase in the incidence of renal tubular carcinomas (NTP, 1995).

There is evidence that the renal tumours observed only in male rats were secondary to interaction with alpha-2u-globulin, followed by its accumulation in proximal tubular cells. In the absence of any human counterpart to this protein at levels sufficient to support a toxicologically relevant interaction, this carcinogenic response is considered not relevant to humans (Cruzan and Kirkpatrick, 2006; TERA, 2009). The follicular cell adenomas in female mice were accompanied by follicular cell hyperplasia. In shorter term studies there was evidence for effects on the liver, consistent with enzyme induction, and reduced levels of circulating T4, suggesting that the adenomas in the thyroid may have been secondary to hepatic enzyme induction with increased clearance of thyroid hormones (Cruzan and Kirkpatrick, 2006).

Developmental and reproductive toxicity

In a 1-generation study of effects on reproduction, groups of 10 male and 10 female, SD rats were exposed (whole body) to tert-butyl acetate (purity > 99 %) at concentrations of 0, 100, 400 and 1 600 ppm for 6 h/day, 7 days/week, for 10 weeks prior to mating. Females were exposed during gestation and lactation (from postnatal day 5). F1 pups were exposed directly from the day of weaning,

on postnatal day (PND) 22, for 5 days. Body weight and body weight gain were reduced in high dose F0 males. The only effect observed in F1 pups was a slight, transient reduction in mean body weight gain in both males and females in the high dose group exposed on PND 22-26. The NOAEC for reproductive and neonatal toxicity was 1 600 ppm, the highest concentration tested.[21]

The developmental toxicity of tert-butyl acetate was investigated in rats. Groups of 22 pregnant SD rats were administered tert-butyl acetate (purity > 99 %) in corn oil by gavage from GD6-19 at doses of 0, 400, 800, 1 000 and 1 600 mg/kg b.w. per day. tert-Butyl acetate was toxic to dams at the highest dose, with increases in the incidences of clinical signs (reflecting mainly central nervous system (CNS) depression) and possibly mortality (2 animals died from unexplained causes), reduced body weight gain and food intake, increases in the weights of adrenal glands (absolute and relative) and liver (relative) and a decrease in absolute thymus weight. There was a statistically significant increase in the number of skeletal variations in offspring in the mid- and high-groups. Variations were typical of those occurring with embryo/fetotoxicity, particularly reduced ossification. There was a decrease in fetal body weight in the high dose group, and increased incidences of supernumerary ribs and a delay in fetal ossification in the mid- and high-dose groups. tert-Butyl acetate was not teratogenic in this study. The NOAEL for maternal toxicity was 800 mg/kg b.w. per day. The NOAEL for developmental toxicity was 400 mg/kg b.w. per day (Yang et al., 2007).

In a further study by the same laboratory to clarify the maternal toxicity of tert-butyl acetate, groups of 22 pregnant SD rats were administered tert-butyl acetate (purity > 99 %) in corn oil by gavage from GD6-19 at doses of 0, 400, 800, 1 000 and 1 600 mg/kg b.w. per day. One dam in the high dose-group died. Clinical signs indicative of effects on the CNS were observed at doses ≥ 800 mg/kg b.w. per day. Reductions in mean body weight, body weight gain and/or food consumption were also observed in these dose groups. The NOAEL for maternal toxicity was 400 mg/kg b.w. per day. Fetal body weight was statistically significantly reduced in the mid- and high-dose groups.[21]

The overall NOAEL for maternal toxicity was 400 mg/kg b.w. per day, based on clinical signs and decreased body weight gain at 800 mg/kg b.w. per day and above. Fetotoxicity appeared to be secondary to maternal toxicity, with an overall NOAEL of 400 mg/kg b.w. per day.

3.6.2.4. Allergenicity

In the Buehler test with guinea pigs, no indications of sensitization were observed (Anonymous, 1997a, as cited in ECHA, online). Available data give no indication that tert-butyl acetate is an allergen or an adjuvant.

3.6.3. Conclusion

The toxicological database on tert-butyl acetate is somewhat limited. The available data on tert-butyl acetate and on acetate and tert-butanol, its major metabolites, do not give rise to concerns regarding systemic toxicity, developmental toxicity or genotoxicity. Any carcinogenic risk would likely be from a non-genotoxic mode of action and would not be of concern at the levels of exposure that might occur from the use of tert-butyl acetate as a previous cargo for edible fats and oils. tert-Butyl acetate is not allergenic. There are no reaction products or impurities of toxicological concern.

The CONTAM Panel therefore concludes that tert-butyl acetate meets the criteria for acceptability as a previous cargo for edible fats and oils.

3.7. n-BUTYL ACETATE (CAS No 123-86-4)

n-Butyl acetate, often termed butyl acetate, is a liquid boiling at 127 °C. It is widely used as a solvent in lacquers, adhesives, cleaning agents and pharmaceutical solvents.

It is prepared by esterification of n-butyl alcohol with acetic acid (with sulphuric acid as catalyst) or acetic anhydride.

3.7.1. Previous evaluations

The SCF evaluated n-butyl acetate as a previous cargo in 1996 and considered it acceptable (SCF, 1997a). This conclusion was based on the fact that n-butyl acetate had a temporary ADI of 0-6 mg/kg b.w. and was temporarily acceptable as an extraction solvent. A temporary ADI was established by the SCF in 1981, based on the results of short term studies. The Committee required information on the levels of residues in extracted food by 1983. In the 2003 SCF evaluation of acceptable previous cargoes, n-butyl acetate was not further evaluated as it was already considered acceptable (SCF, 2003).

n-Butyl acetate was given GRAS status by FEMA in 1965.

The Council of the European Communities approved the use of n-butyl acetate as an extraction solvent for food, and it was included in Part 1 of the Annex to Directive 88/344/EEC.[22]

The SCF issued its second report on extraction solvents in 1992. No further information on levels in food was available, so the SCF extended the temporary ADI of 0-6 mg/kg b.w. The Committee reiterated its request for analytical data on residues in food or for other reassurance that the ADI would not be exceeded (SCF, 1992b).

The Expert Committee on Flavourings of the Council of Europe classified n-butyl acetate as category A, i.e. substances which may be used in foodstuffs (CoE, 1992).

JECFA (1998) evaluated n-butyl acetate as a flavouring agent and concluded that there was 'no safety concern at current levels of intake', estimated to be 170-1 200 µg/person per day. This was because n-butyl acetate is a Cramer class I substance, and can be predicted to be metabolised to innocuous products. Hence, exposures below a TTC of 1 800 µg/person per day (30 µg/kg b.w. per day) would not be expected to be of safety concern.

n-Butyl acetate is included in the EU register of flavouring substances used in or on foodstuffs, according to Commission Decision 2009/163/EC, amending Decision 1999/217/EC, with FL No. 09.004, and a note that no further evaluation is needed.[23]

n-Butyl acetate is on the approved list of substances[24] for making food contact materials, without limit (other than the generic limit of 60 mg/kg food).

n-Butyl acetate has been evaluated under the OECD Screening Information Sata Set (SIDS) programme on High Production Volume (HPV) chemicals (OECD, 2001a). OECD concluded that n-butyl acetate was currently of low priority for further work.

n-Butyl acetate is approved under US Food and Drug Administration (FDA), Title 21 US CFR citations for resinous and polymeric coatings for polyolefin films, without any specific limitations (FDA, 2011b).

3.7.2. Current evaluation

3.7.2.1. Expected impurities

n-Butyl acetate is synthesised from substances, the impurities of which are not expected to be of concern. Also the esterification step is not expected to result in impurities of concern.

[22] Council Directive of 13 June 1988 on the approximation of the laws of the Member States on extraction solvents used in the production of foodstuffs and food ingredients. OJ L 157, 24.6.1988, p. 28.
[23] Database of Flavouring Substances. DG Health and Consumers. European Commission. Available at: http://ec.europa.eu/food/food/fAEF/flavouring/index_en.htm (accessed 18/05/2012).
[24] Commission Regulation (EU) No 10/2011 of 14 January 2011 on plastic materials and articles intended to come into contact with food. OJ L 12, 15.1.2011, p. 1.

3.7.2.2. Reactivity and reaction products

n-Butyl acetate may be hydrolysed to n-butanol and acetic acid or transesterified with lipids. Neither these nor any other reaction products are expected to be of concern when n-butyl acetate is transported as a previous cargo.

3.7.2.3. Toxicological profile

Absorption, distribution, metabolism and excretion

There is little specific information on the absorption and disposition of n-butyl acetate following oral administration. Given its physicochemical characteristics (log P_{ow} 2.3; molecular weight 116.2) it is likely to be readily absorbed from the gastrointestinal tract and distributed throughout the body. n-Butyl acetate partitions more readily into tissues than blood, with tissue/blood ratios of 2-3 for most tissues, but 17 for fat (Kaneko et al., 1994). Metabolism is by hydrolysis to acetic acid and n-butanol, most likely by carboxylesterases, which are found in a variety of tissues, including liver and gastrointestinal tract (Longland et al., 1977; Dahl et al., 1987). Hydrolysis half-lives on addition to whole blood from female rats and male human volunteers were 12 min and 4 min, respectively. As anticipated from its rapid hydrolysis, n-butyl acetate has a very short half-life in rats, as does its hydrolysis products, in the order of minutes (Teeguarden et al., 2005, as cited in ECHA online). Acetic acid is oxidised via the citric acid cycle to carbon dioxide and water. n-Butanol is rapidly metabolised by alcohol dehydrogenase (mainly class 1) to butyraldehyde and then by aldehyde dehydrogenase to butyric acid. These are further oxidised to carbon dioxide. A small amount of n-butanol is excreted as the glucuronide conjugate (WHO/IPCS, 1987; WHO, 2005). Several studies on n-butyl acetate administered by inhalation or by intraperitoneal injection have confirmed the rapid elimination of this compound, with a half-life in rats of the order of minutes [25] (WHO, 2005). There is evidence that the microsomal P450 system, in particular CYP2E1, may play a role in the metabolism of n-butyl acetate (Peng et al., 1995). Barton et al. (2000) have developed a pharmacokinetic model for the disposition of n-butyl acetate and its major metabolites following inhalation exposure.

Acute toxicity

n-Butyl acetate is of low acute toxicity by the oral route, with LD_{50} values of approx. 3-13 g/kg b.w. in mice, rats, guinea pigs and rabbits (OECD, 2001a; WHO, 2005). Rats appear to be slightly less sensitive than some other species.

n-Butyl acetate is not irritating to the skin and at worst only slightly irritating to the eyes (OECD, 2001a; WHO, 2005). n-Butyl acetate has not been classified in the ECHA database for irritation to skin or eyes.[26]

Subacute, subchronic and chronic toxicity studies

No repeat dose toxicity studies on n-butyl acetate administered by the oral route could be identified.

Groups of 15 male and 15 female SD rats were exposed by inhalation (whole body) to n-butyl acetate (purity > 99 %) for 6 h/day, 5 days/week for 13 weeks, at concentrations of 0, 500, 1 500 and 3 000 ppm (to provide target concentrations of 0, 2 400, 7 200 and 14 000 mg/m^3). Groups of 5 animals/sex were killed after 30 days for interim assessment. Exposure to n-butyl acetate had no effects on mortality. Animals in the high-dose group, and minimally in the mid-dose group, showed minor clinical signs indicative of sedation. Males and females in the mid- and high-dose groups

[25] European Chemicals Agency (ECHA). n-Butyl acetate. CAS No 123-86-4. Available at: http://apps.echa.europa.eu/registered/data/dossiers/DISS-9d933481-e0e5-623f-e044-00144f67d249/DISS-9d933481-e0e5-623f-e044-00144f67d249_DISS-9d933481-e0e5-623f-e044-00144f67d249.html

[26] European Chemicals Agency (ECHA). Summary of Classifications and Labelling. Available at: http://clp-inventory.echa.europa.eu/SummaryOfClassAndLabelling.aspx?SubstanceID=56478&HarmOnly=no?DisclaimerAgr=Agree&Index=123-86-4&ExecuteSearch=true&fc=true&lang=en (accesed 20/05/2012).

showed a statistically significant reduction in body weight, body weight gain and food intake. Changes in the weight of a number of organs were observed in mid and/or high-dose males and/or females and included decreased liver and kidney weights, decreased spleen weights, increased adrenal and lung weights, decreased brain weights and increased relative testes weight. The only lesions observed, either macroscopically or histopathologically, were in the stomach and nasal passages, indicative of local irritation and degeneration, apparent in both mid- and high-dose groups. This may be due to local formation of n-butanol and acetic acid. The NOAEC was 2 400 mg/m^3 (ca. 700 mg/kg b.w. per day) (David et al., 2001).

Studies of rats exposed to n-butyl acetate by inhalation (whole body) at concentrations of up 3 000 ppm showed no evidence of neurotoxicity, as assessed by a functional observational battery, motor activity, neurohistopathology and schedule-controlled operant behaviour (WHO, 2005).

Genotoxicity

n-Butyl acetate has been tested relatively extensively for genotoxicity *in vitro*. n-Butyl acetate was negative in an Ames/Salmonella test with *Salmonella typhimurium* strains TA92, TA94, TA97, TA98, TA100, TA1535, TA1537 and TA1538 with and without metabolic activation by hepatic postmitochondrial supernatant (S9 preparation) from rats and/or hamsters treated with Aroclor 1254 (OECD, 2001a; WHO, 2005; CCRIS, 2009). n-Butyl acetate was also negative in tests for genotoxicity using *Escherichia coli* strain WP2 uvrA, with and without metabolic activation by hepatic postmitochondrial supernatant (S9 preparation) from rats treated with a combination of phenobarbital and beta-naphthoflavone, *Saccharomyces cerevisiae* strain D61.M without metabolic activation, in a test for mitotic aneuploidy, and in Chinese hamster lung fibroblasts, without metabolic activation, in a test for clastogenicity (OECD, 2001a; WHO, 2005; CCRIS, 2009).

n-Butanol, a major metabolite of n-butyl acetate, was negative in tests for mutagenicity in *Salmonella typhimurium* strains TA98, TA100, TA102, UTH8413, and UTH8414, with and without metabolic activation with hepatic postmitochondrial supernatant (S9 preparation) from Aroclor 1254 treated rats (CCRIS, 1996), clastogenicity (sister chromatid exchanges) in Chinese hamster ovary (CHO) cells and did not produce any effects on the chromosomes of cultured human lymphocytes (WHO/IPCS, 1987). n-Butanol was also negative in a bone marrow micronucleus test in NMRI mice at doses of up to 2 000 mg/kg b.w. [25] (OECD, 2001a).

Carcinogenicity

n-Butyl acetate has not been tested for its carcinogenic potential.

According to WHO/IPCS (1987), two long-term studies of n-butanol in rats have been recorded by the US National Cancer Institute, but these were not adequate for assessment of the carcinogenicity of the substance.

Developmental and reproductive toxicity

The reproductive toxicity of n-butyl acetate has been investigated in rats following exposure by inhalation. Groups of Crl:CD(SD) rats (30/sex/group) were exposed (whole body) to n-butyl acetate (purity > 99 %), by inhalation for 6 h/day, 7 days per week, for at least 70 days prior to mating. Target concentrations were 750, 1 500 and 2 000 ppm for all three generations. Exposure of the F0 and F1 males continued throughout mating, until termination. Exposure of dams continued until GD 20 and recommenced on lactation day 4. During lactation days 1-4, dams were administered n-butyl acetate by oral gavage at doses of 0, 1 125, 2 250 and 3 000 mg/kg per day (as 3 equal doses, 2 hours apart). F1 animals were exposed by inhalation from PND 22. Adults in the F0, F1 and F2 generations all showed signs of systemic toxicity in the mid- and high-dose groups, with reduced body weight, body weight gain and food consumption. Site of contact degeneration of the olfactory epithelium was apparent on exposure to ≥ 750 ppm. The NOAEC for systemic toxicity in adult rats was 750 ppm.

Exposure to n-butyl acetate had no effect on reproduction. Pups born to dams in the mid- and high-dose groups had lower mean body weights and body weight gains and some delay in attainment of post-weaning developmental landmarks, secondary to the reduction in body weights. The NOAEC for effects on fertility was 2 000 ppm (ca. 4 000 mg/kg b.w. per day), the highest concentration tested, whilst that for developmental toxicity was 750 ppm (ca. 1 500 mg/kg b.w. per day).[25]

Groups of pregnant SD rats (19-21 rats/dose group) were exposed (whole body) to n-butyl acetate by inhalation at concentrations of 0, 500, 1 000, 2 000 and 3 000 ppm 6 h/day from day 6 to 20 of gestation. Maternal toxicity was evident at concentrations of ≥ 1 000 ppm, with reduced food consumption, and at ≥ 2 000 ppm there was a reduction in body weight gain. Exposure of dams to n-butyl acetate had no effects on development other than to cause a reduction in fetal weight at the highest dose, which was maternally toxic. The NOAEC for maternal toxicity was 500 ppm (ca. 1 000 mg/kg b.w. per day), whilst the NOAEC for developmental toxicity was 2 000 ppm (ca. 4 000 mg/kg b.w. per day).[25]

The developmental toxicity of n-butyl acetate has also been studied in rats and rabbits following inhalation exposure at a single high concentration. Groups of female SD rats (37-43 per group) were exposed (whole body) to 1 500 ppm (7 200 mg/m^3) n-butyl acetate (purity > 99 %) for 7 h/day on GD 7-16, GD 1-16, or for 5 days/week for 3 weeks prior to mating and then on GD 1-16. Food consumption of dams was decreased in all exposed groups, with reduced body weight gain noted in the groups exposed for longer. Relative kidney and lung weights were increased in all groups. There were no effects on mating or reproductive performance. Fetal body weights and crown-rump length were reduced in all exposed groups. There was no treatment-related effect on the incidence of malformations (OECD, 2001a; WHO, 2005). The NOAEC for teratogenicity was 1 500 ppm, the only concentration tested (ca. 3 400 and 800 mg/kg b.w. per day for rats and rabbits, respectively).

Groups of 30 artificially inseminated New Zealand White rabbits (21-25 pregnant animals/group at termination) were exposed (whole body) to 1 500 ppm (7 200 mg/m^3, ca. 800 mg/kg b.w. per day) n-butyl acetate (purity > 99 %) by inhalation for 7 h/day on GD 7-19 or GD 1-19. There was no effect on either maternal or fetal body weight. There was no effect of exposure on reproductive performance. There was an increase in the incidences of misaligned sternebrae, retinal folds and clear gall bladders in fetuses of dams exposed from GD1-19. There were no major malformations (OECD, 2001a).

3.7.2.4. Allergenicity

n-Butyl acetate is mildly to moderately irritating (OECD, 2001a; WHO, 2005). n-Butyl acetate showed no sensitization potential in the guinea pig maximization test and in a mouse ear swelling test (Gad et al., 1986). Similarly negative results with regard to dermal sensitization were obtained in humans using a repeated-insult patch test (Roed-Peterson, 1980; Eiermann et al., 1982).

The available data give no indication that n-butyl acetate is an allergen or an adjuvant at concentrations expected from its use as a previous cargo.

3.7.3. Conclusion

The SCF established a temporary ADI of 0-6 mg/kg for n-butyl acetate, on the basis of limited data. The toxicological database has several data gaps (no repeat dose studies by the oral route, no studies of chronic toxicity or carcinogenicity). However, there were sufficient data on its major metabolites, acetate and n-butanol, for the CONTAM Panel to conclude previously that these are not of concern, when used as previous cargoes. n-Butyl acetate is not genotoxic. The CONTAM Panel considers that the available information on the acute effects of n-butyl acetate and on its subchronic, reproductive and developmental toxicity following exposure by the inhalation route, together with information on its major metabolites, was sufficient to conclude that the risk from short-term exposure to *n*-butyl acetate when used as a previous cargo would not give rise to any toxicological concern. There are no concerns regarding the allergenicity of n-butyl acetate. There are no reaction products or impurities of toxicological concern.

The CONTAM Panel therefore concludes that n-butyl acetate meets the criteria for acceptability as a previous cargo for edible fats and oils.

3.8. PROPYLENE TETRAMER (CAS No 6842-15-5)

In the catalogues available on the internet, propylene tetramer has a variety of descriptions. The majority of the sources indicate a linear dodecane with a terminal double bond, which, however, cannot be obtained from propylene. Often dodeca-1,4,7,10-tetraene is given as a synonym, but this is not consistent with the name 1-dodecene and again cannot be obtained from propylene. As it is made by condensation of propylene, it is expected to have the structure of a tetramethyl octane, possibly with a terminal double bond depending on the method of production.

According to the Substance Registry Service of the US-EPA, the systematic name is 1-propene, tetramer with a molecular formula of $(C_3H_6)_4$.

According to the information provided to EFSA (...) 'the material which is shipped seems to be a blend of isomers of which about 65 % are 1-propene (tetramer). Another Material Safety Data Sheet (MSDS) lists a detailed breakdown of the isomers which are present*:* > 71 % C12 alkene, < 22 % C10/C11 olefins and < 15 % C13-C15 alkenes with a total of > 98 % olefins' (see documentation provided to EFSA).

Propylene tetramer is described as a liquid with a melting point of -31 °C.

Propylene tetramer is produced by polymerizing propylene with a phosphate catalyst. This yields a broad mixture from which the tetramer is isolated by fractionation.

As condensation of propylene cannot produce hydrocarbons with 10, 11, 13 or 14 carbon atoms, either highly impure propylene is used or addition reactions interfere. It is concluded that propylene tetramer is a complex and probably variable mixture.

Propylene tetramer is used as a starting substance to make dodecyl phenol, tridecyl alcohol, branched dodecylbenzene sulphonic acids used as surfactants, emulsifiers and to produce plasticizers or lubricating oil additives.

3.8.1. Previous evaluations

The SCF evaluated propylene tetramer as a previous cargo in 1996 and considered it acceptable (SCF, 1997a). This conclusion was based on the fact that some toxicological data were available. It was not of structural concern. Subject to the examination of ongoing genotoxicity studies this substance was acceptable as a previous cargo. Low residue levels were expected, as it is easily removed by tank cleaning and it will easily be removed from vegetable oil if it is refined. In the 2003 SCF evaluation of acceptable previous cargoes, propylene tetramer was not further evaluated as it was already considered acceptable, and no reference was made to the results of ongoing genotoxicity studies (SCF, 2003).

Propylene tetramer is approved under US Food and Drug Administration (FDA), Title 21 US CFR citations for indirect food additives: 'paper and paperboard components', and 'adjuvants, production aids, and sanitizers' (FDA, 2011c, d).

Within the OECD SIDS programme on HPV chemicals, it was concluded that for olefins, amongst which are those comprising propylene tetramer, 'the weight of evidence indicates alpha and internal olefins with carbon numbers between C6 and C24 have a similar and low level of mammalian toxicity, and the toxicity profile is not affected by changes in the location of the double bond or the addition of branching to the structure'. It was further concluded that these compounds are currently of low priority for further work (OECD, 2001b, 2004c).

3.8.2. Current evaluation

3.8.2.1. Expected impurities

Propylene tetramer is a crude mixture largely of olefins (see above).

3.8.2.2. Reactivity and reaction products

Propylene tetramer is not expected to react with edible fats and oils.

3.8.2.3. Toxicological profile

Absorption, distribution, metabolism and excretion

There is little specific information on the absorption and disposition of propylene tetramer or its components following oral administration. Given the physicochemical characteristics of the main olefins present (average molecular weight 168 to 169; highly lipid soluble), they are likely to be absorbed from the gastrointestinal tract to a reasonable extent and distributed throughout the body. Metabolism appears to involve initial microsomal epoxidation by P450 enzymes to an unstable epoxide, which is then either hydrolysed to the corresponding diol, catalysed by epoxide hydrolase, or conjugated with glutathione. The glutathione conjugates are further metabolised to form mercapturic acids, which are excreted in the urine (White et al., 1986; OECD, 2001b). In general, alkenes accumulate in the body with increasing number of carbon atoms, starting at around C6-C7, with the highest concentrations in rats having being observed in brain, liver, kidneys and perirenal fat (OECD, 2004c; EFSA, 2012b).

Acute toxicity

The alkenes comprising propylene tetramer are of low acute toxicity. The oral LD_{50} of individual alkenes and mixtures of alkenes is > 5 g/kg b.w. in rats and, when tested, in mice. In most cases, the LD_{50} was > 10 g/kg b.w. (OECD, 2001b, 2004c).

Some olefins appear to be mildly irritating to rabbit skin when tested as pure chemicals, and slightly to severely irritating when tested as mixtures. Olefins are either non-irritating or slightly irritating to rabbit eyes, regardless of whether tested individually or as mixtures (OECD, 2001b, 2004c). None of the olefins is classified on the ECHA database for irritation to skin or eyes.[27]

Subacute, subchronic and chronic toxicity studies

In general, olefins are not very toxic on repeat dose administration by the oral route. The most common effect observed is on the kidney of male rats, due to binding with alpha-2u-globulin and its accumulation in proximal tubular cells. As there is no equivalent protein in humans at a level sufficient to support such a reaction, the male rat specific renal affects are not considered relevant for human risk assessment (OECD, 2001b, 2004c; EFSA, 2012b). In repeat dose studies in rats with a variety of alkenes administered orally as either the individual compounds or as mixtures, the lowest NOAEL for systemic toxicity other than alpha-2u-dependent renal toxicity in male rats, was for 1-octene administered by gavage. A NOAEL of 50 mg/kg b.w. per day was identified on the basis of marginal effects on kidney weight and serum creatinine in females at 500 mg/kg b.w. per day (OECD, 2001b, 2004c).

Genotoxicity

The olefins found in propylene tetramer and mixtures thereof have been tested for possible genotoxicity *in vitro* and to a lesser extent *in vivo*. The main test systems used were the

[27] European Chemicals Agency (ECHA). Summary of Classification and Labelling. Available at: http://echa.europa.eu/web/guest/information-on-chemicals/cl-inventory-database (accessed 21/05/2012).

Ames/Salmonella assay for bacterial mutagenicity and the mouse micronucleus test *in vivo*. A number of additional test systems were employed with some of the compounds or mixtures. None of the olefins was genotoxic (OECD 2001b; 2004c).

Carcinogenicity

No studies of the potential carcinogenicity of propylene tetramer could be located.

Developmental and reproductive toxicity

1-Hexene and 1-tetradecene have been tested for effects on reproduction in combined studies of reproductive/developmental toxicity in which rats were treated prior to mating and during mating, gestation and lactation by oral gavage with doses of up to 1 000 mg/kg b.w. per day. Neither compound had any effect on reproduction or on development. Hence, the NOAEL was 1 000 mg/kg b.w. per day, the highest dose tested, for both of these compounds (OECD, 2001b). In their evaluation of higher olefins, OECD (2004c) summarised oral studies of reproductive and developmental toxicity of several mixtures of alkenes. These were: alkenes, C6 (internal branched /linear stream); C16/18 internal linear and branched; C18 internal linear and branched. In all cases, the NOAEL for reproductive and developmental toxicity was 1 000 mg/kg b.w., the highest dose tested.

3.8.2.4. Allergenicity

In the Buehler test in guinea pigs, propylene tetramer was not found to be a sensitizer (Cushman et al., 1992). Similarly, in the Buehler test in guinea pigs, 1-dodecene was not found to be a sensitizer (Morris, 1992, as cited in ECB, 2002a). No information has been found regarding adjuvanticity. The available data give no indication that propylene tetramer is an allergen or an adjuvant at concentrations expected from its use as a previous cargo.

3.8.3. Conclusions

Although specific studies on propylene tetramer itself are somewhat limited, data are available on many of its main components and mixtures of these. In general, the toxicological profile of alkenes depends on carbon length, and is similar for those with similar carbon length. The CONTAM Panel considers that propylene tetramer would not be of toxicological concern at the levels that would occur when used as a previous cargo for edible fats and oils. Although there are no studies of carcinogenicity, the CONTAM Panel concludes that in the absence of genotoxicity or of pathological changes in subchronic studies indicative of a potential carcinogenic hazard, there was no concern for possible carcinogenicity from the use of propylene tetramer as a previous cargo. Propylene tetramer is not allergenic. There are no reaction products or impurities of toxicological concern.

The CONTAM Panel therefore concludes that propylene tetramer meets the criteria for acceptability as a previous cargo for edible fats and oils.

3.9. MONTAN WAX (CAS No 8002-53-7)

Montan wax is a hard, brittle, lustrous wax with a melting point around 80 °C extracted with toluene from lignites/brown coal, principally from Central Europe.

Montan wax is formed from resins, waxes and fats of plants. It consists of about 50 % esters of C22-34 fatty acids with C24-C28 alcohols, about 20 % fatty acids and resins of phenols, ketones and asphaltenes.

Montan wax is used for technical purposes, such as sealing concrete, in cleaning agents, lubricants, adhesives, and for electrical insulation in cables.

Montan wax should be distinguished from a variety of products called ‘montan acid esters’ or ‘montanic acid esters’, which are purified (e.g. by bleaching) and modified products. Fatty acids from

montan waxes are esterified, e.g., with ethylene glycol or fatty alcohols. Other isolates from montan wax are partially saponified. This entry does not deal with these purified products.

3.9.1. Previous evaluations

The SCF evaluated montan wax (CAS no. 8002-53-7) as a previous cargo in 1996 and considered it provisionally acceptable, noting its solubility (SCF, 1997a). This conclusion was based on the fact the SCF had concluded that montan wax esters (E192) were temporarily acceptable as a food additive, used as a glazing agent for food (SCF, 1992c). In the 2003 SCF evaluation of acceptable previous cargoes, the Committee reconsidered montan wax and concluded that the information available was inadequate. The SCF therefore maintained their opinion as provisionally acceptable (SCF, 2003).

No previous evaluations of natural montan wax have been carried out, by JECFA, SCF, EFSA or other regulatory agencies. Natural montan wax is not authorised as a food additive in the EU,[15] although montan acid esters are authorised for the surface treatment of certain fruits, with the E number E 912. Montan wax is approved for use as a food contact additive in plastics under Regulation (EU) 10/2011,[24] with no restrictions other than the generic overall migration limit of 60 mg/kg food. Montan wax is also on the US FDA list of approved indirect additives used in food contact materials (FDA, 2011e).

3.9.2. Current evaluation

3.9.2.1. Expected impurities

As montan wax is a complex mixture with a composition depending on its source, the toxicological evaluation should consider the whole mixture, taking into account variability in composition. Anticipated impurities have not been specifically considered in this opinion.

3.9.2.2. Reactivity and reaction products

The large majority if not all of the components in montan wax are not expected to react in edible fats and oils.

3.9.2.3. Toxicological profile

Absorption, distribution, metabolism and excretion

Montan wax has a high melting point relative to other waxes, is insoluble in water and is hydrophobic in nature. Overall the CONTAM Panel considered that absorption of montan wax from the gastrointestinal tract will be limited. Any alkane constituents of the absorbed wax will be slowly metabolised to the corresponding fatty alcohols and then fatty acids, with some metabolism also occurring in the small intestine, and enter normal biochemical pathways (EFSA, 2012b).

Acute toxicity

Montan wax can be anticipated to be of low acute oral toxicity. An LD_{50} of > 12 000 mg/kg b.w. has been reported.[28] Montan wax has been reported to be only very slightly irritating to skin and eyes, based on the results of *in vitro* tests.[28]

Subacute, subchronic and chronic toxicity studies

A 90-day toxicity study in Fisher 344 rats has been carried out with montan wax, administered in the diet at levels of 0, 0.56, 1.67 or 5 % (about 260, 835 or 2 500 mg/kg b.w. per day) (Ikeda et al., 2008). Haematological changes occurred in all treated rats, and aspartate aminotransferase (AST) and

[28] European Chemicals Agency (ECHA). Montan wax. CAS No. 8002-53-7. Available at: http://apps.echa.europa.eu/registered/data/dossiers/DISS-9eb31e9c-8883-2565-e044-00144f67d031/DISS-9eb31e9c-8883-2565-e044-00144f67d031_DISS-9eb31e9c-8883-2565-e044-00144f67d031.html (consultation date: 2012-01-20).

alanine aminotransferase (ALT) in serum were elevated. Liver, spleen, lung and kidney weights relative to body weight were also increased. Diffuse multiple granulomatous change occurred in the liver in all treated rats, together with severe hepatocyte damage and lymphocytic infiltration. A NOAEL could not therefore be identified in this study.

No chronic toxicity study is available on montan wax.

Genotoxicity

Montan wax was non-mutagenic in a bacterial mutagenicity study using *Salmonella typhimurium* with and without metabolic activation.[28]

Carcinogenicity

No carcinogenicity study is available on montan wax.

3.9.2.4. Allergenicity

Montan wax was tested in the mouse local lymph node assay (LLNA) according to OECD Guideline 429. Montan wax did not induce skin sensitization in this test (Anonymous, 2009, as cited in ECHA, online). No other information has been found regarding sensitization, adjuvanticity or irritancy of Montan wax. The available data give no indication that montan wax is an allergen or an adjuvant at concentrations expected from its use as a previous cargo.

3.9.3. Conclusion

No ADI or TDI has been established for montan wax by the SCF, JECFA or EFSA. Data recently provided to ECHA indicate that montan wax is not mutagenic in a bacterial mutagenicity test, and the CONTAM Panel considers that it is not likely to be a significant sensitizer, adjuvant or irritant. In a subchronic toxicity study in rats, haematological changes and hepatotoxicity were observed at the lowest dose tested, of approximately 260 mg/kg b.w. per day, and hence no NOAEL could be identified. There are no data on chronic toxicity or carcinogenicity.

Montan wax is an ill-defined material for which it cannot be excluded that it contains components of concern.

The CONTAM Panel therefore concludes that, given the deficiencies in the available data on montan wax, it does not meet the criteria for acceptability as a previous cargo.

3.10. PARAFFIN WAX (CAS No 8002-74-2 / 63231-60-7)

Waxes are mixtures of mineral hydrocarbons having a melting point above ambient temperature. There are hard waxes (like those used in candles), but also soft waxes, e.g. used for cosmetics. For chemists, the term ‘paraffin’ suggests that the wax consists of saturated, open-chain hydrocarbons, i.e. that it neither contains saturated cyclic components (naphthenes) nor aromatic components. The term is also used, however, to distinguish waxes of mineral sources from waxes of other origin and may, therefore, not in itself exclude appreciable amounts of aromatic components.

CAS No 8002-74-2 has entries as ‘paraffin wax’, but also as ‘paraffin wax and other hydrocarbon waxes’, which means that aromatic hydrocarbons can be present. CAS No 63231-60-7 refers to microcrystalline wax. Microcrystalline waxes differ from paraffin waxes in the size and structure of crystals: microcrystalline wax is almost amorphous, whereas paraffin wax is macrocrystalline. To achieve these properties, they contain a higher proportion of saturated hydrocarbons other than n-alkanes. Microcrystalline waxes used in foods (E 905) are hydrogenated to remove the aromatic compounds. However, microcrystalline waxes are not per se food grade.

Waxes are obtained by solvent crystallisation from mineral oil fractions. To be solids they must have a high concentration of n-alkanes (usually > 90 %) and be of molecular masses above about C20. Crystallisation reduces the content of aromatics to at most a few percent. Other characteristics may vary, such as the molecular mass distribution. The higher the molecular mass, the higher may be the percentage of the branched and cyclic hydrocarbons still resulting in a melting point above ambient.

Waxes are used e.g. for candles, tyres and other rubber articles, treatment of surfaces to improve water-resistance, cosmetics and electrical insulation. This includes both the paraffin waxes and the microcrystalline waxes.

3.10.1. Previous evaluations

The SCF evaluated paraffin wax as a previous cargo in 1996 and considered it provisionally acceptable (SCF, 1997a), noting that 'Existing SCF opinion on mineral hydrocarbons - waxes states that there are insufficient data to establish the safety of paraffin waxes. (SCF, 37th report, 1997). However given the nature of the toxicity of paraffin waxes it would not be expected that very low residues would give rise to problems. The normal cleaning process involving heating of the tank should ensure the removal of paraffin waxes to acceptable residual levels'. In the 2003 SCF evaluation of acceptable previous cargoes, the Committee reconsidered paraffin wax and concluded that the information available was inadequate. SCF therefore maintained their opinion on paraffin wax as provisionally acceptable previous cargo (SCF, 2003).

Mineral hydrocarbons including paraffin wax and microcrystalline wax (E 905) have been evaluated several times for the safety for use as food additives by both the Scientific Committee on Food (SCF) in 1990 and 1995 (SCF, 1992d, 1997b) and the Joint FAO/WHO Expert Committee on Food Additives (JECFA) on several occasions, most recently in 2009 (JECFA, 2010).

JECFA noted at its 39th meeting that long-term toxicity studies had indicated that petroleum-derived paraffin waxes and microcrystalline waxes were non-toxic and non-carcinogenic (JECFA, 1992, 1993a). The Committee therefore established an ADI 'not specified' for these waxes for the following uses: chewing-gum base, protective coating, defoaming agent, and surface finishing agent. The ADI 'not specified' for paraffin waxes was withdrawn in 1995, and an ADI of 0-20 mg/kg b.w. was established for hydrotreated, high-melting point microcrystalline wax and clay-treated microcrystalline wax at the 44th JECFA meeting, based on new short-term feeding studies showing no adverse effects up to the highest dose tested of 2 % microcrystalline wax in the diet (JECFA, 1995, 1996). Based on the same studies, the SCF likewise established an ADI of 0-20 mg/kg b.w. (SCF, 1997b). Only microcrystalline wax is authorised as a food additive within the EU.

In the USA petroleum wax including microcrystalline wax is classified as Generally Recognized As Safe (GRAS) by the US FDA, and is permitted in chewing gum base, on cheese and raw fruits and vegetables and as a defoamer in food (FDA, 1977).

Microcrystalline wax is approved for use as a food contact additive in plastics under Commission Regulation 10/2011[24] with the name waxes, refined, derived from petroleum based or synthetic hydrocarbon feedstocks and with no restrictions other than the generic overall migration limit of 60 mg/kg food.

3.10.2. Current evaluation

In view of concerns regarding the toxicity and carcinogenicity of aromatic hydrocarbons, the current evaluation is restricted to paraffin waxes that have been treated to remove aromatic hydrocarbons and which otherwise meet relevant standards to be considered as 'food grade'.

3.10.2.1. Expected impurities

Waxes of mineral origin predominantly consist of n-alkanes. Branched and cyclic hydrocarbons may reach a few percent of the wax (mostly < 10 %). The food grade waxes being considered here as

previous cargoes for edible fats and oils will always contain less than 3 % highly alkylated aromatic hydrocarbons. No other impurities of concern are anticipated.

3.10.2.2. Reactivity and reaction products

Mineral waxes do not react with edible fats and oils.

3.10.2.3. Toxicological profile

Absorption, distribution, metabolism and excretion

In a 90-day study in which rats were fed five different microcrystalline or lower melting point paraffin waxes (LMPW) at a level of 2 mg/kg in the diet, mineral hydrocarbons were found in liver, mesenteric lymph nodes, and perirenal fat of all groups with the exception of animals fed microcrystalline waxes (Smith et al., 1996). The SCF concluded from this study that microcrystalline wax is not absorbed after oral administration but is excreted unchanged in the faeces (SCF, 1997b), in contrast to mineral hydrocarbon oils and lower melting point paraffin waxes. It has been reported that absorption of aliphatic hydrocarbons was inversely proportional to the number of carbon atoms and ranged from 60 % for C14 compounds to 5 % for C28 compounds, while no absorption was detected for carbon numbers greater than C30 (Albro and Fishbein, 1970). The results of a number of extraction and migration tests on waxes and wax-bearing products were used by JECFA as indirect evidence that hydrocarbon waxes consumed in the diet are unlikely to be absorbed or metabolized in detectable or significant amounts (JECFA, 1993a). Any absorbed paraffin wax (high carbon number alkanes) will be slowly metabolised to the corresponding fatty alcohols and then fatty acids, with some metabolism also occurring in the small intestine, and enter normal biochemical pathways (EFSA, 2012b).

Acute toxicity

Paraffin waxes are anticipated to be of low acute oral toxicity. An LD_{50} of greater than 5 000 mg/kg b.w. has been reported[29] (US-EPA, 2011). They have been reported to be only very slightly irritant to skin and eyes.[29]

Subacute, subchronic and chronic toxicity studies

Both JECFA and the SCF have extensively reviewed the results of subacute, subchronic and chronic oral toxicity studies and human data on a number of mineral and synthetic oils and waxes including paraffin waxes (JECFA, 1993a; SCF, 1997b). The SCF (1997b) reported some of these substances 'not only accumulate with repeated dosing, but also give rise to effects which are not confined solely to localised foreign body reactions and provide clear evidence of toxicity in animals. […]. The following effects were observed: increased organ weights, especially liver and lymph nodes; altered serum enzyme levels; increased monocyte and neutrophil counts; reduced red blood cells, haemoglobin, haematocrit, mean corpuscular hemoglobin concentration (MCHC). The main histopathological findings were granulomata in the liver and focal collections of vacuolated macrophages (histiocytosis) in the lymph nodes. In animals dosed with certain of the waxes, an inflammatory lesion at the base of the mitral valve in the heart was observed'.

In the most recent of these studies (Smith et al., 1996), a range of mineral oils and waxes were administered in the diet to groups of F344 rats (20/sex) at levels of 0.002, 0.02, 0.2 or 2 % for 90 days (equivalent to 2, 20, 200 or 2 000 mg/kg b.w. per day). The results confirmed the toxicity of the mineral oils and low melting point wax tested, as described by the SCF (1997b), however no treatment-related effects were associated with administration of the high melting point wax and high sulphur wax (both microcrystalline waxes) other than minor haematological changes in females only, receiving the high sulphur wax. A NOAEL of 0.002 % in diet (about 1.5 mg/kg b.w. per day) was

[29] European Chemicals Agency (ECHA). Paraffin waxes and hydrocarbon waxes. CAS No 8002-74-2. Available at: http://apps.echa.europa.eu/registered/data/dossiers/DISS-9eb27f4b-c95d-44a9-e044-00144f67d031/DISS-9eb27f4b-c95d-44a9-e044-00144f67d031_DISS-9eb27f4b-c95d-44a9-e044-00144f67d031.html (consultation date: 2012-01-23).

identified for the low melting point wax, while for the microcrystalline waxes the NOAEL was ≥ 2 % in diet (about 1 500 mg/kg b.w. per day).

In a 60-day study with Fischer-344 (F-344) and SD rats, 2 % LMPW (low melting point paraffin wax) was administered in the diet for 60 day (Hoglen et al., 1998). The results of this study indicated that 2 % LMPW altered the morphology and functional capacity of Kupffer cells of F-344 rats, but not of SD rats. The authors suggested that these effects may ultimately lead to the formation of hepatic granuloma.

No treatment-related effects were reported in a chronic toxicity/carcinogenicity study in which SD rats were fed 5 types of refined waxes (three of the waxes were microcrystalline and the other two were refined paraffin waxes, not further specified) at a dietary concentration of 10 % (about 5 000 mg/kg b.w. per day) for two years (Shubik et al., 1962).

Genotoxicity

The results of a range of *in vitro* genotoxicity studies conducted with paraffin wax and reported in the ECHA database,[29] including a bacterial mutagenicity study with *Salmonella typhimurium* and *Escherichia coli*, a mouse lymphoma mutation assay and a chromosome aberration test in CHO cells, all conducted with and without metabolic activation, indicate no genotoxic potential. In genotoxicity studies, high viscosity and medium viscosity white oils also do not show genotoxic effects (EFSA, 2009c).

Carcinogenicity

In a chronic toxicity/carcinogenicity study in which rats were fed 5 types of refined waxes (three of the waxes were microcrystalline and the other two were refined paraffin waxes, not further specified) at a dietary concentration of 10 % (about 5 000 mg/kg b.w. per day) the incidence of tumours was comparable in test animals and controls (Shubik et al., 1962). The polycyclic aromatic hydrocarbon (PAH) content of the waxes tested was determined analytically, and the two refined paraffin waxes were found to have detectable levels of PAHs, while the three microcrystalline waxes did not. As reported by the authors, however, all five waxes were negative in the 2-year oral carcinogenicity study and also in a skin painting study in mice (Shubik et al., 1962). Both JECFA and the SCF concluded that (microcrystalline) paraffin wax is not carcinogenic, based on the results of this study. EFSA has also concluded that, in chronic toxicity/carcinogenicity studies conducted with high viscosity and medium viscosity white oils, no carcinogenic effects were observed in any of the studies in F344 rats or in skin painting studies in mice (EFSA, 2009c).

Developmental and reproductive toxicity

No data are available on the reproductive and developmental toxicity of paraffin wax or microcrystalline wax. There are also no data on high viscosity or medium viscosity white oils. EFSA concluded, however, that studies on low viscosity white mineral oils can be used to support the lack of reproductive or developmental effects for white oils (EFSA, 2009c). The CONTAM Panel considered that this could also be applied to the paraffin waxes.

3.10.2.4. Allergenicity

In the guinea pig maximization test, no skin reactions were observed in groups treated with 100 % or 50 % paraffin wax in liquid paraffin (Anonymous, 1997b, 2007, both as cited in ECHA, online). Negative results for paraffin wax have been recorded also in a human patch-test study (Dooms-Goosens and Degreef, 1983, as cited in ECHA, online).

Clinical studies in humans with two undiluted paraffin waxes and formulated products containing various concentrations of paraffinic (5-16 %) and microcrystalline (4.35-15 %) waxes recorded, at most, slight erythema, and none of the test substances caused skin sensitization (Elder, 1984). No data

on adjuvanticity or irritancy have been found. The available data give no indication that paraffin wax is an allergen or an adjuvant at concentrations expected from its use as a previous cargo.

3.10.3. Conclusion

Paraffin wax may contain aromatic hydrocarbons, some of which are genotoxic carcinogens. Hence, the CONTAM Panel concluded that this entry to the Annex should be restricted to paraffin waxes that have been treated to remove aromatic hydrocarbons and which also meet other relevant standards to be considered as 'food grade'. Accordingly, the CONTAM Panel recommends that the entry for these waxes in Annex to Commission Directive 96/3/EC be amended to 'Paraffin Wax (CAS No 8002-74-2 / 63231-60-7) (food grade)'.

An ADI of 0-20 mg/kg b.w. has been established by both JECFA and the SCF for high molecular mass food-grade microcrystalline wax, with specifications as laid down according to Commission Directive 2008/84/EC[30] and JECFA. The CONTAM Panel (EFSA, 2012b) noted that this ADI was established from toxicological studies in which no effects were observed at any tested dose. Food grade paraffin wax is not genotoxic or allergenic. It will not give rise to any reaction products with fats and oils of toxicological concern. No impurities of toxicological concern are known or anticipated.

The CONTAM Panel therefore concludes that paraffin wax (food grade, CAS No. 8002-74-2 / 63231-60-7) meets the criteria for acceptability as a previous cargo.

3.11. CARNAUBA WAX (Brazil wax) (CAS No 8015-86-9)

Carnauba wax is one of the hardest and highest-melting point natural waxes, with a melting point range between 82 and 86 °C. It is modestly soluble in solvents, virtually insoluble in water, i.e. difficult to remove from a container in solid form. The cleaning of a vessel might be inefficient.

Carnauba wax is mechanically obtained from the leaves of the Brazilian palm trees *Copernicia prunifera* and *Copernicia cerifera*. For purification it is melted and filtered.

Carnauba wax contains about 85 % esters of long chain fatty acids, hydroxy fatty acids and cinnamic acid with long chain alcohols and diols. The remaining material consists of long chain free acids, long chain fatty alcohols and saturated hydrocarbons.

Carnauba wax is used for polishing surfaces (e.g. shoes, furniture, floors, cars), as a release agent for bakery ware and sugar products, in chewing gums, as coatings of fruits, in cosmetics or to protect printed surfaces.

3.11.1. Previous evaluations

The SCF evaluated carnauba wax as a previous cargo in 1996 and considered it acceptable (SCF, 1997a). This conclusion was based on the fact that carnauba wax was temporarily acceptable as a food additive, E903, for use as a glazing agent for food (SCF, 1992d, 1997c). The SCF noted the insolubility of carnauba wax. In the 2003 SCF evaluation of acceptable previous cargoes, carnauba wax was not further evaluated as it was already considered acceptable (SCF, 2003).

The SCF has evaluated carnauba wax as a food additive on several occasions (SCF, 1992d, 1997c, 2001). The SCF did not establish an ADI for carnauba wax, and in its 1992 and 1997 opinions considered its use as a glazing agent as temporarily acceptable. In 2001, based on new toxicological and exposure data the SCF accepted the use of carnauba wax as a glazing agent up to a maximum use level of 200 mg/kg of food and withdrew its temporary status (SCF, 2001).

An ADI of 0-7 mg/kg b.w. for carnauba wax was established by JECFA in 1993 (JECFA, 1993b).

[30] Commission Directive 2008/84/EC of 27 August 2008 laying down specific purity criteria on food additives other than colours and sweeteners. OJ L 253/1. p. 175.

In USA carnauba wax is classified as GRAS and is permitted with no other limitation than good manufacturing practice (GMP) in a variety of food products (FDA, 1983a).

Carnauba wax is approved for use as a food contact additive in plastics under Commission Regulation (EU) 10/2011,[24] with no restrictions other than the generic overall migration limit of 60 mg/kg food.

EFSA re-evaluated carnauba wax (E 903) as a food additive in 2012 (EFSA, 2012c). The Panel on Food Additives and Nutrients added to Food (ANS Panel) did not establish an ADI due to the lack of long-term toxicity data. It noted, however, that available toxicity studies consistently reported no adverse effects associated with carnauba wax intake, and that the available data suggests no concern for genotoxicity. In addition, the exposure estimates to carnauba wax indicated sufficient 'margins of safety', and therefore concluded that its use as a food additive within the currently authorised uses would not be of safety concern.

3.11.2. Current evaluation

3.11.2.1. Expected impurities

Carnauba wax is not expected to contain impurities of concern when transported as a previous cargo.

3.11.2.2. Reactivity and reaction products

Carnauba wax is not expected to produce reaction products with edible fats and oils which are of concern when it is transported as a previous cargo.

3.11.2.3. Toxicological profile

Absorption, distribution, metabolism and excretion

Carnauba wax has a high melting point relative to other waxes, is insoluble in water and is hydrophobic in nature. There are no specific experimental data on the absorption, distribution, metabolism and elimination of carnauba wax (EFSA, 2012c). Overall the CONTAM Panel considered, however, that absorption of carnauba wax from the gastrointestinal tract will be low, if any, and that the wax is unlikely to be susceptible to metabolism by digestive enzymes or the intestinal microbiota. Any degradation products, e.g. long-chain aliphatic esters which are the main components of carnauba wax, will be incorporated into normal cellular metabolic pathways and eliminated thereafter.

Acute toxicity

Carnauba wax is of low acute toxicity, an oral LD_{50} of greater than 1 100 mg/kg b.w. has been reported (Liebert, 1984). Carnauba wax is not anticipated to have irritant properties.

Subacute, subchronic and chronic toxicity studies

As reported by the SCF (2001) and EFSA (2012c), a 90-day oral study in Wistar rats was carried out with carnauba wax (Rowland et al., 1982) at levels of up to 10 % in the diet, in which no treatment-related effects were reported. A NOAEL of 8 800 mg/kg b.w. per day, the highest dose tested, was identified in this study. A further 90-day feeding study in Fischer F-344 rats was designed to investigate whether components of carnauba wax could be absorbed and accumulate in the liver and other organs of this strain, as seen with high molecular mass mineral oils and other waxes (Edwards, 1998). Groups of 20 male and 20 female rats were fed diets containing carnauba wax corresponding to intakes of 0, 15, 150 and 1 500 mg/kg b.w. per day. No treatment-related effects were identified, there were no dose-related histopathological changes in liver and other tissues, and a NOAEL of 1 500 mg/kg b.w. per day, the highest dose tested, can be identified in this study (Edwards, 1998). A 6-month feeding study has also been carried out in Beagle dogs, using dietary levels of up to 1 % in

the diet (equivalent to up to 250 mg/kg b.w. per day) (Parent et al., 1983a). No treatment-related effects were identified. No studies on the chronic toxicity of carnauba wax are available (EFSA, 2012c).

Genotoxicity

As reported by JECFA (1993b) and the SCF (2001), carnauba wax was not mutagenic in *in vitro* tests with *Salmonella typhimurium* and *Saccharomyces cerevisiae*, with and without metabolic activation. As reported by SCF (2001), there was no evidence of clastogenicity of carnauba wax in *in vitro* chromosome aberration tests using human lymphocytes (Edwards, 1996, 1998). The SCF and, more recently, the EFSA ANS Panel (EFSA, 2012c) concluded that carnauba wax was not genotoxic *in vitro*, based on the results of these studies. There are no *in vivo* genotoxicity data available on carnauba wax.

Carcinogenicity

No studies on the carcinogenicity of carnauba wax are available (EFSA, 2012c).

Developmental and reproductive toxicity

No treatment-related effects were reported in a reproductive toxicity study with carnauba wax in which Wistar rats were administered levels of 0, 0.1, 0.3 or 1 % in the diet for 4 weeks prior to mating and through gestation and lactation (Parent et al., 1983b). This study was used by JECFA as the basis for setting the ADI of 7 mg/kg b.w. per day for carnauba wax (rounded up), by applying a 100 uncertainty factor to the NOAEL of approximately 670 mg/kg b.w. per day. As reported by the SCF (2001), no developmental toxicity was evident in a study in which rats were fed 0, 0.1, 0.3 or 1 % carnauba wax in the diet for two weeks before mating and throughout gestation.

3.11.2.4. Allergenicity

One report of a test-proven case of sensitization to carnauba wax has been published (Chowdhury, 2002). In addition, Jacob et al. (2008) report one case of supposed sensitization to carnauba wax, based on reaction to a product containing propolis and carnauba wax and test-proven sensitization to cinnamic acid/cinnamaldehyde, which is a component of both the mentioned substances. However, no testing with carnauba wax was performed. Chowdhury (2002) state that sensitization to carnauba wax is very rare. No other information on sensitizing properties, adjuvanticity or irritancy has been found. The CONTAM Panel considers that taking into account the scarcity of reports of sensitization in the literature as well as the relevant dilution factor, carnauba wax when used as a previous cargo is not likely to be a significant sensitizer, adjuvant or irritant.

3.11.3. Conclusion

JECFA has established an ADI of 0-7 mg/kg b.w. for carnauba wax, while the SCF concluded that its use as a glazing agent up to a maximum use level of 200 mg/kg of food was acceptable. The EFSA ANS Panel noted that available toxicity studies consistently reported no adverse effects associated with carnauba wax intake, and that the available data suggests no concern for genotoxicity. In addition, the exposure estimates to carnauba wax indicated sufficient 'margins of safety', and therefore concluded that its use as a food additive within the currently authorised uses would not be of safety concern. The CONTAM Panel considered, based on the outcome of these expert evaluations, the likely limited absorption of carnauba wax and the toxicological profile of its main component groups of chemicals, that this wax will not pose any toxicological concern when used as a previous cargo, based on normal assumptions regarding worst case carryover. There is no evidence that it is genotoxic and there is no allergenic potential of concern. It will not give rise to any reaction products with fats and oils of toxicological concern. No impurities of toxicological concern are known or anticipated.

The CONTAM Panel noted however, the insolubility of carnauba wax in water, its high melting point (82 to 86 °C) and the fact that heating of ships' tanks is normally to a maximum of 80 °C. The CONTAM Panel therefore has concerns regarding the feasibility of tank cleaning following transport of carnauba wax as a previous cargo, such that carryover may exceed the worst case normally assumed.

The CONTAM Panel concludes that carnauba wax does not meet the criteria for acceptability as a previous cargo because of doubts concerning the efficiency of tank cleaning following transport of carnauba wax as a previous cargo.

According to the information provided to EFSA, carnauba wax does not appear to be transported as a previous cargo.

3.12. CANDELILLA WAX (CAS No 8006-44-8)

Candelilla wax is yellowish to brown, hard (melting point around 70 °C), brittle, aromatic and opaque to translucent. It is insoluble in water, but soluble in many organic solvents.

Candelilla wax is obtained from the leaves and stems of a shrub from the family Euphorbiaceae growing in Mexico and the south-western United States by boiling with dilute sulphuric acid. The resulting 'cerote' is skimmed and purified.

Candelilla wax consists mainly of n-alkanes C29-33 (about 50 %), wax esters, sterol esters, free acids and resins.

Candelilla wax is used for making varnish. It is an approved food additive (glazing agent for fruits and sweets, E 902), and is also used in cosmetics. One of its major uses is as a binder for chewing gums. It is often used to replace the more expensive beeswax.

3.12.1. Previous evaluations

The SCF evaluated candelilla wax as previous cargo in 1996 and considered it acceptable (SCF, 1997a). This conclusion was based on the fact that candelilla wax was temporarily acceptable as a food additive, E902, for use as a glazing agent for food (SCF, 1992e). In the 2003 SCF evaluation of acceptable previous cargoes, candelilla wax was not further evaluated as it was already considered acceptable (SCF, 2003).

The SCF evaluated the safety of candelilla wax as a food additive in 1990 (SCF, 1992e). The Committee did not establish an ADI for candelilla wax, but took into consideration the available toxicity data, its long established use without apparent adverse effects and the expected limited intake when used as a glazing agent, and accepted the temporary continued use of candelilla wax (SCF, 1992e).

JECFA evaluated the use of candelilla wax as a glazing agent, chewing gum base component, surface finishing agent and carrier for flavours in 1993 and again in 2005 (JECFA, 1993c, 2006). JECFA estimated dietary exposure to candelilla wax using the conservative assumption that an individual would consume all the foods (and tablets or capsules) containing candelilla wax at the highest percentile in each food category and that all those foods contained candelilla wax, and calculated that the dietary exposure would be < 650 mg per person per day. JECFA concluded that the functional uses indicated did not raise any toxicological concerns provided the dietary exposure was less than 650 mg per person per day.

EFSA re-evaluated candelilla wax (E 902) as a food additive in 2012 (EFSA, 2012d). The Panel on Food Additives and Nutrients added to Food (ANS Panel) did not establish an ADI due to the lack of long-term toxicity data. It noted, however, that the available toxicity studies consistently reported no adverse effects associated with intake of the main components constituting candelilla wax, and that the

available data suggest that candelilla wax is not genotoxic. In addition, the exposure estimates (using the maximum permited levels of carnauba wax) indicated a sufficient 'margin of safety' and therefore concluded that its use as a food additive within the currently authorised uses would not be of safety concern.

In the USA candelilla wax is classified as GRAS and is permitted with no other limitation than GMP in a variety of food products (FDA, 1983b).

Candelilla wax is approved for use as a food contact additive in plastics under Commission Regulation (EU) 10/2011,[24] with no restrictions other than the generic overall migration limit of 60 mg/kg food.

3.12.2. Current evaluation

3.12.2.1. Expected impurities

Candelilla wax does not include impurities that would be of concern when it is used as a previous cargo.

3.12.2.2. Reactivity and reaction products

Candelilla wax does not contain substances which could react with edible fats and oils to produce compounds of concern.

3.12.2.3. Toxicological profile

Absorption, distribution, metabolism and excretion

No specific data on absorption, distribution, metabolism or excretion of candelilla wax were available to the Panel for evaluation. Overall, the CONTAM Panel considered that absorption of candelilla wax from the gastrointestinal tract will be low, if any, and that degradation by digestive enzymes or the intestinal microbiota would be limited. The components of candelilla wax, e.g. straight-chain hydrocarbons (C29-C33 n-alkanes) together with esters of acids and alcohols with even-numbered carbon chains (C28-C34) (JECFA, 2006), are also expected to have limited absorption and if absorbed, will be incorporated into normal cellular metabolic pathways and eliminated thereafter (EFSA, 2012d).

Acute toxicity

Candelilla wax is of low acute toxicity. As reported by the EFSA ANS Panel in 2012, the SCF reviewed a number of acute oral toxicity studies on candelilla wax (no further details) and reported that 'none of the studies reported any adverse treatment-related toxicological findings' (SCF, 1992e). Liebert (1984) reported that the acute oral toxicity of candelilla wax following gavage administration has been investigated in SD and Hooded Long Evans rats and other rats of undefined strain without report of any toxic effects. JECFA reported an oral LD_{50} of > 5 000 mg/kg b.w. for candelilla wax in rats (JECFA, 1993c).

Subacute, subchronic and chronic toxicity studies

JECFA in their evaluation of candelilla wax described four unpublished short-term studies (8-27 weeks in duration) in rats and one study in dogs (6 months in duration) (JECFA, 1993c). The studies in rats used a mixture of candelilla wax and either gum base or a butadiene-styrene polymer. The composition of the mixtures administered is not clear from the JECFA report, but the intakes of candelilla wax could have been up to 2 400 mg/kg b.w. per day in rats. No treatment-related effects were reported in any of these studies (JECFA, 1993c). In the 6-month study in dogs, candelilla wax was given in a gum base in the diet at levels equivalent to up to 600 mg candelilla/kg b.w. per day; again, no treatment-related effects were reported.

As also reported by JECFA (1993c), in a study in which groups of 30 rats were fed diets containing 0, 0.8, 2.0 or 5.0 % mixture of gum base containing 25 % candelilla wax for 89 weeks, no significant differences were reported between the groups regarding food intake, urinalysis, haematology or histopathology of major organs (Harrisson, 1953).

Genotoxicity

As reported by JECFA (1993c), candelilla wax was not mutagenic in four bacterial mutagenicity studies using *Salmonella typhimurium*, at test concentrations of up to 10 000 µg/plate, with and without metabolic activation. Candelilla wax also gave negative results in two other studies respectively using *Escherichia coli* and *Saccharomyces cerevisiae* D4 (JECFA, 1993c). No other *in vitro* or *in vivo* genotoxicity studies appear to have been carried out with candelilla wax. Available studies on the main components of candelilla wax (e.g. straight-chain hydrocarbons (C29-C33 n-alkanes) together with esters of acids and alcohols with even-numbered carbon chains (C28-C34) (JECFA, 2006)) do not give rise to concern regarding genotoxicity.

Carcinogenicity

As reported by JECFA (1993c), a mixture of gum base containing 25 % candelilla wax was administered to mice at levels of 0, 0.8 or 5.0 % in the diet, corresponding to 0, 1 200 or 7 500 mg/kg b.w. per day of gum mixture and approximately 0, 300 or 1 900 mg candelilla wax/kg b.w. per day for a period of 12-13 months (Hodge, 1973). The number of deaths in the 5 % dose group was reported by the authors to exceed those in the lower or control groups, but the cause of death was not defined. The authors concluded that there was no evidence of a carcinogenic effect of candelilla wax in this study (JECFA, 1993c).

JECFA concluded that the long term study of Harrisson (1953) in rats described above under 'Subacute, subchronic and chronic toxicity studies' also did not provide any evidence of carcinogenicity.

The CONTAM Panel noted that the main components of candelilla wax (e.g. straight-chain hydrocarbons (C29-C33 n-alkanes) together with esters of acids and alcohols with even-numbered carbon chains (C28-C34) (JECFA, 2006)) do not give rise to concern with respect to carcinogenicity.

Developmental and reproductive toxicity

As reported by JECFA (1993c), in a very limited short-term study three male and three female rats were fed a diet containing a 1:1 mixture of styrene-butadiene polymer and candelilla wax at concentrations of 0, 680 or 3 420 mg/kg b.w. per day for 5 months prior to mating (Harrisson, 1949). The authors reported that two of the three females from each dose group conceived and produced normal litters.

3.12.2.4. Allergenicity

No information has been found regarding sensitizing capacity, adjuvanticity or irritancy of candelilla wax. The CONTAM Panel considers that it is unlikely that candelilla wax after dilution when used as a previous cargo will be of concern with regard to sensitization, adjuvanticity or irritancy.

3.12.3. Conclusions

JECFA concluded that dietary exposures to candelilla wax of less than 650 mg/person per day (approximately 10 mg/kg b.w. per day), the intake calculated by JECFA from a conservative exposure estimate based on the indicated uses of candelilla wax as a food additive, do not raise concern about safety. The EFSA ANS Panel noted that the available toxicity studies consistently reported no adverse effects associated with intake of the main components constituting candelilla wax and that the exposure estimates allowed to conclude that candelilla wax, within the currently authorised uses as

food additive, would not be of safety concern. The CONTAM Panel agreed with this position, and concluded that given the likely limited absorption of candelilla wax and the toxicological profile of its main component groups of chemicals, this wax will not pose any toxicological concern when used as a previous cargo. There is no evidence that it is genotoxic and there is no allergenic potential of concern. It will not give rise to any reaction products with fats and oils of toxicological concern. No impurities of toxicological concern are known or anticipated.

The CONTAM Panel therefore concludes that candelilla wax meets the criteria for acceptability as a previous cargo.

According to the information provided to EFSA, the CONTAM Panel noted that candelilla wax does not appear to be transported as a previous cargo.

3.13. WHITE MINERAL OILS (CAS No 8042-47-5)

White mineral oil (CAS 8042-47-5) is defined by ECHA[31] as 'a highly refined petroleum mineral oil consisting of a complex combination of hydrocarbons obtained from the intensive treatment of a petroleum fraction with sulfuric acid and oleum, or by hydrogenation, or by a combination of hydrogenation and acid treatment. Additional washing and treating steps may be included in the processing operation. It consists of saturated hydrocarbons having carbon numbers predominantly in the range of C15 through C50'. Often white mineral oils are deparaffinated (removal of n-alkanes) to ensure liquid properties.

White mineral oils are used mainly in the food industry (e.g. as release agents and for dedusting of grain and rice) and for pharmaceuticals.

Most edible oils contain mineral oil hydrocarbons from the environment, harvesting and/or processing. Concentrations around 10-50 mg/kg are common, but some edible oils also regularly contain above 100 mg/kg mineral oil (such as olive pomace oil, grapeseed oil or cottonseed oil; Wagner et al., 2001; Moret et al., 2003, Biedermann et al., 2009; EFSA 2012b). Mostly the mineral oils also contain aromatic components.

3.13.1. Previous evaluations

The SCF evaluated white mineral oils as previous cargo in 1996 and considered that oils with a carbon number of not less than 25, an average molecular mass not less than 480 and a viscosity not less than 8.5 centistokes at 100 °C were provisionally acceptable pending submission of further data on chronic toxicity/carcinogenicity (SCF, 1997a). The SCF considered that there were insufficient data to establish the safety of other mineral oils. In the 2003 SCF evaluation of acceptable previous cargoes, the Committee reconsidered white mineral oils and concluded that the information available was inadequate. The SCF therefore maintained their opinion as provisionally acceptable previous cargo (SCF, 2003).

Mineral oil hydrocarbons have been evaluated on a number of occasions for their safety for use as food additives by the SCF, EFSA and JECFA.

An ADI of 0-20 mg/kg b.w. was established by JECFA (1995) for high viscosity (> 11 mm^2/s at 100 °C) mineral oils (synonyms: liquid paraffin; liquid petrolatum; food grade mineral oil; white mineral oil). In 2002 JECFA established an ADI of 0-10 mg/kg b.w. for medium- and low-viscosity, class I (8.5-11 mm^2/s at 100 °C) mineral oils (synonyms: liquid paraffin; liquid petrolatum; food grade mineral oil; white mineral oil) (JECFA, 2002). A temporary group ADI of 0-0.01 mg/kg b.w. was established by JECFA (2002) for medium- and low-viscosity, class II (7.0-8.5 mm^2/s at 100 °C) and

[31] European Chemicals Agency (ECHA), online. White mineral oil. CAS 8042-47-5. Available at: http://apps.echa.europa.eu/registered/data/dossiers/DISS-9ea08dfc-55a5-3699-e044-00144f67d031/DISS-9ea08dfc-55a5-3699-e044-00144f67d031_DISS-9ea08dfc-55a5-3699-e044-00144f67d031.html (consultation date: 2012-01-23).

class III (3.0-7.0 mm^2/s at 100 °C) mineral oils, but this was withdrawn in 2012, due to the absence of suitable information to enable an ADI to be established or confirmed (JECFA, 2012).

The EFSA ANS Panel evaluated the safety of high viscosity white mineral oils (CAS Registry Number 8042-47-5, chain lengths C22-C60, average molecular weight: > 500 g/mol, viscosity at 100 °C ≥ 11 mm^2/s, carbon number > 25 at 5 % distillation point) when used as food additives and established an ADI of 12 mg/kg b.w. based on a NOAEL of 1 200 mg/kg b.w. per day in a chronic (12 months) study in Fischer 344 rats (highest dose tested) (EFSA, 2009c).

The CONTAM Panel has provided a scientific opinion on Mineral Oil Hydrocarbons in Food, concluding that revision of the existing ADIs for some food grade mineral oil saturated hydrocarbons is warranted on the basis of new toxicological information (EFSA, 2012b). EFSA (2012b) noted that established ADIs are based on toxicological studies with poorly characterised products with regard to chemical composition. The CONTAM Panel concluded that for high-viscosity mineral oils and medium- and low viscosity class I mineral oils, the ADIs established by SCF, FAO/WHO and EFSA were based on toxicological studies in which no effects were observed at any tested dose. For those grades, it was concluded that although based on products with poor chemical characterisation, the existing ADIs were of low priority for revision. The upper bounds of the ADIs were all ≥ 4 mg/kg b.w.

White mineral oils, paraffinic, derived from petroleum-based hydrocarbon feedstocks, are approved for use as a food contact additive in plastics under Commission Regulation (EU) No 10/2011,[24] with no restrictions other than the generic overall migration limit of 60 mg/kg food.

For white mineral oil used as an active substance in pesticides, EFSA concluded that 'In line with the low toxicity of paraffin oils (of high purity), no ADI, AOEL[32] or ARfD[33] would be proposed, nor considered necessary, and no risk assessment for operators, workers and bystanders would be required' (EFSA, 2008b, c).

3.13.2. Current evaluation

3.13.2.1. Expected impurities

White mineral oils are not expected to contain impurities of concern.

3.13.2.2. Reactivity and reaction products

White mineral oils do not react with edible fats and oils.

3.13.2.3. Toxicological profile

Absorption, distribution, metabolism and excretion

Gastrointestinal absorption of white mineral oils is dependent on the physical properties and molecular composition of the oil, absorption decreasing with increasing carbon number and extent of side chain branching (EFSA, 2012b). Given the carbon numbers of high viscosity and medium and low viscosity (P70) white mineral oils, of > 28 and > 25 respectively, absorption will be limited. Any mineral oil absorbed is deposited mainly in the liver, mesenteric lymph nodes, spleen and perirenal fat, as shown by the results of toxicokinetic and toxicological studies (EFSA, 2012b). Deposited mineral oils will be slowly metabolised in the liver to the corresponding fatty alcohols and then fatty acids, with some metabolism also occurring in the small intestine, and will enter normal biochemical pathways (EFSA, 2012b).

[32] Acceptable operator exposure level.
[33] Acute reference dose.

Acute toxicity

Mineral oils (high viscosity) and mineral oils (medium and low viscosity) have low acute toxicity, with LD_{50} values > 5 000 mg/kg b.w. [31](EFSA, 2012b). They are non-irritant or slightly irritant to skin and eyes.[31]

Subacute, subchronic and chronic toxicity studies

As reported by SCF (1995), JECFA (2002) and EFSA (2009c, 2012b), repeated ingestion of mineral oils results in accumulation of the oils in various tissues, both in humans and in experimental animals, in a dose- and time-dependent manner, depending on the molecular composition of the particular oils, the carbon number and the extent of side chain branching (EFSA, 2012b). This accumulation results in an inflammatory response, characterised by focal histiocytosis, particularly in the mesenteric lymph nodes, and granulomas or microgranulomas in the liver and mesenteric lymph nodes. Increases in relative organ weights of liver, lymph nodes, spleen and kidneys also occur, together with haematological changes indicative of a chronic inflammatory reaction and biochemical changes associated with mild hepatic damage. It has been demonstrated in a number of studies that the Fischer 344 rat is markedly more susceptible to the development of these changes than Sprague Dawley rats or other strains. The CONTAM Panel in their evaluation of mineral oil hydrocarbons considered that 'the presence of microgranulomas/histocytosis in MLN[34] is a non specific, adaptative change of low toxicological concern' (EFSA, 2012b). The CONTAM Panel concluded however that the liver microgranulomas induced by mineral oils in Fischer 344 rats could be potentially relevant to humans and were the critical effect for risk assessment of mineral oils. The NOAEL for the critical effect in studies showing these effects was at least 100-fold greater than that for histiocytosis in the mesenteric lymph nodes. The lowest NOAEL identified for development of liver microgranulomas following administration of mineral hydrocarbons was 19 mg/kg b.w. per day, in a 90-day study in Fischer rats (Smith et al., 1996). This was however for mineral waxes, whereas in general the NOAEL for class II and II mineral oils was one order of magnitude greater.

These changes were not seen in toxicological studies with high viscosity mineral oils (e.g. P100) and medium and low viscosity class I mineral oils (e.g. P70(H)) and P100(H). For the high viscosity P100(H) mineral oils, the ADI of 20 mg/kg b.w. established by JECFA (2002) was based on a no-observed-effect level (NOEL) of 2 000 mg/kg b.w. per day, the highest dose tested in a 90 day study in Fischer rats. For the class I intermediate and low viscosity P70 mineral oils, the ADI of 10 mg/kg b.w. per day was based on an increased incidence of pigmented macrophages in male rats at a dose level of 2 000 mg/kg b.w per day, an effect considered of doubtful biological significance. A temporary group ADI of 0-0.01 mg/kg b.w. was established by JECFA (2002) for class II and III mineral oils, based on the occurrence of histiocytosis of mesenteric lymph nodes in 90-day studies in rats, with a NOAEL of 2 mg/kg b.w. per day and an uncertainty factor of 200. This effect is now considered to be of no toxicological relevance (EFSA, 2012b), and JECFA withdrew the ADIs of these classes in 2012, due to the absence of suitable information to enable an ADI to be established or confirmed (EFSA, 2012b).

Genotoxicity

The expert reviews carried out by the SCF, JECFA and EFSA have all concluded that refined high viscosity mineral oils (e.g. P100) and medium and low viscosity mineral oils with a very low content of aromatic compounds are not genotoxic. Negative results were obtained in bacterial mutagenicity tests without or with metabolic activation (Granella and Clonfero, 1991; Mackerer et al., 2003). Highly refined base oil was negative in a mouse lymphoma assay, with and without metabolic activation.[31] As reported by EFSA (2009c), a series of five paraffinic base stocks and two naphthenic base stocks were tested in the rat bone marrow cytogenetic assay (CONCAWE, 1984, as cited in

[34] Mesentheric lymph nodes.

EFSA, 2009c). Negative findings in these base stock oils, all of which are less refined than white mineral oils, supports the lack of genotoxicity in refined white mineral oils.

Carcinogenicity

Refined high viscosity mineral oils (e.g. P100) and medium and low viscosity class I (e.g.P70) mineral oils (with a very low content of aromatics) have not shown any effects of toxicological significance, including carcinogenicity, in chronic toxicity/carcinogenicity studies. In the pivotal carcinogenicity study for these mineral oils, rats were administered P70H and P100H mineral oils at doses of 0, 60, 120, 240, or 1 200 mg/kg b.w. per day via the diet. No carcinogenic potential or chronic toxicity was observed (Exxon Biomedical Sciences, 2001, as cited in JECFA, 2002). EFSA has also concluded that, in chronic toxicity/carcinogenicity studies conducted with high viscosity and medium viscosity white oils, no carcinogenic effects were observed in any of the studies in F344 rats or in skin painting studies in mice (EFSA, 2009c, 2012b).

Developmental and reproductive toxicity

Refined high viscosity mineral oils (e.g. P100) and medium and low viscosity (e.g.P70) mineral oils are not considered to show developmental or reproductive toxicity, although there are limited data following administration by the oral route (EFSA, 2012b). As reported by EFSA (2012b), in a developmental toxicity study, a sample of white mineral oil (no detail available) was administered to female SD rats (20 rats/group) at dose levels of 0 or 5 000 mg/kg b.w. per day from days 6 through 19 of gestation. No maternal or fetal toxicity were observed [31]. As also reported by EFSA (2012b), a light paraffinic distillate extract with a low viscosity and carbon numbers predominantly in the range of C15 to C30 was administered by gavage at a dose level of 1000 mg/kg per day in a screening reproductive and development toxicity study to rats. [31] There were no treatment-related effects on pup body weights, sex ratios, live litter sizes, viability indices, and general physical conditions and no treatment-related effects were observed on the parental animals. Studies by other routes of administration support the lack of developmental or reproductive toxicity of white mineral oils (EFSA, 2012b).

3.13.2.4. Allergenicity

In a skin sensitization study in guinea pigs undiluted highly refined base oil was tested, and found not to be a sensitizer (Anonymous, 1987g, as cited in ECHA, online). White mineral oil was found not to be sensitizing in the guinea pig maximization test (Magnusson and Kligman, 1969; Exxon Corporation, 1994, as cited in ECB, 2000b).

White mineral oil appears to be a non-irritant or only slightly irritating for the skin (Hoekstra and Phillips, 1963; Anonymous, 1987c, as cited in ECHA, online; Exxon Corporation, 1994, as cited in ECB, 2000b). However, the use of mineral oils of unspecified purity in cutting fluid has been associated with dermatitis in metal workers (Pryce at al., 1989). Emulsions of purified mineral oil with allergens have been much used as immune adjuvants in particular in animals (White, 1963) and the question has been raised whether mineral oil exposure may under some circumstances promote autoimmunity (Whitehouse, 2012).

Considering the high dilution factor, the CONTAM Panel considers that white mineral oils are not of concern with regard to sensitization, irritancy or adjuvanticity when used as a previous cargo.

3.13.3. Conclusions

The SCF, JECFA and/or EFSA have established ADIs of ≥ 4 mg/kg b.w. for high viscosity and medium- and low-viscosity, class I mineral oils. Whilst the CONTAM Panel considers that these may need to be revised as they were based on products with poor chemical characterisation, this is not a high priority given their toxicological profile, and there would be no toxicological concern from their use as previous cargoes. There are no ADIs for class II and III mineral oils. However, the lowest

relevant NOAEL available is 19 mg/kg b.w. per day from a 90-day study in Fischer rats. This was for mineral waxes, whereas in general the NOAEL for class II and III mineral oils was one order of magnitude greater. White mineral oils are not genotoxic and they would not be expected to be of concern for allergenicity when used as previous cargoes. They will not give rise to any reaction products with fats and oils of toxicological concern. The only potential impurities of toxicological concern are PAHs, which are controlled to low levels in these mineral oils.

The CONTAM Panel notes that some aliphatic hydrocarbons bioaccumulate in the body, such as branched and cyclic species in the mass range of 16-35 carbon atoms. However, since exposure to mineral oil hydrocarbons via contamination of edible fats and oils from previous cargoes occurs only rarely and mostly at levels lower than those observed in edible oils, it will contribute little to overall exposure. Further, humans are exposed to mineral oil hydrocarbons from numerous sources.

The CONTAM Panel therefore concludes that white mineral oils meet the criteria for acceptability as a previous cargo.

3.14. GLYCERINE (glycerol; glycerin) (CAS No 56-81-5)

The CONTAM Panel noted that the term glycerine is rarely used to refer to this substance. It is more normally referred to as glycerol (glycerin is the German name of the substance), and this is the preferred name. The IUPAC name is propane-1,2,3-triol.

Glycerol is a viscous liquid, miscible with water. It is the backbone of triglycerides (fats and oils). It is obtained from fats and oils, either from saponification or from transesterification with methanol (biodiesel; today the main source). It is also produced from propene via allyl chloride, dichloropropanol and epichlorohydrine. Synthetic glycerol is used only when the highest purity is required, as in pharmaceuticals and some food grade products.

Glycerol is used to produce e.g. glycerol trinitrate (nitroglycerol, dynamite), alkyd resins, polyurethanes, hydraulic fluids, antifreeze, cosmetics, humectants (e.g. in foods) and for the production of various food components, such as emulsifiers.

3.14.1. Previous evaluations

The SCF evaluated glycerol as a previous cargo in 1996 and considered it as acceptable (SCF, 1997a). This conclusion was based on the fact that glycerol was a food additive, E 422, and component of food, with an ADI not specified (SCF, 1981). In the 2003 SCF evaluation of acceptable previous cargoes, glycerol was not further considered as it was already considered acceptable (SCF, 2003).

JECFA evaluated glycerol as a food additive and established an ADI 'not specified' at its 20th meeting (JECFA, 1976). JECFA evaluated glycerol again in 2001 as a flavouring substance and maintained the ADI 'not specified' (JECFA, 2001).

The SCF evaluated glycerol as a food additive and as an extraction solvent for food, and agreed with the JECFA 1976 evaluation, that an ADI need not be specified (SCF, 1981).

The CONTAM Panel has evaluated crude glycerol derived from biodiesel production and concluded that such glycerol up to a level of 15 % in the diet of ruminants and up to 10 % in the diet of monogastric animals had no adverse effects on animal health (EFSA, 2010). Glycerol is considered as a feed material under Commission Regulation (EU) 892/2010,[35] with no maximum levels assigned.

Glycerol has been evaluated under the OECD SIDS programme on HPV chemicals (OECD, 2002). Overall, it was concluded that it was of low priority for further work.

[35] Commission Regulation (EU) No 892/2010 of 8 October 2010 on the status of certain products with regard to feed additives within the scope of Regulation (EC) No 1831/2003 of the European Parliament and of the Council, OJ L 266, 08.10.2010, p.8.

Glycerol is approved for use as a food contact additive in plastics under Commission Regulation (EU) No 10/2011,[24] with no restrictions other than the generic overall migration limit of 60 mg/kg food.

3.14.2. Current evaluation

3.14.2.1. Expected impurities

Crude glycerol from transesterification will contain alkali and methanol as the main impurities. When prepared by saponification it will contain alkali and free fatty acids as impurities. These impurities will not be of any concern when glycerol is used as a previous cargo.

Crude glycerol obtained by chemical synthesis could contain some unreacted allyl chloride, dichloropropanol and epichlorohydrin. Epichlorohydrin is fairly reactive in the presence of acid, but it is uncertain whether it reacts with components of edible fats and oils. However, as synthetic glycerol is only used after substantial purification, these impurities are not expected to be of concern when glycerol is used as a previous cargo.

3.14.2.2. Reactivity and reaction products

Glycerol may react with fats and oils through transesterification, but this is not expected to yield products of concern.

3.14.2.3. Toxicological profile

Absorption, distribution, metabolism and excretion

Glycerol occurs endogenously in the body as a result of hydrolysis of glycerol esters in the intestine, followed by absorption from the intestinal mucosa (JECFA, 2001). Following metabolism to glycerol-3-phosphate in the liver and to a minor extent in the kidney, intestine and other tissues, it is oxidized in several steps to pyruvic acid. Glycerol also combines with free fatty acids in the liver to form triglycerides. There is generally no excretion of free glycerol in the urine, due to complete metabolic conversion to other products (JECFA, 2001; OECD, 2002).

Acute toxicity

As reported by OECD (2002), glycerol is of low acute oral toxicity, with LD_{50}s > 20 000 mg/kg b.w. in rats, mice and rabbits. At doses approaching the LD_{50}, signs of toxicity include tremors, convulsions, CNS depression and hyperaemia of the gastrointestinal tract (OECD, 2002). Glycerol is slightly irritant to skin and eyes (OECD, 2002).

Subacute, subchronic and chronic toxicity studies

Rats were administered glycerol in the diet at levels of up to 60 %, providing intakes of 0, 1 000, 3 000, 6 000, 10 000, 15 000, 20 000, 30 000, 40 000, 500 00 or 60 000 mg/kg b.w. per day for 20 weeks (Guerrant and Whitlock, 1947, as cited in JECFA, 2001). Treatment-related changes were restricted to reduced body-weight gain in rats receiving > 40 000 mg/kg b.w. per day and hydropic and fatty degeneration of hepatocytes in rats receiving > 10 000 mg/kg b.w. per day. The NOAEL in this study was identified as 6 % glycerol in the diet, equivalent to 6 000 mg/kg b.w. per day (Guerrant and Whitlock, 1947, as cited in JECFA, 2001).

JECFA in 1976 reported the results of a long-term study in which rats were given glycerol in the diet at a concentration of 0, 5, 10 or 20 % (equivalent to 0, 2 500, 5 000, or 10 000 mg/kg b.w. per day) for 2 years, also including an interim kill at 12 months. No treatment-related effects were reported on body weight or on histological examination of major organs. The only treatment-related change was an increase in relative kidney weights at 10 000 mg/kg b.w. per day, unaccompanied by histopathological changes. The author of the study identified a NOEL of 10 000 mg/kg b.w. per day, the highest dose tested (Atlas Chemical Co., 1969, as cited in JECFA, 1976).

In another 2-year rat study reported by both JECFA (2001) and OECD (2002) male rats received 2 000, 4 000 or 8 000 mg/kg b.w. per day glycerol in the diet and females received 2 500, 5 000 and 10 000 mg/kg b.w. per day. No treatment-related effects were reported in this study other than a slight increase in food consumption in males receiving 4 000 or 8 000 mg/kg b.w. per day glycerol. The author of the report concluded that the NOAEL was greater than 10 000 mg/kg b.w. (Hine et al., 1953, as cited in JECFA, 2001 and OECD, 2002).

Genotoxicity

As reported by both JECFA (2001) and OECD (2002), glycerol did not induce mutations in a bacterial mutagenicity study, with and without metabolic activation and was negative in a mammalian cell gene mutation test (HGPRT). Glycerol did not induce chromosomal aberrations or sister chromatid exchanges in CHO cells (JECFA, 2001; OECD, 2002). In a bone marrow chromosome aberration test with rats, glycerol did not induce a statistically significant increase in chromosomal aberrations compared to controls (Varilyak and Kozachuk, 1985). OECD noted however that no reliable conclusions could be drawn from this study due to the limited details available, the small number of animals used and the absence of a positive control (OECD, 2002). Overall, glycerol is considered to possess no genotoxic potential.

Carcinogenicity

There was no evidence of carcinogenicity in two 2-year oral toxicity studies in the rat, reported under 'chronic toxicity' above. Data from tumour promotion studies in male mice indicated that oral administration of glycerol for up to 20 weeks had a weak promotion effect on the incidence of lung tumour formation (Nagahara, 1987; Inayama, 1986, as cited in OECD, 2002). Overall, these data do not indicate that glycerol has carcinogenic potential.

Developmental and reproductive toxicity

As reported by OECD (2002), a two generation study was conducted with glycerol administered by gavage as a 20 % solution in water (providing 2 000 mg/kg b.w. per day). No effects were found on the reproductive efficiency of the parents, nor on the growth, fertility or reproductive performance of the untreated F1 generation, and no histological changes occurred in the tissues of either the F1 or F2 generation. The NOAEL was therefore identified as 2 000 mg/kg b.w., the highest dose tested (Wegener, 1953, as cited in OECD, 2002).

In an oral gavage study, rats, mice and rabbits were administered glycerol at doses of 1 310, 1 280 and 1 180 mg/kg b.w. during part of the gestation period. No maternal toxicity or teratogenic effects were seen at the highest dose levels tested (N.T.I.S., 1974, as cited in OECD, 2002).

A study of fertility in 64 male workers involved in glycerol manufacture reported no significant effects on sperm quality parameters (Venable et al., 1980). The CONTAM Panel noted that although the workers were involved in glycerol manufacture, exposure to epichlorhydrin, allyl chloride and 1,3-dichloropropene was the specific focus of the study.

3.14.2.4. Allergenicity

Glycerol has low irritancy and is considered to be a weak sensitiser based on human data (El-Nagdy et al., 1973; Preston and Finch, 2003; Fairhurst and Wilkinson, 2007; Tamagawa-Mineoka et al., 2007). A guinea pig study on glycerol found no capacity for sensitization (Hine et al., 1953, as cited in JECFA, 2001 and OECD, 2002). No information has been found regarding adjuvanticity. The CONTAM Panel considers that the available data indicate that glycerol when used as a previous cargo would be of no concern as an allergen or adjuvant.

3.14.3. Conclusions

The CONTAM Panel notes that the name glycerine is rarely used to refer to this substance. It is more normally referred to as glycerol, which is the preferred name. The IUPAC name is propane-1,2,3-triol. The CONTAM Panel therefore recommends that the entry for the substance in the Annex to Commission Directive 96/3/EC[5] is amended to 'Glycerol (glycerine; glycerin; propane-1,2,3-triol) (CAS No 56-81-5)'.

Both JECFA and the SCF have established an ADI not specified for glycerol, which the CONTAM Panel considers appropriate. Glycerol is not genotoxic and there are no concerns regarding its allergenicity when it is used as a previous cargo. There are no reactions of concern with edible fats and oils, nor are any anticipated impurities likely to be present at levels of toxicological relevance.

The CONTAM Panel therefore concludes that glycerol meets the criteria for acceptability as a previous cargo.

CONCLUSIONS AND RECOMMENDATIONS

CONCLUSIONS

- Substances transported in bulk as previous cargoes are often rather crude and usually no specific information is available on the impurities present. Hence, the EFSA Panel on Contaminants in the Food Chain (CONTAM Panel) often had to determine which impurities might be present primarily from assessment of the source or starting material and method of preparation of the substance to be transported. Chemicals transported as previous cargoes may vary in composition, depending on their method of preparation, details for which were obtained, in part, from information obtained from FOSFA. The CONTAM Panel based its evaluations on worst case assumptions on these aspects.[36]

- The CONTAM Panel considered that it should be possible to measure the relevant components of a previous cargo in the edible oil or fat transported later. However, it is unrealistic to expect that corresponding analytical methods are immediately available, since fats and oils are not routinely analysed for the presence of most previous cargoes. It is sufficient that the development of a corresponding method is feasible with standard techniques. [36]

- **Sodium silicate (water glass) solution (CAS No 1344-09-8)**. Toxicological effects of sodium silicate following acute and repeat dosing are mostly due to high alkalinity. However, following ingestion it will be diluted and buffered by the neutralising capacity of the gastrointestinal tract. Thus the CONTAM Panel considered that the levels that would occur following oral ingestion of fats and oils transported subsequent to sodium silicate as a previous cargo would not give rise to any toxicological concern. Although there are no carcinogenicity studies available sodium silicate did not show any genotoxic activity in a variety of *in vitro* and *in vivo* assays thus indicating no genotoxic potential. Available data give no indication that sodium silicate is an allergen or an adjuvant at concentrations expected from its use as a previous cargo. Exposure to sodium silicates can be irritating or corrosive to the skin, however the potential levels arising in fats and oils following its transport as previous cargo would be of no concern. There are no reactions of concern with edible fats and oils, nor are any anticipated impurities likely to be present at levels of toxicological concern. The CONTAM Panel therefore concludes that sodium silicate solution meets the criteria for acceptability as a previous cargo for edible fats and oils.

[36] The addition of this bullet point aims to clarify the evaluation performed by the CONTAM Panel in relation to the impurities and the analytical methods. The clarification applies also to the previous two opinions by the CONTAM Panel on this topic (Part I of III (EFSA, 2011) and Part II of III (EFSA, 2012a)).

- **Iso-octanol (isooctyl alcohol) (CAS no 26952-21-6), iso-nonanol (isononyl alcohol) (CAS no 27458-94-2) and iso-decanol (isodecyl alcohol) (CAS no 25339-17-7)**. Iso-octanol, iso-nonanol and iso-decanol were classified by the former Scientific Committee on Food (SCF) in its last re-evaluation in 2003 as provisionally acceptable as previous cargoes because the information available was considered inadequate or limited. The CONTAM Panel used a 'read across' from the assessment profile of oxo-alcohols C9-C13 category (OECD, 2006) to fill data gaps on the toxicological profile of iso-octanol, iso-nonanol and iso-decanol. They are of a low order of toxicity following acute and repeated exposures upon oral, dermal or inhalational exposure. The lack of effects found in the limited studies available suggests that they are not genotoxic. They are not allergenic and there are no reactions of concern with edible fats and oils, nor are any anticipated impurities likely to be present at levels of toxicological concern. The CONTAM Panel therefore concludes that iso-decanol, iso-nonanol or iso-octanol meet the criteria for acceptability as previous cargoes for edible fats and oils.

- **1,3-Propanediol (1,3-Propylene glycol; trimethylene glycol) (CAS No 504-63-2).** 1,3-Propanediol is of low systemic toxicity when administered by the oral route. There are no carcinogenicity data but the available evidence indicates that 1,3-propanediol does not have any genotoxic potential. 1,3-Propanediol is not an allergen. There are no reactions of concern with edible fats and oils, nor are any anticipated impurities likely to be present at levels of toxicological concern. Therefore, the CONTAM Panel concludes that 1,3-propanediol meets the criteria for acceptability as a previous cargo for edible fats and oils.

- **Isobutyl acetate (2-methylpropyl acetate) (CAS No 110-19-0)**. The toxicity of acetate, one of the major metabolites of isobutyl acetate, was addressed in a previous Opinion of the CONTAM Panel (EFSA, 2012a), when it was considered that there would be no health concerns following the maximum potential carryover into edible fats and oils when it is transported as a previous cargo. In its evaluation of previous cargoes in 1996, the SCF concluded that isobutanol, the other major metabolite, was 'not acceptable', because 'limited toxicological data indicates a suspicion of carcinogenic concerns.' In a re-evaluation in 2003, the SCF maintained its previous opinion that this substance was not acceptable as a previous cargo because the Committee was aware of a number of issues that still needed clarification. The CONTAM Panel considered isobutanol as a previous cargo for edible fats and oils in 2009, and concluded that it was acceptable, based on the low level of toxicity observed in a more recent chronic study, as well as its volatility and ease of tank cleaning (EFSA, 2009b). Although the toxicological database for isobutyl acetate is limited, available data on this substance and on its hydrolysis products, acetic acid and isobutanol, suggest that isobutyl acetate is of relatively low systemic toxicity. It is not genotoxic or allergenic. There are no reaction products or impurities expected to be of toxicological concern. The CONTAM Panel therefore concludes that isobutyl acetate meets the criteria for acceptability as a previous cargo for edible fats and oils.

- **Sec-butyl acetate (CAS No 105-46-4)**. There are no data on repeated-dose toxicity of sec-butyl acetate. It is a Cramer class I substance, with a threshold of toxicological concern of 1 800 µg/person per day. It is rapidly metabolised to acetate and sec-butanol, which can be further metabolised to methyl ethyl ketone (MEK). The CONTAM Panel has previously evaluated acetic acid and MEK for their suitability as previous cargoes for edible fats and oils and concluded that they meet the criteria for acceptability (EFSA, 2012a). sec-Butanol is not genotoxic. The information available on sec-butanol does not indicate any toxicological concern at the exposure levels that might occur from the transport of sec-butyl acetate as a previous cargo to edible fats and oils. sec-Butyl acetate is not allergenic. There are no reaction products or impurities of toxicological concern. The CONTAM Panel therefore concludes that sec-butyl acetate meets the criteria for acceptability as a previous cargo for edible fats and oils.

- **Tert-butyl acetate (CAS No 540-88-5)**. The toxicological database on tert-butyl acetate is somewhat limited. The available data on tert-butyl acetate and on acetate and tert-butanol, its major metabolites, do not give rise to concerns regarding systemic toxicity, developmental toxicity or genotoxicity. Any carcinogenic risk would likely be from a non-genotoxic mode of action and would not be of concern at the levels of exposure that might occur from the use of tert-butyl acetate as a previous cargo for edible fats and oils. tert-Butyl acetate is not allergenic. There are no reaction products or impurities of toxicological concern. The CONTAM Panel therefore concludes that tert-butyl acetate meets the criteria for acceptability as a previous cargo for edible fats and oils.

- **n-Butyl acetate (CAS No 123-86-4)**. The SCF established a temporary acceptable daily intake (ADI) of 0-6 mg/kg for n-butyl acetate, on the basis of limited data. The toxicological database has several data gaps (no repeat dose studies by the oral route, no studies of chronic toxicity or carcinogenicity). However, there were sufficient data on its major metabolites, acetate and n-butanol, for the CONTAM Panel to conclude previously that these are not of concern, when used as previous cargoes. n-Butyl acetate is not genotoxic. The CONTAM Panel considers that the available information on the acute effects of n-butyl acetate and on its subchronic, reproductive and developmental toxicity following exposure by the inhalation route, together with information on its major metabolites, was sufficient to conclude that the risk from short-term exposure to n-butyl acetate when used as a previous cargo would not give rise to any toxicological concern. There are no concerns regarding the allergenicity of n-butyl acetate. There are no reaction products or impurities of toxicological concern. The CONTAM Panel therefore concludes that n-butyl acetate meets the criteria for acceptability as a previous cargo for edible fats and oils.

- **Propylene tetramer (CAS No 6842-15-5)**. Although specific studies on propylene tetramer itself are somewhat limited, data are available on many of its main components and mixtures of these. In general, the toxicological profile of alkenes depends on carbon length, and is similar for those with similar carbon length. The CONTAM Panel considers that propylene tetramer would not be of toxicological concern at the levels that would occur when used as a previous cargo for edible fats and oils. Although there are no studies of carcinogenicity, the CONTAM Panel concludes that in the absence of genotoxicity or of pathological changes in subchronic studies indicative of a potential carcinogenic hazard, there was no concern for possible carcinogenicity from the use of propylene tetramer as a previous cargo. Propylene tetramer is not allergenic. There are no reaction products or impurities of toxicological concern. The CONTAM Panel therefore concludes that propylene tetramer meets the criteria for acceptability as a previous cargo for edible fats and oils.

- **Montan wax (CAS No 8002-53-7)**. No ADI or tolerable daily intake (TDI) has been established for montan wax by the SCF, the Joint FAO/WHO Expert Committee on Food Additives (JECFA) or the European Food Safety Authority (EFSA). Data recently provided to the European Chemicals Agency (ECHA) indicate that montan wax is not mutagenic in a bacterial mutagenicity test, and the CONTAM Panel considers that it is not likely to be a significant sensitizer, adjuvant or irritant. In a subchronic toxicity study in rats, haematological changes and hepatotoxicity were observed at the lowest dose tested, of approximately 260 mg/kg body weight (b.w.) per day, and hence no no-observed-adverse-effect level (NOAEL) could be identified. There are no data on chronic toxicity or carcinogenicity. Montan wax is an ill-defined material for which it cannot be excluded that it contains components of concern. The CONTAM Panel therefore concludes that, given the deficiencies in the available data on montan wax, it does not meet the criteria for acceptability as a previous cargo.

- **Paraffin wax (food grade) (CAS No 8002-74-2 / 63231-60-7)**. Paraffin wax may contain aromatic hydrocarbons, some of which are genotoxic carcinogens. Hence, the CONTAM Panel concluded that this entry to the Annex should be restricted to paraffin waxes that have

been treated to remove aromatic hydrocarbons and which otherwise meet relevant standards to be considered as 'food grade'.

An ADI of 0-20 mg/kg b.w. has been established by both JECFA and the SCF for high molecular mass food-grade microcrystalline wax, with specifications as laid down according to Commission Directive 2008/84/EC and JECFA (2008). The CONTAM Panel (EFSA, 2012b) noted that this ADI was established from toxicological studies in which no effects were observed at any tested dose. Food grade paraffin wax is not genotoxic or allergenic. It will not give rise to any reaction products with fats and oils of toxicological concern. No impurities of toxicological concern are known or anticipated. The CONTAM Panel therefore concludes that paraffin wax (food grade, CAS No. 8002-74-2 / 63231-60-7) meets the criteria for acceptability as a previous cargo.

- **Carnauba wax (Brazil wax) (CAS No 8015-86-9)**. JECFA have established an ADI of 0-7 mg/kg b.w. for carnauba wax, while the SCF concluded that its use as a glazing agent up to a maximum use level of 200 mg/kg of food was acceptable. The EFSA Panel on Food Additives and Nutrient Sources added to Food (ANS Panel) noted in its re-evaluation of carnauba wax as a food additive carried out in 2012, that available toxicity studies consistently reported no adverse effects associated with carnauba wax intake, and that the exposure estimates to carnauba wax allowed the conclusions that, within the currently authorised as a food additive, it would not be of safety concern. The CONTAM Panel considered, based on the outcome of these expert evaluations, the likely limited absorption of carnauba wax and the toxicological profile of its main component groups of chemicals, that this wax will not pose any toxicological concern when used as a previous cargo, based on normal assumptions regarding worst case carryover. There is no evidence that it is genotoxic and there is evidence that the allergenic potential is very low and therefore of no concern in the context of previous cargoes. It will not give rise to any reaction products with fats and oils of toxicological concern. No impurities of toxicological concern are known or anticipated. The CONTAM Panel noted however, the insolubility of carnauba wax in water, its high melting point (82 to 86 °C) and the fact that heating of ships' tanks is normally to a maximum of 80 °C. The CONTAM Panel therefore has concerns regarding the feasibility of tank cleaning following transport of carnauba wax as a previous cargo, such that carryover may exceed the worst case normally assumed. The CONTAM Panel concludes that carnauba wax does not meet the criteria for acceptability as a previous cargo because of doubts concerning the efficiency of tank cleaning following transport of carnauba wax as a previous cargo.

- **Candelilla Wax (CAS No 8006-44-8)**. JECFA concluded that dietary exposures to candelilla wax of less than 650 mg/person per day (approximately 10 mg/kg b.w. per day), the intake calculated by JECFA from a conservative exposure estimate based on the indicated uses of candelilla wax as a food additive, do not raise concern about safety. The ANS Panel noted in its re-evaluation of candelilla wax as a food additive carried out in 2012, that the available toxicity studies consistently reported no adverse effects associated with intake of the main components constituting candelilla wax and that the exposure estimates allowed the conclusion that, within the currently authorised uses as a food additive, it would not be of safety concern. The CONTAM Panel agreed with this position, and concluded that given the likely limited absorption of candelilla wax and the toxicological profile of its main component groups of chemicals, this wax will not pose any toxicological concern when used as a previous cargo. There is no evidence that it is genotoxic and there is no allergenic potential of concern. It will not give rise to any reaction products with fats and oils of toxicological concern. No impurities of toxicological concern are known or anticipated. The CONTAM Panel therefore concludes that candelilla wax meets the criteria for acceptability as a previous cargo.

- **White mineral Oils (CAS No 8042-47-5)**. The SCF, JECFA and/or EFSA have established ADIs of ≥ 4 mg/kg b.w. for high viscosity and medium- and low-viscosity, class I mineral oils. Whilst the CONTAM Panel considers that these may need to be revised as they were

based on products with poor chemical characterisation, this is not a high priority given their toxicological profile, and there would be no toxicological concern from their use as previous cargoes. There are no ADIs for class II and III mineral oils. However, the lowest relevant NOAEL available is 19 mg/kg b.w. per day from a 90-day study in Fischer rats. This was for mineral waxes, whereas in general the NOAEL for class II and III mineral oils was one order of magnitude greater. White mineral oils are not genotoxic and they would not be expected to be of concern for allergenicity when used as previous cargoes. They will not give rise to any reaction products with fats and oils of toxicological concern. The only potential impurities of toxicological concern are polycyclic aromatic hydrocarbons (PAHs), which are controlled to very low levels in these mineral oils. The CONTAM Panel notes that some aliphatic hydrocarbons bioaccumulate in the body, such as branched and cyclic species in the mass range of 16-35 carbon atoms. However, since exposure to mineral oil hydrocarbons via contamination of edible fats and oils from previous cargoes occurs only rarely and mostly at levels lower than those observed in edible oils, it will contribute little to overall exposure. The CONTAM Panel therefore concludes that white mineral oils meet the criteria for acceptability as a previous cargo

- **Glycerol (Glycerine; glycerine; propane-1,2,3-triol) (CAS No 56-81-5)**. Both JECFA and the SCF have established an ADI not specified for glycerol, which the CONTAM Panel considers appropriate. Glycerol is not genotoxic and there are no concerns regarding its allergenicity when it is used as a previous cargo. There are no reactions of concern with edible fats and oils, nor are any anticipated impurities likely to be present at levels of toxicological relevance. The CONTAM Panel therefore concludes that glycerol meets the criteria for acceptability as a previous cargo.

RECOMMENDATIONS

The CONTAM Panel recommends that a number of amendments be made to the entries of the substances in the Annex to Commission Directive 96/3/EC.[5]

- The entry for 'Sodium silicate (water glass) (CAS No 1344-09-8' be amended to **'Sodium silicate (water glass) solution (CAS No 1344-09-8)'** to reflect contemporary shipping practices.

- The entry for '1,3-Propylene glycol (trimethylene glycol; 1.3-propanediol) (CAS No 504-63-2)' be amended to **'1,3-Propanediol (1,3-propylene glycol; trimethylene glycol (CAS No 504-63-2)'** to reflect accepted chemical nomenclature.

- The entry for 'iso-Butyl acetate (CAS No 110-19-0)' be amended to **'Isobutyl acetate (2-methylpropyl acetate) (CAS No 110-19-0)'** to reflect accepted chemical nomenclature.

- The entry for 'Paraffin wax (CAS No 8002-74-2 / 63231-60-7)' be amended to **'Paraffin wax (food grade) (CAS No 8002-74-2 / 63231-60-7)'** since other grades may contain aromatic hydrocarbons which could pose an unacceptable risk if such waxes were to be transported as previous cargoes to edible fats and oils.

- The CONTAM Panel recommends that the entry for 'Glycerine (glycerol; glycerin) (CAS No 56-81-5)' be amended to **'Glycerol (glycerine; glycerin; propane-1,2,3-triol) (CAS No 56-81-5)'** to reflect accepted chemical nomenclature.

The entries in the Annex to Commission Directive 96/3/EC for the substances evaluated in this Opinion as previous cargoes for edible fats and oils are listed in Table 4, amended as recommended by the CONTAM Panel.

Table 4: Substances in the list to Annex to Commission Directive 96/3/EC[5] listed as acceptable previous cargoes for edible fats and oils with amendments recommended by the CONTAM Panel (entries in bold).

Substance (synonyms)	CAS Number
Sodium silicate (water glass) solution	**1344-09-8**
iso-Octanol (isooctyl alcohol)	26952-21-6
iso-Nonanol (isononyl alcohol)	27458-94-2
iso-Decanol (isodecyl alcohol)	25339-17-7
1,3-Propanediol (1,3-propylene glycol; trimethylene glycol)	**504-63-2**
Isobutyl acetate (2-methylpropyl acetate)	**110-19-0**
sec-Butyl acetate	105-46-4
tert-Butyl acetate	540-88-5
n-Butyl acetate	123-86-4
Propylene tetramer	6842-15-5
Paraffin wax (food grade)	**8002-74-2 / 63231-60-7**
Candelilla wax	8006-44-8
White mineral oils	8042-47-5
Glycerol (Glycerine; glycerine; propane-1,2,3-triol)	**56-81-5**

The CONTAM Panel recommends that when new substances are to be evaluated as previous cargoes for the bulk transport by sea of edible fats and oils, the interested party should provide information adequate for EFSA to carry out a scientific evaluation, including information on:

- the identity and specification (including impurities) of the substances to be evaluated,
- their chemical composition,
- the form in which they are transported (e.g. in solution),
- the chemical reactivity with fats and oils,
- published data on toxicological studies (including acute and chronic toxicity studies, reproductive and developmental toxicity studies, carcinogenicity and genotoxicity studies) and allergenicity and adjuvanticity.
- similar information on the toxicity of any significant impurities and reaction products with fats and oils.
- where an impurity (or reaction product) is not considered significant, an explanation for this conclusion.

Information should also be supplied on ease of tank cleaning, including any need for heating of the transfer equipment.

DOCUMENTATION PROVIDED TO EFSA

1. **FOSFA International. Response from FOSFA International following a meeting the EFSA Working Group on Previous Cargoes, 3 April 2012. Submitted to EFSA on 18 April 2012.**

WAXES

Question: the WG requested information on the current transport of the different waxes listed as acceptable previous cargoes for edible fats and oils.

With regard to the various waxes, the IBC Code does not differentiate but simply contains an entry "Waxes", which is pollution Category Z and ship type 3 (lowest safety requirement ship). My contacts understand that in most cases where wax is carried, it is petroleum wax. They have never heard of anyone carrying beeswax, candelilla wax or carnauba wax, but they will check with the trade association membership to ensure they are not carried.

(*Follow-up reply submitted by FOSFA to EFSA on 30.05.2012*). I have made further enquiries into the carrying of waxes in bulk by sea. As far as I can determine, these waxes are not carried in bulk. There is not enough shipment to justify bulk cargoes. I believe that they are not carried in bulk by sea. Also, these products do not appear in the IBC Code, and products which do not appear in the code, and are not covered by a tripartite agreement (an agreement between the exporting country, the importing country and the flag state of the ship carrying the cargo) cannot be carried in bulk by sea.

PROPYLENE TETRAMER

Question: the WG requested information on the identity of the material that is carried as previous cargo for edible fats and oils.

Propylene Tetramer is a branched olefin produced by the polymerization of propylene. It is also commonly referred to as dodecene. Propylene Tetramer is used in the production of dodecylphenol, tridecyl alcohol, branched dodecylbenzene sulfonic acid, and dodecylsuccinic anhydride which in turn are used to produce plasticizers, surfactants, lube oil additives, emulsifiers for herbicides, and corrosion inhibitors in alkyd and epoxy coatings.

The material which is shipped seems to be a blend of isomers of which about 65% are 1-propene. Another MSDS lists a detailed breakdown of the isomers which are present:

Components	CAS Registration Number	Weight %
Trimethylheptene Isomers	102943-77-1	0.5 to 2
Tetramethylheptene Isomers	103982-56-5	3 to 6
Trimethyloctene Isomers	103985-01-9	3 to 6
Tetramethyloctene Isomers	105902-19-0	20 to 25
Trimethylnonene Isomers	54410-98-9	40 to 50
Dimethyldecene Isomers	55170-80-4	20 to 25
Tetramethylnonene Isomers	55771-41-0	0.5 to 2

I have not been able to get much information about the material which is shipped apart from a Material Safety Data Sheet (MSDS) which is rather vague on the various components. Thus, I have attached the detailed MSDS from TEXAS PETROCHEMICALS LP which gives much more information about the product.

2. FOSFA International. Response from FOSFA International. Submitted to EFSA on 16 July 2012.

1,3-PROPYLENE GLYCOL

Question: the WG requested information on the grade(s) of 1,3-propylene glycol most commonly transported.

The vast majority of propylene glycol carried by the chemical tanker fleet is 1,2-propylene glycol. The 1,3-propylene glycol which is carried is typified by the attached MSDS from Du Pont (1). This has a composition of > 99.7 % purity although many manufacturers quote 99% minimum, and occasionally 98 % min. It has been available in commercial quantities in the past, but is not an important product now. It was obtained as a by-product in the production of glycerol by either saponification or fermentation of animal fats, but is also produced from acrylaldehyde.

ISO-DECANOL, ISO-NONANOL, ISO-OCTANOL

Question: the WG requested information on the composition of the iso-decanols, iso-nonanols and iso-octanols as traded.

The iso-decanol, iso-nonanol, iso-octanol products which are traded are mixtures of isomers and are mainly produced by Oxo-process from olefins by addition of CO and hydrogen. They are generally described as, for example, 'ALCOHOLS, C9–C11 -ISO, C10-RICH', or 'C9-RICH'. The compositions are typified by the MSDS for Exxal 10 (2) and Neodol 9 (3). The purity is difficult to define. The multinational manufacturers such as Exxon have 99.0 % minimum purity, but some just state "rich", meaning that this is the majority chemical present. I believe that both types are carried in bulk by sea. Octanol Technical Grade (4) is sometimes carried and is described as 99.5 % minimum 2 ethyl-hexanol isomers.

PARAFFIN WAX - EDIBLE GRADE

Question: It was noted that this entry appears in the FOSFA list of acceptable previous cargoes as 'Paraffin wax - edible grade'. The WG requested information on the specifications understood by FOSFA for 'edible grade'? (The same applies for the entry White Mineral Oils).

Paraffin wax - edible grade is a highly refined paraffin wax. When a manufacturer states that their product is edible, FOSFA understands that it complies with all the relevant food ingredient legislation of the country in which it is to be used.

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ABBREVIATIONS

ACGIH	American Conference of Industrial Hygienists
ADH	Alcohol dehydrogenase
ADI	Acceptable daily intake
ALDH	Aldehyde dehydrogenases
ALT	Alanine aminotransferase
ANS Panel	EFSA Panel on Food Additives and Nutrient Sources added to Food
AST	Aspartate aminotransferase
b.w.	Body weight
CAC	Codex Alimentarius Commission
CCFO	Codex Committee for Fats and Oils
CHO	Chinese hamster ovary
CONTAM Panel	EFSA Panel on Contaminants in the Food Chain
CNS	Central nervous system
DIDP	Diisodecyl phthalate
DINP	Diisononyl phthalate
ECHA	European Chemicals Agency
EFSA	European Food Safety Authority
EU	European Union
FAO	Food and Agriculture Organization of the United Nations
FDA	United States Food and Drug Administration
FEMA	Flavor and Extract Manufacturers Association of the US
FOSFA	Federation of Oils, Seeds and Fats Associations
GD	Gestation day
GMP	Good manufacturing practice
GRAS	Generally Recognized As Safe
HPV	High Production Volume
IUCLID	International Uniform Chemical Information Database
JECFA	Joint FAO/WHO Expert Committee on Food Additives
LLNA	Local lymph node assay
LMPW	Low melting point paraffin wax
LMWPW	Lower melting point paraffin waxes
LOAEL	Lowest-observed-adverse-effect level
MCHC	Mean corpuscular hemoglobin concentration
MEK	Methyl ethyl ketone
MSDS	Material Safety Data Sheet
MTBE	Methyl tertiary butyl ether
NOAEC	No-observed-adverse-effect concentration
NOAEL	No-observed-adverse-effect level
NOEL	No-observed-effect level
OECD	Organisation for Economic Co-operation and Development
PAH	Polycyclic aromatic hydrocarbon
PCE	Polychromatic erythrocytes
PND	Postnatal day
PTT	Polytrimethylene terephthalate
SCF	Scientific Committee on Food
SD	Sprague-Dawley (rats)
SIDS	Screening Information Sata Set
TDI	Tolerable daily intake
TTC	Threshold of toxicological concern
WHO	World Health Organization