

SCIENTIFIC OPINION

Scientific Opinion on the re-evaluation of microcrystalline wax (E 905) as a food additive¹

EFSA Panel on Food Additives and Nutrient Sources added to Food (ANS)^{2, 3}

European Food Safety Authority (EFSA), Parma, Italy

ABSTRACT

Following a request from the European Commission, the Panel on Food Additives and Nutrient Sources added to Food (ANS) was asked to deliver a scientific opinion on microcrystalline wax (E 905) when used as a food additive. Microcrystalline wax (E 905) is authorised *quantum satis* as a surface treatment agent on non-chocolate confectionery, chewing gum and decorations, coatings and fillings, except fruit based fillings. It is also permitted as a surface treatment of melons, papaya, mango and avocado. The substance was evaluated by the Scientific Committee on Food (SCF) in 1990 and 1995 and by the Joint FAO/WHO Expert Committee on Food Additives (JECFA), the latest in 1995. The JECFA established a group ADI of 20 mg/kg bw/day for mineral oils, paraffins and microcrystalline waxes. The Panel noted that all mineral oil products accumulated in tissues in a dose- and time-dependent manner with the exception of microcrystalline waxes. The Panel concluded that there is no concern for genotoxicity from microcrystalline wax (E 905). The Panel also considered that the available toxicity studies with mineral hydrocarbons, closely related from a chemical point of view with microcrystalline waxes, consistently reported no effects of concern associated with the intake of microcrystalline wax. The Panel further concluded that since no long-term toxicity and carcinogenicity studies with microcrystalline wax E 905 were available, no ADI could be established. The Panel also concluded that the conservative exposure estimates to microcrystalline wax (E 905) from its use at maximum permitted level (following *quantum satis* rules), resulted in a sufficient margin of safety compared to the NOAEL established by the Panel for the closely related high viscosity mineral oils, and therefore the use microcrystalline wax (E 905) as a food additive with the currently authorised uses would not be of safety concern.

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KEY WORDS

Petroleum wax, microcrystalline, CAS Registry Number 63231-60-7; Microcrystalline paraffin waxes and hydrocarbon waxes.

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² Panel members: Fernando Aguilar, Riccardo Crebelli, Birgit Dusemund, Pierre Galtier, David Gott, Ursula Gundert-Remy, Jürgen König, Claude Lambré, Jean-Charles Leblanc, Alicja Mortensen, Pasquale Mosesso, Agneta Oskarsson, Dominique Parent-Massin, Martin Rose, Ivan Stankovic, Paul Tobback, Ine Waalkens-Berendsen, Rudolf Antonius Woutersen and Matthew Wright. Correspondence: ans@efsa.europa.eu

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SUMMARY

Following a request from the European Commission, the Panel on Food Additives and Nutrient Sources added to Food (ANS) was asked to deliver a scientific opinion on microcrystalline wax (E 905) when used as a food additive.

The Panel was not provided with a newly submitted dossier and based its evaluation on previous evaluations and additional literature that became available since then and the data available following a public call for data. The Panel noted that not all original studies on which previous evaluations were based were available.

Microcrystalline wax (E 905) is authorised *quantum satis* as a surface treatment agent on non-chocolate confectionery, chewing gum and decorations, coatings and fillings, except fruit based fillings. It is also permitted as a surface treatment of melons, papaya, mango and avocado.

The substance was evaluated previously by the Scientific Committee on Food (SCF) in 1990 and 1995 and by the Joint FAO/WHO Expert Committee on Food Additives (JECFA), the latest in 1995.

Microcrystalline wax (E 905) is a refined mixture of solid, saturated hydrocarbons, mainly branched paraffin, obtained from petroleum. The hydrocarbons are characterised by carbon numbers predominantly in the range between C41-C51, a kinematic viscosity of ≥ 11 mm²/s at 100°C, an average molecular weight of ≥ 650 g/mol and a carbon number at 5 % distillation point of ≥ 25 .

The Panel noted that microcrystalline wax has physico-chemical characteristics very similar to high viscosity mineral oils (kinematic viscosity of > 11 mm²/s at 100 °C, average molecular weight of ≥ 500 g/mol and a carbon number at 5 % distillation point of ≥ 28), previously evaluated by EFSA.

Absorption, distribution, metabolism and elimination (ADME) studies show that gastrointestinal absorption of purified hydrocarbons from different origin is dependent on their physical properties and molecular composition (e.g. chain length) of the constituting hydrocarbons, with no absorption occurring for hydrocarbon fractions with carbon numbers above C32. In addition, less than 5 % of the carbon fraction above C28 is expected to be absorbed. Due to the large carbon number of microcrystalline wax (46-50) the Panel considered that these compounds are not significantly absorbed.

The Scientific Panel on Contaminants in the Food Chain (CONTAM) observed that all mineral oil products accumulated in tissues in a dose- and time-dependent manner with the exception, however, of microcrystalline waxes.

The Panel noted that subchronic (90-day) feeding studies on a wide range of white oils and waxes were conducted in F344 rats and that subchronic studies in Long Evans rats and Beagle dogs on a related white mineral oil are available. The studies showed that microcrystalline waxes and high viscosity mineral oils were found to be without statistically significant biological effects at doses up to 1620 mg/kg bw/day for the male rats and up to 1820 mg/kg bw/day for the female rats.

No genotoxicity studies on microcrystalline wax E 905 were available; however, some studies with the closely related high viscosity mineral oils show that high viscosity mineral oils and also the medium viscosity mineral oils are neither mutagenic nor genotoxic.

No long-term toxicity and carcinogenicity with microcrystalline wax E 905 were available. However, a 2-year study in male and female Sprague-Dawley rats on the toxicity of three petroleum waxes with a kinematic viscosity comparable to that of microcrystalline wax E 905 was considered. Based on the results of this study, JECFA concluded that the waxes administered at a level of 10 % in the feed (equivalent to 4500 mg/kg bw/day for the male rats and to 5800 mg/kg bw/day for the female rats) were devoid of carcinogenic or other toxic effects.

Trimmer et al. (2004) assessed long-term toxicity and carcinogenicity of two mineral oils: a medium viscosity mineral oil (kinematic viscosity 8.97 mm²/s at 100 °C) and a high viscosity mineral oil (kinematic viscosity 11 mm²/s at 100 °C) in a 2-year study, conducted in male and female F344 rats. The Panel considered that, given the chemical nature of the high viscosity mineral oil used in the study, any effect observed with that substance could provide useful information for a read across for the evaluation of microcrystalline wax E 905. Based on the results of these studies the EFSA in 2009 concluded that no carcinogenic effects were observed in any of the studies in F344 rats. Non-neoplastic effects were limited to infiltration of histiocytes in mesenteric lymph nodes and oil deposition in the liver. These effects are considered to be an indication of white oil exposure rather than an adverse effect. There were no adverse effects on survival, body weight, food consumption, clinical signs, clinical chemistry, haematology, and no treatment-related changes were seen at gross necropsy.

Based on the No Observed Adverse Effect Level (NOAEL) of 1200 mg/kg bw/day of the study, EFSA (EFSA Panel on Food Additives and Nutrient Sources added to Food (ANS), 2009) derived an Acceptable Daily Intake (ADI) of 12 mg/kg bw/day for high viscosity mineral oils.

No study on treatment related and developmental toxicity on microcrystalline were available. However, chronic toxicity studies on various oils did not show histopathological changes on male and female reproductive organs. In addition, several reproductive and developmental toxicity studies using low viscosity mineral oils as a solvent control are available. In 2009, EFSA reviewed these studies and concluded that they were useful in providing evidence of the lack of reproductive or developmental effects of white mineral oils.

The SCF (1997) stated that some mineral hydrocarbons have accumulated in humans, but no further details were provided. JECFA (1995) stated that the limited data on mineral hydrocarbons available from human studies indicated that mineral-oil-induced lesions similar to those seen in rats, had (?) been identified in human tissues, but that it was not possible to assess the level of intake of mineral oil associated with hydrocarbon accumulation in humans.

The Panel considered that the generalised conclusion, from the literature of human mineral oil tissue deposition and concurrent histopathological changes, is that none of the investigations have clearly demonstrated any clinical significance due to the observed pathological changes and the presence of oil.

Exposure estimates derived using the MPL (following *quantum satis* rules), showed that the mean intake of microcrystalline wax from use as food additive ranged from 0.3-1.4 mg/kg bw/day in toddlers, 0.5-1.8 mg/kg bw/day in children, 0.2-1.3 mg/kg bw/day in adolescents, 0.03-0.6 mg/kg bw/day in adults and 0.05-0.2 mg/kg bw/day in the elderly. High intake for estimates derived using the maximum permitted levels ranged from 1.8-6.7 mg/kg bw/day in toddlers, 1.1-5.5 mg/kg bw/day in children, 0.5-4.4 mg/kg bw/day in adolescents, 0.3-11 mg/kg bw/day in adults and 0.3-1.8 mg/kg bw/day in the elderly.

For the highest consumers (95th percentile), given the NOAEL of 1200 mg/kg bw/day for the closely related high viscosity mineral oils, these exposures would result in a margin of safety of approximately 177 for toddlers and of approximately 108 for adults.

The Panel concluded that there is no concern for genotoxicity for microcrystalline wax (E 905).

The Panel also considered that the available toxicity studies with mineral hydrocarbons, closely related from a chemical point of view with microcrystalline waxes, and consistently reported no effects of concern associated with the intake of microcrystalline wax.

The Panel further concluded that since no long-term toxicity and carcinogenicity studies with microcrystalline wax E 905 were available, no ADI could be established.

The Panel also concluded that the conservative exposure estimates to microcrystalline wax (E 905) from its use at maximum permitted level (following *quantum satis* rules), resulted in a sufficient margin of safety compared to the NOAEL identified by the Panel for the closely related high viscosity mineral oils, and therefore the use of microcrystalline wax (E 905) as a food additive with the currently authorised uses would not be of safety concern.

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BACKGROUND AS PROVIDED BY THE EUROPEAN COMMISSION

Regulation (EC) No 1333/2008⁴ of the European Parliament and of the Council on food additives requires that food additives are subject to a safety evaluation by the European Food Safety Authority (EFSA) before they are permitted for use in the European Union. In addition, it is foreseen that food additives must be kept under continuous observation and must be re-evaluated by EFSA.

For this purpose, a programme for the re-evaluation of food additives that were already permitted in the European Union before 20 January 2009 has been set up under Regulation (EU) No 257/2010⁵. This Regulation also foresees that food additives are re-evaluated whenever necessary in light of changing conditions of use and new scientific information. For efficiency and practical purposes, the re-evaluation should, as far as possible, be conducted by group of food additives according to the main functional class to which they belong.

The order of priorities for the re-evaluation of the currently approved food additives should be set on the basis of the following criteria: the time since the last evaluation of a food additive by the Scientific Committee on Food (SCF) or by EFSA, the availability of new scientific evidence, the extent of use of a food additive in food and the human exposure to the food additive taking also into account the outcome of the Report from the Commission on Dietary Food Additive Intake in the EU⁶ of 2001. The report “Food additives in Europe 2000⁷” submitted by the Nordic Council of Ministers to the Commission, provides additional information for the prioritisation of additives for re-evaluation. As colours were among the first additives to be evaluated, these food additives should be re-evaluated with a highest priority.

In 2003, the Commission already requested EFSA to start a systematic re-evaluation of authorised food additives. However, as a result of adoption of Regulation (EU) 257/2010 the 2003 Terms of References are replaced by those below.

TERMS OF REFERENCE AS PROVIDED BY THE EUROPEAN COMMISSION

The Commission asks the European Food Safety Authority to re-evaluate the safety of food additives already permitted in the Union before 2009 and to issue scientific opinions on these additives, taking especially into account the priorities, procedures and deadlines that are enshrined in the Regulation (EU) No 257/2010 of 25 March 2010 setting up a programme for the re-evaluation of approved food additives in accordance with the Regulation (EC) No 1333/2008 of the European Parliament and of the Council on food additives.

⁴ Regulation (EC) No 1333/2008 of the European Parliament and of the Council of 16 December 2008 on food additives, OJ L 354, 31.12.2008, p. 16.

⁵ Commission Regulation (EU) No 257/2010 of 25 March 2010 setting up the program for the re-evaluation of approved food additives in accordance with Regulation (EC) No 1333/2008 of the European Parliament and of the Council on food additives, OJ L 80, 26.03.2010, p.19.

⁶ Report from the Commission on Dietary Food Additive Intake in the European Union, Brussels, 01.10.2001, COM (2001) 542 final.

⁷ Food Additives in Europe 2000, Status of safety assessments of food additives presently permitted in the EU, Nordic Council of Ministers. TemaNord 2002:560.

ASSESSMENT

1 Introduction

The present opinion deals with the re-evaluation of the safety of microcrystalline wax (E 905) when used as a food additive.

Microcrystalline wax (E 905) is a mineral hydrocarbon authorised as a food additive in the EU. The substance has been evaluated previously by the Scientific Committee on Food (SCF) in 1990 and 1995 (SCF, 1992, 1997) and several times by the Joint FAO/WHO Expert Committee on Food Additives (JECFA), the latest in 1995 (JECFA 1995). Microcrystalline wax was also reviewed by TemaNord in 2002 (TemaNord, 2002).

The Panel was not provided with a newly submitted dossier and no new toxicological or biological information was submitted for the present re-evaluation neither following a public call for data⁸. The Panel based its evaluation on previous evaluations and additional literature that became available since then. Not all original studies on which previous evaluations were based were available for the present re-evaluation.

2 Technical data

2.1 Identity of the substance

Microcrystalline wax (E 905) is a refined mixture of solid, saturated isoprenic (branched) and cyclic compounds (naphthenes, alkyl- and naphthenes-substituted aromatic units). The branched isoparaffins and the naphthenes chains are located at random along the main carbon chain. The presence of the (large number) of side chains inhibit crystallisation and gives the substance its microcrystalline structure (Heinrich, 2005).

Microcrystalline waxes have as the empirical formula C_nH_{2n+z} where n is predominantly in the range of 41 – 51.

Microcrystalline wax has the CAS Registry Number 63231-60-7 and the EINECS Registry number 264-038-1 (Bennett, 1975; ChemIdplus 2011). The average molecular weight is in the range of 650 up to above 700 g/mol (CONCAWE, 1984).

In Table 1 the chemical characteristics, as provided by the producers, of six different samples of microcrystalline waxes that meet the specifications, are listed. The producers stated that such types of microcrystalline waxes will be used for the requested applications (CONCAWE, 2012).

⁸ Call for scientific data on miscellaneous waxes permitted as food additives in the EU (published: 23 November 2009). Available from: <http://www.efsa.europa.eu/en/dataclosed/call/ans091123b.htm>

Table 1: Chemical characteristics of microcrystalline waxes (CONCAWE 1984)

Microcrystalline waxes						
Origin of crude feedstock	Middle East			North America		
Manufacturing process	Hydrotreating (catalytic hydrogenation)		Conventional ⁹	Hydrotreating (catalytic hydrogenation)		Conventional
Sample number in CONCAWE report 84/60	4	5 (fresh catalyst)	6 (used catalyst)	9	3	10
Boiling range (°C)	>500	>500	>500	>500	>500	>500
Refractive index at 100°C (n_D^{100})	1.4437	1.4463	1.4440	1.4467	1.4424	1.4437
Viscosity at 100°C (mm ² /s)	16.3	15.5	15.2	16.4	14.7	14.7
Average molecular weight (g/mol)	729	702	693	709	673	680
Number of carbons (C_n)	50.1	47.9	50.3	48.7	46.3	47.9
z-number ^a in general formula	-0.03	-0.18	0.46	0.22	0.65	0.75
1. C_nH_{2n+z}						
Number of saturated rings	1.02	1.09	0.77	0.89	0.67	0.62
Sum of 6 PAHs ^b µg/kg	1.4 – 3.3	0.8 – 4.5	0.9 – 1.7	1.4-3.3	0.8 – 1.2	1.0-4.9

^a z-number: parameter indicating the deficiency of hydrogen atoms relative open chain structures

^b Fluoranthene; Benzo(b)fluoranthene; Benzo(d)fluoranthene; Benzo(a)pyrene; Benzo(ghi)perylene; Indeno(1,2,3-cd)pyrene

The Panel noted that the PAHs listed in the last row of Table 1 do not fully concur with those considered most relevant by EFSA for food risk assessment (EFSA, 2008).

According to FAO/WHO (2002) the highly refined mineral hydrocarbons, including microcrystalline wax, intended for use in food, can be classified as shown in Table 2.

Table 2: Classification of highly refined mineral hydrocarbons intended for use in food (from FAO/WHO, 2002)

Name	Viscosity at 100 °C (mm ² /s)	Average relative molecular mass	Carbon number at 5 % distillation point
Microcrystalline wax	≥ 11	≥ 500	≥ 25

2.2 Specifications

Specifications have been defined in Commission Regulation (EU) No 231/2012¹⁰. Specifications have

⁹ See section 2.3.

¹⁰ Commission Regulation (EU) No 231/2012 of 9 March 2012 laying down specifications for food additives listed in Annexes II and III to Regulation (EC) No 1333/2008 of the European Parliament and of the Council. OJ L 83, 22.3.2012, p 1-295.

also been defined by JECFA (JECFA, 2000) established specifications for microcrystalline wax (E 905/INS 905c) used as food additive. In Table 3 these specifications are listed.

Table 3: Chemical specifications for microcrystalline wax (E 905) according to Commission Regulation (EU) No 231/2012 and JECFA (JECFA, 2000)

	Commission Regulation (EU) No 231/2012	JECFA 55 th meeting 2000										
DEFINITION	Microcrystalline wax is a refined mixture of solid, saturated hydrocarbons, mainly branched paraffin, obtained from petroleum	Microcrystalline Wax is a refined mixture of solid, saturated hydrocarbons, mainly branched paraffin, obtained from petroleum										
DESCRIPTION	White to amber, odourless wax	Colourless or white, somewhat translucent, tasteless and odourless wax										
IDENTIFICATION												
Solubility	Insoluble in water, very slightly soluble in ethanol	Insoluble in water, very slightly soluble in ethanol, sparingly soluble in diethyl ether and hexane										
Refractive Index	n_D^{100} : 1.434-1.448 Alternative n_D^{120} : 1,426-1,440	n_D^{100} : 1.434 – 1.448										
Infrared absorption	not listed	The infrared absorbance spectrum of the sample melted and prepared on a caesium or potassium bromide plate corresponds to the spectrum in the Appendix [not included]										
PURITY												
Molecular weight (g/mol)	Average not less than 500	[average] not less than 500										
Viscosity at 100° C ¹¹	Not less than $1.1 \times 10^{-5} \text{ m}^2 \text{ s}^{-1}$ Alternative: Not less than $0,8 \times 10^{-5} \text{ m}^2 / \text{s}$ at 120 °C, if solid at 100 °C	Not less than 11 mm ² /s										
Residue on ignition	Not more than 0.1 %	Not more than 0.1 %										
Carbon number at 5 % distillation point	Not more than 5 % of molecules with carbon number less than 25	Not more than 5 % of molecules with carbon number less than 25										
Colour	Passes test	Passes test										
Sulphur	Not more than 0.4 %	Not more than 0.4 %										
Arsenic	Not more than 3 mg/kg	-										
Lead	Not more than 3 mg/kg	Not more than 3 mg/kg										
	Benzo(a)pyrene not more than 50 µg/kg	The sample shall meet the following ultraviolet absorbance limits when subjected to the analytical procedure										
Polycyclic aromatic compounds		<table border="1"> <thead> <tr> <th>nm</th> <th>Maximum absorbance per cm path length</th> </tr> </thead> <tbody> <tr> <td>280-289</td> <td>0.15</td> </tr> <tr> <td>290-299</td> <td>0.12</td> </tr> <tr> <td>300-359</td> <td>0.08</td> </tr> <tr> <td>360-400</td> <td>0.02</td> </tr> </tbody> </table>	nm	Maximum absorbance per cm path length	280-289	0.15	290-299	0.12	300-359	0.08	360-400	0.02
nm	Maximum absorbance per cm path length											
280-289	0.15											
290-299	0.12											
300-359	0.08											
360-400	0.02											

¹¹ Dynamic (absolute) viscosity: measure of the internal resistance of a fluid. Unit: N s/m² or kg/m s. Kinematic viscosity: ratio of the dynamic (absolute) viscosity to the density of a fluid. Unit: m²/s or Stoke (St).

2.3 Manufacturing process

A detailed description of the manufacturing process is available from Heinrich (2005). The process can be summarised as follows.

Microcrystalline waxes are prepared from crude petroleum feed stock of different origin (Middle East, North America). The feed stock is subjected to vacuum distillation and the residues obtained after this treatment are further subjected to de-asphalting, refining, and de-waxing to produce high-value bright stock slack waxes (petrolatum). These crude bright stock slack waxes are subsequently de-oiled by fractional crystallisation.

As de-oiled micro-waxes are still dark yellow to dark brown and not completely odorless, further refining is required.

Refining is carried out either by the conventional method (i.e. solvent extraction followed by discolorisation using clay or bauxite) or by catalytic hydrogenation in the presence a specific catalyst (hydrotreating).

The hydrogenated products are further refined by adsorptive decolourisation or stripping, to completely remove odorous materials and volatile components. Products differ in their congealing point¹², drop point¹³, hardness, viscosity, and colour. They are available in a liquid (molten) form or as solids in the form of slabs, pellets and powder.

The producers provided data showing that the physical and chemical characteristics of microcrystalline waxes obtained either via the conventional method or via the catalytic hydrogenation process are essentially similar. This conclusion was based on the analysis of corresponding pairs of waxes of different origin (CONCAWE, 1984).

2.4 Methods of analysis in food

No official analytical method for the determination of microcrystalline wax in/on food has been identified in literature.

Methods to detect mineral hydrocarbons, including microcrystalline wax, have been described in literature. In these methods, a fatty extract is analysed by GC/FID (Gas Chromatography with Flame Ionisation Detector) calibrated with n-alkanes solutions in the C₂₅-C₆₀ range. The authors indicate that the analysis of mineral oils in foods is very complex and, even after extensive clean-up, the hydrocarbons appear as a complex envelope of peaks in capillary GC/MS. The lack of a suitable chromophore makes the analysis prone to interference with co-extracted compounds. The absence of suitable standards makes the analysis only semi-quantitative (Castle et al., 1993a, 1993b; Castle et al., 1994; Lanzon et al., 1994; Grob et al., 1997).

2.5 Reaction and fate in food

Although the components of microcrystalline wax are more sensitive to chemical attack at elevated temperatures than paraffin wax it is unlikely that any change will take place when used in or on foods at normal temperatures (Bennett, 1975; Heinrichs, 2005; Class, 2010).

¹² The temperature at which a molten petroleum wax ceases to flow, when allowed to cool under prescribed conditions.

¹³ The temperature at which a petroleum wax passes from a semi-solid state to a liquid state under specific test conditions.

2.6 Case of need and proposed uses

2.6.1 Actual levels of use

Maximum permitted levels (MPLs) of microcrystalline wax have been defined in the Commission Regulation (EU) No 1129/2011¹⁴ on food additives for use in foodstuffs.

Currently, microcrystalline wax is an authorised glazing agent in the EU for 4 *quantum satis* applications.

Table 4 summarises the foods that are permitted to contain microcrystalline wax and the corresponding MLs as set by Commission Regulation (EU) No 1129/2011.

Table 4: MLs of microcrystalline wax in foods according to the Commission Regulation (EU) No 1129/2011

Category number	Foods	Maximum permitted level (mg/L or mg/kg as appropriate)	restrictions/exception
4.1.1	Entire fresh fruit and vegetables	<i>quantum satis</i>	only surface treatment of melons, papaya, mango, and avocado
5.2	Other confectionery including breath refreshing microsweets	<i>quantum satis</i>	surface treatment only
5.3	Chewing gum	<i>quantum satis</i>	surface treatment only
5.4	Decorations, coatings and fillings, except fruit based fillings covered by category 4.2.4	<i>quantum satis</i>	surface treatment only

2.6.2 Reported use levels or data on analytical levels of microcrystalline wax

Most food additives in the EU are authorised at a specific MPL. However, a food additive may be used at a lower level than the MPL. For those additives where no MPL is set and which are authorised as *quantum satis*, information on actual use levels is required. In the framework of Regulation (EC) No 1333/2008¹⁵ on food additives and of Regulation (EC) No 257/2010¹⁶ regarding the re-evaluation of approved food additives, EFSA issued a public call for scientific data on microcrystalline wax (E 905) including present use and use patterns (i.e. which food categories and subcategories, proportion of food within categories/subcategories in which it is used, actual use levels (typical and maximum use levels), especially for those uses which are only limited by *quantum satis*).

2.6.3 Summarised data on reported use levels in foods from industries and other sources

No data on usage of microcrystalline wax was submitted by industry. Table 5 therefore only shows the levels used for the exposure assessment identified by the Panel based on data for several food categories in finished products from the rules followed to deal with *quantum satis* (QS) authorisation as indicated in Annex A (Figure 1).

¹⁴ Commission Regulation (EU) No 1129/2011 of 11 November 2011 amending Annex II to Regulation (EC) N°1333/2008 of the European Parliament and of the Council establishing a Union list of food additives. The Panel noted that the Commission Regulation (EU) No 1129/2011 of 11 November 2011 will enter into force on June, 1st 2013 but confirms the approved uses of SSL and CSL as food additive as described in previous Directives still active until end of May 2013.

¹⁵ Regulation (EC) No 1333/2008 of the European Parliament and of the Council of 16 December 2008 on food additives, OJ L 354, 31.12.2008, p. 33.

¹⁶ Commission Regulation (EU) No 257/2010 of 25 March 2010 setting up the program for the re-evaluation of approved food additives in accordance with Regulation (EC) No 1333/2008 of the European Parliament and of the Council on food additives, OJ L 80, 26.03.2010, p. 19-27.

Table 5: Summary of levels used in the refined exposure assessment

Matching FAIM Foodcodes	Food items		Maximum permitted levels	Level used for calculation (mg/kg)	comments
4.1 - Unprocessed fruit and vegetables	melons, papaya, mango and avocado	q.s.	50 mg/kg for surface treated fresh fruit Source Codex Alimentarius	-	Peel not consumed, therefore not taken into account
5.2.1 - Other confectionery with added sugar 5.2.2 - Other confectionery without added sugar	confectionery excluding chocolate	q.s.	2000 mg/kg of high and medium/low viscosity mineral oils used as surface treatment for confectionery including hard and soft candy, nougats, etc. Source: Codex Alimentarius	2000	
5.3.1 - Chewing gum with added sugar 5.3.2 - Chewing gum without added sugar	chewing gum	q.s.	20 000 mg/kg in chewing gum used as surface treatment Source: Codex Alimentarius	20 000	
7.2 - Fine bakery wares	Decorations, coatings and fillings, except fruit based fillings	q.s..	2000 mg/kg of high and medium/low viscosity mineral oils used as surface treatment for confectionery including hard and soft candy, nougats, etc. Source: Codex Alimentarius	2000	A 10 % weight factor was applied to account for the coating/decoration part of fine bakery ware

* Industries reported no use in this food category

** *quantum satis* rules data.

number of analysed samples

FCM = Food Contact Material

2.7 Information on existing authorisations and evaluations

According to Directive No 98/72/EC¹⁷, amending Directive No 95/2/EC¹⁸, microcrystalline wax (E 905) is permitted in the EU, at *quantum satis* levels, for the surface treatment on confectionery (except chocolate), chewing gum and a few fruits: melon, papaya, mango and avocado. Regulation (EC) No 1333/2008 of the European Parliament and of the Council of 16 December 2008 on food additives extends this use to Decorations, coatings and fillings, except fruit based fillings covered by category 4.2.4 as of 1st June 2013.

According to EU Directive No 2002/72/EC¹⁹ microcrystalline wax is permitted for plastics in contact with food and is defined as ‘*waxes, refined, derived from petroleum based or synthetic hydrocarbon (Ref No 95859)*’. No specific migration limit (SML) was set.

JECFA (1992 and 1993) allocated an Acceptable Daily Intake (ADI) ‘not specified’ for microcrystalline wax (INS 905(c). In 1995 (JECFA, 1995) this ADI was changed to an ADI of 0-20 mg/kg bw based on new short-term feeding studies showing no adverse effects up to the highest dose tested of 2 % microcrystalline wax in the diet. Based on the same studies, the SCF allocated an ADI of 0-20 mg/kg bw (SCF, 1997).

¹⁷ European Parliament and Council Directive 98/72/EC of 15 October 1998 amending Directive 95/2/EC on food additives other than colours and sweeteners. OJ L 295, 4.11.1998 p 18-30.

¹⁸ European Parliament and Council Directive 95/2/EC of 20 February 1995 on food additives other than colours and sweeteners. OJ L 61, 18.3.1995, p. 1-40.

¹⁹ Commission Directive No 2002/72/EC of 6 August 2002 relating to plastic materials and articles intended to come into contact with foodstuffs. OJ L 220, 15.8.2002, p. 18.

In the USA microcrystalline wax is included in the definition of petroleum wax, which is permitted in chewing gum base, on cheese and raw fruits and vegetables and as an anti-foaming agent in foods

In Canada microcrystalline wax is not listed as such as a permitted food additive but, as both mineral oil and paraffin wax are permitted for various purposes, the Panel considered that this will cover also microcrystalline wax.

<http://laws.justice.gc.ca/eng/C.R.C.-c.870/page-1.html#anchorbo-ga:l B-gb:l 16>).

In Japan microcrystalline wax is listed as a permitted food additive with the number 310 <http://www.ffcr.or.jp/zaidan/FFCRHOME.nsf/pages/list-exst.add>).

In Australia and New Zealand microcrystalline wax as such is not listed, but only petrolatum or petroleum jelly (INS 905b).

<http://www.foodstandards.gov.au/srcfiles/Food%20Additives%20numeric.pdf>).

2.8 Exposure

2.8.1 Food consumption data used for exposure assessment

In 2010, the EFSA Comprehensive European Food Consumption Database (Comprehensive Database) has been built from existing national information on food consumption at a detailed level. Competent authorities in the European countries provided EFSA with data on the level of food consumption by the individual consumer from the most recent national dietary survey in their country (cf. Guidance of EFSA 'Use of the EFSA Comprehensive European Food Consumption Database in Exposure Assessment' (EFSA, 2011b).

Overall, the food consumption data gathered at EFSA were collected by different methodologies and thus direct country-to-country comparison should be made with caution.

For calculation of chronic exposure, intake statistics have been calculated based on individual average consumption over the total survey period excluding surveys with only one day per subject. High level consumption was only calculated for those foods and population groups where the sample size was sufficiently large to allow calculation of the 95th percentile (EFSA, 2011b). The Panel estimated chronic exposure for the following population groups: toddlers, children, adolescents, adults and the elderly. Calculations were performed using individual body weights.

Thus, for the present assessment, food consumption data were available from 23 different dietary surveys carried out in 17 different European countries as mentioned in the Table 6.

Table 6: Population groups considered for the exposure estimates of microcrystalline wax

Population	Age range	Countries with food consumption surveys covering more than one day
Toddlers	from 12 up to and including 35 months of age	Bulgaria, Finland, Germany, Netherlands
Children ²⁰	from 36 months up to and including 9 years of age	Belgium, Bulgaria, Czech Republic, Denmark, Finland, France, Germany, Greece, Italy, Latvia, Netherlands, Spain, Sweden
Adolescents	from 10 up to and including 17 years of age	Belgium, Cyprus, Czech Republic, Denmark, France, Germany, Italy, Latvia, Spain, Sweden
Adults	from 18 up to and including 64 years of age	Belgium, Czech Republic, Denmark, Finland, France, Germany, Hungary, Ireland, Italy, Latvia, Netherlands, Spain, Sweden, UK
The elderly ²⁰	Older than 65 years	Belgium, Denmark, Finland, France, Germany, Hungary, Italy

Consumption records were codified according to the FoodEx classification system (EFSA, 2011a). Nomenclature from FoodEx classification system has been linked to the Food Classification System as presented in the Commission Regulation (EU) No 1129/2011, part D, to perform exposure estimates.

2.8.2 Exposure to microcrystalline wax from its use as food additive

Exposure to microcrystalline wax from its use as food additive has been calculated by using MPLs following *quantum satis* rules as listed in Table 4 combined with national consumption data for the five population groups (Table 6).

High level exposure (typically 95th percentile of consumers only) was calculated by adding the 95th percentile of exposure from one food group (i.e. the one having the highest value) to the mean exposure resulting from the consumption of all other food groups.

This is based on the assumption that an individual might be a high level consumer of one food category and would be an average consumer of the others. This approach has been tested several times by the ANS Panel in re-evaluation of food colours and has shown reasonable correlation with high level total intakes when using the raw food individual consumption data. Therefore, this approach was preferred for the calculations based on the maximum permitted levels and maximum reported use levels in order to avoid excessively conservative estimates.

However, the Panel noted that its estimates should be considered as being conservative, since it is assumed that all processed foods contain microcrystalline wax added at the maximum permitted levels.

Table 7 summarises the estimated exposure to microcrystalline wax from its use as food additive of all five population groups.

²⁰ The terms “children” and “the elderly” correspond respectively to “other children” and the combination of “elderly” and “very elderly” in the Guidance of EFSA on the ‘Use of the EFSA Comprehensive European Food Consumption Database in Exposure Assessment’ (EFSA, 2011b).

Table 7: Summary of anticipated exposure to microcrystalline wax from its use as food additive using maximum permitted levels in five population groups (mg/kg bw/day)

Estimated exposure (mg/kg bw/day) using maximum permitted levels					
	Toddlers (12-35 months)	Children (3-9 years)	Adolescents (10-17 years)	Adults (18-64 years)	The elderly (>65 years)
Mean	0.3-1.4	0.5-1.8	0.2-1.3	0.03-0.6	0.05-0.2
High level ^[1]	1.8-6.7	1.1-5.5	0.5-4.4	0.3-11.1	0.3-1.8

^[1] typically 95th percentile of consumers only

For estimates derived using the maximum permitted levels (following quantum satis rules), mean intake of microcrystalline wax from use as food additive ranged from 0.3-1.4 mg/kg bw/day in toddlers, 0.5-1.8 mg/kg bw/d in children, 0.2-1.3 mg/kg bw/day in adolescents, 0.03-0.6 mg/kg bw/day in adults and 0.05-0.2 mg/kg bw/day in the elderly. High intake for estimates derived using the maximum permitted levels ranged from 1.8-6.7 mg/kg bw/day in toddlers, 1.1-5.5 mg/kg bw/day in children, 0.5-4.4 mg/kg bw/day in adolescents, 0.3-11 mg/kg bw/day in adults and 0.3-1.8 mg/kg bw/day in the elderly.

The derived intake estimates are likely to present an overestimate of intake, as it was assumed that all confectionery, decorations, fillings and coatings and chewing gum contain microcrystalline wax at the highest permitted level (following *quantum satis* rules). It was further assumed that all fine bakery ware contain ten percent of coating and/or decoration. A number of studies reported in the literature, which predominantly focus on the migration of mineral oils and waxes from food contact materials, and which aim to estimate intake from the overall diet have reported considerably lower intake estimates. In these studies, concentration data found in various food categories were found to be lower than the maximum permitted levels used in this opinion. Whilst the aim of these studies was to estimate migration of food contact materials, it is reasonable to assume that these studies would have also picked up microcrystalline wax used as food additive. Therefore, the intake estimates derived in this opinion should be considered as conservative.

JECFA made an overall estimate of mineral hydrocarbons from all sources through the diet at their meeting in 2002 (JECFA, 2003). They concluded that the average daily intake from food uses (including packaging) of microcrystalline wax would be 0.01 and 0.02 mg/kg bw/day in UK and the USA respectively. The high percentile even for children would be below 1 mg/kg bw/day.

Tennant (2004) estimated that the average exposure (consumers only) to microcrystalline wax from all food use sources (additive, in cheese rind and from packaging) could amount to 0.012 mg/kg bw/day for adults and 0.079 mg for preschool children. The 97.5th percentiles being 0.056 and 0.404 mg/kg bw/day respectively.

2.8.3 Main food categories contributing to exposure of microcrystalline wax using MLs

As shown in Table 8, for all population groups, confectionery with added sugar and fine bakery ware (decorations, fillings and coatings) presented the major dietary contributor to microcrystalline wax.

Table 8: Main food categories contributing to exposure to microcrystalline wax using MPLs (> 5 % of the total mean exposure) and number of surveys in which each food categories is contributing

Food Categories	Toddlers	Children	Adolescents	Adults	The elderly
	% contribution to total exposure (Number of Surveys)				
5.2.1 - Other confectionery with added sugar	21.7-64 (4)	7.3-72.5 (15)	5.9-75.8 (12)	8.3-54.9 (13)	7.8-59.7 (6)
5.2.2 - Other confectionery without added sugar	5.3 (1)	0	0	0	10.6 (1)
5.3.1 - Chewing gum with added sugar	0	6.8-13.9 (3)	5.2-19.9 (4)	21.8 (1)	11.9 (1)
5.3.2 - Chewing gum without added sugar	49.8 (1)	7.5-40.4 (6)	12.2-21.5 (5)	8.5-40.9 (7)	11.9-32.5 (2)
7.2 - Fine bakery wares	8-73.1 (4)	22.8-86.6 (13)	20.9-88.5 (11)	31.8-99.2 (13)	16.6-98.2 (6)

**Total number of surveys may be greater than total number of countries as listed in Table 3, as some countries submitted more than one survey for a specific age range.

2.9 Uncertainty analysis

Uncertainties in the exposure assessment of microcrystalline wax were discussed in section 2.8.2. According to the guidance provided in the EFSA opinion related to uncertainties in dietary exposure assessment (EFSA, 2007), the following sources of uncertainties have been considered and are summarised below:

Table 9: Qualitative evaluation of influence of uncertainties

Sources of uncertainties	Direction *
Consumption data: different methodologies / representativeness / under reporting / misreporting / no portion size standard	+/-
Extrapolation from food consumption survey of few days to estimate chronic exposure	+
Linkage between reported use levels and food items in the consumption database: uncertainties on which precise types of food the use levels refer.	+/-
Occurrence data: maximum reported use levels within a food category	+
Exposure model: uncertainty in possible national differences in use levels of food categories, data set not fully representative of foods on the EU market, exposure calculations based on the maximum reported use levels (no use of typical use levels when available)	+

* + = uncertainty with potential to cause over-estimation of exposure; - = uncertainty with potential to cause underestimation of exposure.

3 Biological and toxicological data

No new toxicological or biological information was submitted for the re-evaluation of microcrystalline wax following an EFSA public call for data or following calls targeted to relevant professional organisations.

Not all of the original unpublished study reports forming part of the evaluations of the SCF and JECFA were available for this pre-evaluation document (SCF, 1992, 1997) (JECFA, 1993, 1996, 2003). Although not dealing with microcrystalline wax as such some of the studies examined by EFSA (EFSA Panel on Food Additives and Nutrient Sources added to Food (ANS), 2009) in its opinion on high viscosity mineral oil have been included as they are found to add supporting evidence of the safety of the wax.

A literature search was conducted on the most commonly available online databases for toxicological and biological information (PubMed, Toxline, BIOSIS and Web of Science), but no new relevant information was identified on microcrystalline wax.

The present document summarises the relevant toxicological studies on microcrystalline wax evaluated previously by JECFA and SCF, with the latest evaluation in 2003 and 1997 respectively.

In addition the present evaluation also summarises the toxicological studies that were evaluated by the ANS Panel in its opinions on high viscosity mineral oils (EFSA Panel on Food Additives and Nutrient Sources added to Food (ANS), 2009) and on medium viscosity mineral oils with a kinematic viscosity between 8.5-11 mm²/s at 100 °C (EFSA Panel on Contaminants in the Food Chain (CONTAM), 2012).

3.1 Absorption, distribution, metabolism and excretion

Studies on the absorption, distribution, metabolism and elimination of microcrystalline wax (E 905) have not been found in literature.

Albro and Fishbein (1970) in a systematic study examined the relationship between carbon number of hydrocarbons and their absorption. A number of hydrocarbons (saturated, unsaturated, linear, branched-chain and cycloalkanes) were administered by gastric intubation to male CD rats at dose levels of up to 500 mg/kg bw/day and their retention (defined as the dose administered minus the percentage excreted, using squalane as a non-absorbable lipid marker) was examined. A linear relationship was demonstrated: C₁₄ hydrocarbons were absorbed to ca. 60 % while no absorption of hydrocarbons with a carbon number >C₃₀ was observed. This contrasts with the findings of Kolattukudy and Hankin (1966) who observed 25 % absorption of nonacosane fed in rat diets. According to Albro and Fishbein it appears that higher absorption values are obtained when hydrocarbons are fed as an integral part of the diet.

In the Albro and Fishbein (1970) study, the site of absorption of hydrocarbons in the gastrointestinal tract was also examined; it was demonstrated that the small intestine is the major site of absorption and that all areas of the small intestine are similarly efficient in this respect as judged by everted sac experiments. Lymph appeared to be the major route of transport of the ¹⁴C of labelled hydrocarbons fed to rats, though some portal venous transport of ¹⁴C occurred after ¹⁴C-hexadecane feeding, probably as palmitic acid.

Barrowman et al. (1989) reviewed the intestinal absorption and metabolism of the major chemical classes of hydrocarbons (aliphatic and aromatic hydrocarbons of different chain length) showing that these classes of hydrocarbons are well absorbed by the gastrointestinal tract in various species.

JECFA (1993), evaluating the safety of microcrystalline wax and paraffin wax, uses as indirect proof for the non-absorption of waxes, the results of extraction and migration tests that have been performed on waxes and wax-bearing products, which are claimed to indicate that hydrocarbon waxes consumed in the diet are unlikely to be absorbed or metabolized in detectable or significant amounts. For example, gum base waxes do not leach into saliva at a detection limit of 1 mg/kg, and hydrocarbons are not extractable by gastric and pancreatic fluids at a detection limit of 0.5 mg/kg. (van Battum and Rijk, 1979; van den Berg et al., 1989; Kelly and Castle, 1989; Orfan and Bonica, 1989; Woldhuis and Kemp, 1989; Eldred, 1990; Eldred and Modderman, 1990; European Wax Federation, 1990; Orfan, 1990; van den Berg, 1990).

EFSA (EFSA Panel on Food Additives and Nutrient Sources added to Food (ANS), 2009) refers to several studies on the metabolic fate of mineral oils and uses also studies on the metabolism of hydrogenated poly-1-decene, but the Panel considered these studies to be less relevant for the safety evaluation of microcrystalline wax.

Due to the large carbon number of microcrystalline wax (46-50) the Panel considered that these compounds are not likely to be significantly absorbed.

3.2 Toxicological data

3.2.1 Acute oral toxicity

No acute oral toxicity studies were used by JECFA or the SCF and similarly none were identified in the literature search. The Panel considers that given the inertness of microcrystalline the wax and the lack of intestinal absorption it can be assumed that the substance has a very low acute toxicity.

3.2.2 Short-term and subchronic toxicity

Subchronic (90-day) feeding studies on a wide range of white oils and waxes have been conducted in F344 rats (Baldwin et al., 1992; Smith et al., 1996; Scotter et al., 2003; Griffis et al., 2010). In addition, subchronic studies in Long Evans rats and Beagle dogs on four related white mineral oils are available (Smith et al., 1995). In this study two white mineral oils have a kinematic viscosity of respectively 3.1 and 3.5 mm²/s at 100 °C and carbon numbers respectively between C₁₄-C₃₈ and between C₁₆-C₃₄. The other two mineral oils have kinematic viscosities of respectively 31.6 and 65.9 mm²/s at 40 °C (values at 100 °C not given) and carbon numbers respectively between C₂₀-C₃₆ and between C₂₃-C₄₄.

The Panel noted that only the study by Smith et al. (1996) has been carried out with test substances that fall within the specifications set for microcrystalline wax.

In the Smith et al. (1996) 90-day feeding study, the safety of twelve different highly refined petroleum-derived food-grade white oil and waxes was tested in male and female Fisher-344 rats (20 rats/sex/dose for the treated groups; 60 rats/sex/dose for the controls). Only two of the test materials fall within the specifications set forward for the additive E 905, namely a high sulphur microcrystalline wax (HSW) (kinematic viscosity 13.7 mm²/s at 100 °C) and a high melting point microcrystalline wax (HMPW) (kinematic viscosity 15.4 mm²/s at 100 °C). These test materials were mixed in the diet at doses of 20, 200, 2 000 and 20 000 mg/kg premix maintenance diet (equivalent to 1.62, 16.2, 162.0 and 1620 mg/kg bw/day for the male rats and to 1.82, 18.2, 182.0 and 1820 mg/kg bw/day for the female rats). A reversal group (10 rats/sex for the treated groups and 20 rats/sex for the untreated groups, at the highest dose only) was added to assess whether or not effects observed at 90 days would reverse following a 28-day period without treatment. The authors stated that the tests were designed and conducted in compliance with international regulatory guidelines. The results of the study showed that paraffinic waxes with a kinematic viscosity between 3.3 and 6.3 mm²/s and low- to mid-viscosity oils with a kinematic viscosity between 3.1 to below 11 mm²/s, produced biological effects that were inversely related to molecular weight, viscosity and melting point.

The microcrystalline waxes and high viscosity mineral oils (i.e. substances with a kinematic viscosity >11 mm²/s) were found to be without statistically significant biological effects at any of the doses tested.

3.2.3 Genotoxicity

No studies on genotoxicity of microcrystalline wax E 905 have been found in the literature; however, some studies using high viscosity mineral oils are available.

In vitro studies with high viscosity mineral oils

High viscosity white mineral oil (kinematic viscosity >11 at 100 °C; carbon number at 5 % boiling point >28; average molecular weight >500 g/mol) was tested in the modified Ames assay in bacteria. The study was conducted according to OECD 471 Guideline. In this study, the Mutagenicity Index (MI) of the high viscosity oil was 0.1 indicating that there is essentially no induction of gene mutations (Exxon Mobil Biomedical Sciences, 2001).

In vivo studies with high viscosity mineral oils

A series of five paraffinic base stocks (viscosities ranging from <4 mm²/s 100 °C up to 19 mm²/s at 100 °C) and two naphthenic base stocks (viscosities ranging from less <4 mm²/s 100 °C up to 29 mm²/s 100 °C), were tested in the rat bone marrow cytogenetic assay. Male and female Sprague-Dawley rats (5/sex/dose) were given by gavage 500 to 2000 mg/kg bw/day paraffinic base oils and 500 to 5000 mg/kg naphthenic base oils for 5 days. Corn oil control samples and a positive control chemical, (triethylenemelamine) were tested concurrently. The percentage of aberrant bone marrow cells from treated rats were at or the below corn-oil treated control levels, indicating a lack of cytogenicity for these oils. Negative findings in these base stock oils, all of which are less refined than white mineral oils, supports the lack of genotoxicity in white mineral oils (CONCAWE, 1984).

The Panel concurred with the EFSA (EFSA Panel on Food Additives and Nutrient Sources added to Food (ANS), 2009) opinion, considering that these studies suggest that high viscosity (kinematic viscosity ≥ 11 mm²/s at 100 °C) and medium viscosity (kinematic viscosity 8.5 – 11 mm²/s) are neither mutagenic nor genotoxic.

3.2.4 Chronic toxicity and carcinogenicity

No reports on long-term toxicity and carcinogenicity studies with microcrystalline wax E 905 were available in literature.

JECFA (1993) refers to a report by Shubik et al. (1962) on the toxicity petroleum waxes. This study was designed in first place to analyse 32 commercially available petroleum waxes for their polycyclic aromatic hydrocarbons content. However, from these 32 petroleum waxes, five waxes were further tested in a 2-year study in male and female Sprague-Dawley rats. As regards their kinematic viscosity, the five substances can be classified as follows: three have a kinematic viscosity of respectively 14.3, 15.1 and 17.02 mm²/s at 100 °C and two have a kinematic viscosity of 3.71 and 4.08 mm²/s at 100 °C.

The Panel noted that only three of the substances have a kinematic viscosity comparable to that set forward for the microcrystalline wax E 905.

Groups of 50, 6-8 week old male and female Sprague-Dawley rats, were fed diets containing 10 % ground wax (equivalent to 4500 mg/kg bw/day for the male rats and to 5800 mg/kg bw/day for the female rats) for two years. In addition, 157 female and 140 male rats served as untreated controls. Waxes were chosen to represent the range of polycyclic aromatic hydrogen content of waxes in commercial use (i.e. 0-0.64 mg/kg). The rats were observed and weighed every other week, and all gross lesions were recorded. Rats were observed for 2 years, and subsequently until spontaneous death occurred or were killed when dying. Necropsies were performed on all animals and histological examination was performed on all abnormal tissues (no details given on number of organs and which organs were examined).

The results of the study show that survival rates and average weights of experimental groups did not differ significantly from those of control animals, and the incidence of tumours observed in experimental animals was consistently similar to incidences of these tumours in control animals. No pathologic finding attributable to the treatment was observed over the 2-year period or afterwards when observed until death.

According to JECFA, the study indicates that the five waxes, tested via administration at a level of 10 % in the feed of male and female rats, are devoid of carcinogenic or other toxic action by this route of administration.

Trimmer et al. (2004) assessed long-term toxicity and carcinogenicity of two mineral oils: a medium viscosity mineral oil (kinematic medium 8.97 mm²/s at 100 °C) and a high viscosity mineral oil (kinematic viscosity 11 mm²/s at 100 °C) in a 2-year study, conducted in male and female F344 rats.

The Panel considered that, given the chemical nature of the high viscosity mineral oil used in the study, any effect observed with that substance could provide useful information for a read across for the evaluation of microcrystalline wax E 905.

The study was conducted in compliance with OECD guidelines for chronic toxicity/carcinogenicity (OECD 453) and OECD Good Laboratory Practice (GLP) principles. The study consisted of three phases: a carcinogenic phase, a chronic toxicity phase and a recovery phase. In the carcinogenic phase 50 rats/sex/group were used and were sacrificed after a 24-month exposure. In the chronic phase 10 rats/sex/group were used and were sacrificed after a 12-month exposure. In the reversibility phase 20 rats/sex/group used and were sacrificed after 24 months; the rats were first exposed to the treated diet for 12 months followed by and exposure to the control diet for an additional 12 months. In addition, a satellite group of 5 females were included at each dosage level for each phase. These rats were sacrificed at 3, 6, 12, 18 and 24 months for analysis of the tissues for the presence of mineral hydrocarbons.

The high viscosity white mineral was administered in the diet at levels of 60, 120, 240 or 1200 mg/kg bw/day.

The parameters investigated included body weight, food consumption, clinical observations, serum chemistry, haematology, ophthalmology, urine parameters and organ weights, including mesenteric lymph nodes. Analyses for MHC were performed on the liver, kidneys, mesenteric lymph nodes and spleen from female animals. Detailed histopathological examination of 48 tissues, including the liver, spleen, mesenteric and mandibular lymph nodes, Peyer's patches, kidney, bone marrow and male and female reproductive tissues was conducted for all animals in the control group and at the highest dose in the main (2 year) study and at the 12 month sacrifice. From animals at 60, 120 or 240 mg/kg bw/day in the main study, only the lungs, liver, mesenteric lymph nodes, spleen and kidneys were examined; the mesenteric lymph nodes and livers of animals in all groups in the recovery study were also examined. Immune function was not tested, but standard end-points considered to reflect immune function (i.e. total and differential leukocyte count, albumin: globulin ratio, the weights and histological appearance of the thymus, spleen and mesenteric lymph nodes, histopathological evaluation of Peyer's patches and bone-marrow cellularity) were assessed.

Administration of the high viscosity mineral oil did not affect survival. No treatment-related effects were seen on clinical signs, body weight, food consumption, food conversion efficiency, ophthalmic, haematological, serum chemical or urinary parameters, and no treatment related changes were seen at gross necropsy. Dietary administration of the oil was associated with increased weight of mesenteric lymph nodes and increased grade of infiltrating cell histiocytosis; increased incidence and grade of vacuolation of periportal hepatocytes; increased incidence of combined cystic degeneration or angiectasis of the livers from male rats (with no dose-response relationship); and a quantifiable, reversible accumulation of MHCs in the liver to a similar level regardless of dose but dependent on the type of mineral oil. The high viscosity mineral oil was not carcinogenic in this assay.

Treatment-related non-neoplastic lesions in this study were seen in the mesenteric lymph nodes. Infiltrating histiocytes were observed in the mesenteric lymph nodes of all groups, including the controls. With the P70(H) medium viscosity white mineral oil a slight increase in severity score from "minimal" to "mild" was observed in all treatment groups compared to the control group after 24 months of exposure. Similar severity scores were observed in the recovery groups. No significant increase in severity was seen after 12 months of exposure. With the high viscosity mineral oil, no change in severity of infiltrating histiocytes was observed at 12 months. At 24 months, the severity was increased by a statistically significant amount from minimal to mild in all the female groups. Higher but non-statistically significant scores were noted in the males.

A few other non-neoplastic lesions were observed in this study but were not considered to be biologically important, e.g., a dose-related increase in the incidence and grade of vacuolation of periportal hepatocytes was observed in the livers of males in all treated groups after 12 and 24 months

of exposure. In view of the nature and severity of the response, the investigators did not consider the increased grade of vacuolation to be indicative of an adverse effect but rather a marker of prolonged administration of white oil. An increased incidence of combined angiectasis and cystic degeneration (focal sinusoidal dilatation) was also observed in all treated male groups compared to the control group at the 24 month sacrifice. This lesion was of minimal grade, and of similar incidence in all treated groups, and it was, according to the authors, a common finding in F344 rats. An increased incidence of mononuclear cell leukemia was observed in treated females. However, this was not considered treatment-related, as the incidence in treated groups was not dose-related and was within the range for other control female F344 rats.

Although effects were observed in the mesenteric lymph nodes and the liver, even at the lowest dose level, these did not progress to more serious changes and were not detrimental to the life or health status of the rat. These effects are considered to be more an indication of exposure to white oils rather than adverse effects. The No Observed Adverse Effect Level (NOAEL) for both the high viscosity mineral oil in this study was considered to be 1 200 mg/kg bw/day - the highest dose tested.

Based on the results of these studies, EFSA concluded in 2009 that no carcinogenic effects were observed in any of the studies in F344 rats. Non-neoplastic effects were limited to infiltration of histiocytes in mesenteric lymph nodes and oil deposition in the liver. These effects are considered to be an indication of white oil exposure rather than an adverse effect. There were no adverse effects on survival, body weight, food consumption, clinical signs, clinical chemistry, haematology, and no treatment-related changes were seen at gross necropsy.

Further, based on the NOAEL of 1 200 mg/kg bw/day the EFSA, (EFSA, EFSA Panel on Food Additives and Nutrient Sources added to Food (ANS), 2009) derived an ADI of 12 mg/kg bw/day for high viscosity mineral oils.

3.2.5 Reproductive and developmental toxicity

No study on reproductive and developmental toxicity of microcrystalline wax was identified from the literature search.

However, the chronic toxicity studies on various oils, as evaluated by EFSA (EFSA Panel on Food Additives and Nutrient Sources added to Food (ANS), 2009), did not show treatment related histopathological changes on female and male reproductive organs (i.e. ovaries, oviducts, uterus (corpus, cervix), vagina, testes, prostate, or seminal vesicles).

In addition, several reproductive and developmental toxicity studies using low viscosity mineral oils as a solvent control are available (Schreiner et al., 1997; McKee et al., 1987a; McKee et al., 1987b). In 2009, EFSA reviewed these studies and concluded that, although there are no specific reproductive or developmental toxicity studies of high viscosity mineral oils, the studies performed with low viscosity white mineral oils are useful in providing evidence of the lack of reproductive or developmental effects of white mineral oils.

The Panel also considered that the studies, performed with low viscosity white mineral oils, are useful in providing evidence for the lack of reproductive or developmental effects for high viscosity mineral oils and microcrystalline wax.

3.2.6 Other studies

Observations in humans

The SCF (1997) stated that some mineral hydrocarbons have accumulated in humans, but no further details were provided.

JECFA (1995) stated that the limited data on mineral hydrocarbons available from human studies indicate that mineral-oil-induced lesions similar to those seen in rats, have been identified in human tissues. Vacuoles of accumulated mineral oil have been found in the liver, spleen and lymph nodes. Some studies reported the presence of an accompanying inflammatory or granulomatous reaction, while others reported no tissue reaction to the accumulated material. However, none of the studies contained detailed information about the individuals' history of use of liquid paraffin as a medicine or their dietary intake. JECFA therefore concluded that it was not possible to assess the level of intake of mineral oil associated with hydrocarbon accumulation in humans.

EFSA (EFSA Panel on Food Additives and Nutrient Sources added to Food (ANS), 2009) indicated that mineral hydrocarbons have been found visually, chemically and analytically in a number of human tissues at autopsy and biopsy. For decades, the presence of mineral hydrocarbon oils has been observed in human liver, spleen, lymph nodes and other tissues, and it is believed to occur from both natural and man-made sources of mineral hydrocarbons in the diet. Stryker (1941) proposed that deposits of mineral oil in tissues such as the lung, liver, spleen, etc. are associated with histopathological changes in these same tissues. The nomenclature, severity and causality of tissue mineral hydrocarbon and histopathological changes have varied, but there does not appear to be any major controversy in the published literature. These conclusions are essentially supported by various investigators (Boitnott and Margolis, 1966; Rose and Liber, 1966; Boitnott and Margolis, 1970; Dincsoy et al., 1982; Cruickshank, 1984; Cruickshank and Thomas, 1984; Fleming et al., 1998).

The Panel noted that the histopathology findings from tissues have been variously described in the literature. Follicular lipidosis (oil globules in follicles of the spleen), lipogranuloma of the liver, lipophage clusters, hepatic granulomata, histiocytosis, etc., have all been associated with the presence of oil in tissues (Klatskin, 1977) described problems in interpreting hepatic granulomata and indicated that they did not pose a diagnostic problem unless the pathologist was unfamiliar with their appearance. He indicated that mineral oil lipogranulomata persist for years, but do not appear to progress, and that the hepatic lipogranulomata may have no clinical or diagnostic significance. Cruickshank (1984) reported cellular reactions in the lymph nodes that were not considered granulomatous due to the absence of fibroblasts or significant fibrosis. Fleming et al. (1998) compared the lipogranulomas associated with the ingestion of mineral oil reported in humans, to the morphology of the hepatic lesions seen in the Fischer rat studies treated with certain mineral hydrocarbon products. The lesions in humans were not believed to progress to lesions of clinical significance.

The authors concluded that the majority, if not all, of the lesions in the rats were of no significance for humans (Fleming et al., 1998). A generalised conclusion from the literature of human mineral oil tissue deposition and concurrent histopathological changes is that none of the investigations have clearly demonstrated any clinical significance due to the pathological changes and presence of oil.

Special pathology studies

In 2001, a group of medical and veterinary pathologists (Carlton et al., 2001) reviewed published and unpublished reports dealing with studies of various white mineral oils (including high viscosity and Class 1 medium viscosity white oils) and waxes in both F344 and SD rats. They also studied histological slides from both subchronic and chronic studies of certain mineral hydrocarbons (90-day oral study of Low Melting Point Wax (LMPW) (kinematic viscosity 3.3 mm²/s at 100 °C) in female F344 and SD rats; 90-day studies of low viscosity (P15) and medium viscosity (P70) white oil and HMPW (kinematic viscosity 15.4 mm²/s at 100 °C) in male and female F344 rats; and a 24-month study of P70 white oil in male and female F344 rats). These pathologists also reviewed mineral oil-induced alterations in tissues from human patients (liver, hepatic lymph node and spleen). They agreed that certain mineral hydrocarbons produced lesions in the mesenteric lymph nodes and liver of the F344 rat and that these lesions were best described as microgranulomas/granulomas. The lesions were fundamentally similar in both organs, although varying in severity with dose and type of mineral hydrocarbons. They also agreed that hepatic lesions with inflammatory cell infiltration, necrosis, and fibrosis were produced only by feeding of LMPW and that the lesions were confined to F344 rats and

were not found in SD rats. The most severe granulomatous lesions in the mesenteric lymph nodes were found in high dose LPMW-fed F344 rats. The microgranulomas were similar in subchronic and chronic studies. Also, little difference existed between controls and treated F344 rats in the incidence and severity of the lesions after 2 years of feeding P70 white oil. It was agreed that some slight reversibility existed for these lesions, but that the lesions observed in the liver and mesenteric lymph nodes of F344 rats exposed to mineral hydrocarbons, especially the LMPW, were morphologically different from changes observed in the lymph nodes, liver, and spleen of humans that were mineral oil-users. These changes in humans are usually found incidentally in tissues taken at biopsy or autopsy.

The overall conclusions drawn by the pathologists were that granulomatous lesions are produced in rats by mineral hydrocarbon-feeding, especially in the livers of the F344 rat with certain mineral hydrocarbons, but are not found in human tissues. This suggests a heightened and perhaps different type of toxic response in the rat compared to humans. The mineral hydrocarbon-associated alterations in humans are present after a certain age in most, if not all cases, and consist of intra-and-extra-cellular oil droplets with a minimal macrophage (including giant cells) response. These mineral hydrocarbon-induced lesions were considered by the authors as incidental and inconsequential.

4 Discussion

The Panel was not provided with a newly submitted dossier and based its evaluation on previous evaluations, additional literature that became available since then and the data available following a public call for data. The Panel noted that not all original studies on which previous evaluations were based were available for re-evaluation by the Panel.

Microcrystalline wax (E 905) is authorised *quantum satis* as a surface treatment agent on non-chocolate confectionery, chewing gum and decorations, coatings and fillings, except fruit based fillings. It is also permitted as a surface treatment of melons, papaya, mango and avocado.

The substance was evaluated previously by the Scientific Committee on Food (SCF) in 1990 and 1995 (SCF, 1992, 1997) and by the Joint FAO/WHO Expert Committee on Food Additives (JECFA), the latest in 1995, (JECFA, 1995).

Microcrystalline wax (E 905) is a refined mixture of solid, saturated hydrocarbons, mainly branched paraffin, obtained from petroleum. The hydrocarbons are characterised by carbon numbers predominantly in the range between C41-C51, a kinematic viscosity of ≥ 11 mm²/s at 100 °C, an average molecular weight of ≥ 650 g/mol and a carbon number at 5 % distillation point of ≥ 25 .

The Panel noted that, unlike other refined white mineral oils, microcrystalline wax has physico-chemical characteristics very similar to the (liquid) high viscosity minerals oils (kinematic viscosity of >11 mm²/s at 100 °C, average molecular weight of ≥ 500 g/mol and a carbon number at 5 % distillation point of ≥ 28), previously evaluated by EFSA (EFSA Panel on Food Additives and Nutrient Sources added to Food (ANS), 2009).

ADME studies show that gastrointestinal absorption of purified hydrocarbons from different origin is dependent on their physical properties and molecular composition (e.g. chain length) of the constituting hydrocarbons, with no absorption occurring for hydrocarbon fractions with carbon numbers above C32. In addition, less than 5 % of the carbon fraction above C28 is expected to be absorbed (Albro and Fishbein, 1970). Due to the large carbon number of microcrystalline wax (46-50) the Panel considered that these compounds are not significantly absorbed.

The Panel noted that subchronic (90-day) feeding studies on a wide range of white oils and waxes were conducted in F344 rats (Baldwin et al., 1992; Smith et al., 1996; Scotter et al., 2003; Griffis et al., 2010). In addition, subchronic studies in Long Evans rats and Beagle dogs on a related white mineral oil are available (Smith et al, 1995). The studies showed that microcrystalline waxes and high

viscosity mineral oils were found to be without statistically significant biological effects at doses up to 1620 mg/kg bw/day for the male rats and up to 1820 mg/kg bw/day for the female rats.

As regards genotoxicity, no studies on microcrystalline wax E 905 have been found in literature; however, some studies with the closely related high viscosity mineral oils are available. These studies show that high viscosity and also the medium viscosity white mineral oils are neither mutagenic nor genotoxic.

As regards long-term toxicity and carcinogenicity, no reports on microcrystalline wax E 905 were available in literature. However, JECFA (1993) refers to a report by Shubik et al. (1962) on the toxicity of petroleum waxes. In this study, three substances with a kinematic viscosity comparable to that of microcrystalline wax E 905 were tested in a 2-year study in male and female Sprague-Dawley rats. Based on the results of this study, JECFA concluded that the waxes administered at a level of 10 % in the feed (equivalent to 4500 mg/kg bw/day for the male rats and to 5800 mg/kg bw/day for the female rats) were devoid of carcinogenic or other toxic effects.

Trimmer et al. (2004) assessed long-term toxicity and carcinogenicity of two mineral oils: a medium viscosity mineral oil (kinematic viscosity 8.97 mm²/s at 100 °C) and a high viscosity mineral oil (kinematic viscosity 11 mm²/s at 100 °C) in a 2-year study, conducted in male and female F344 rats. The Panel considered that, given the chemical nature of the high viscosity mineral oil used in the study, any effect observed with that substance could provide useful information for a read across for the evaluation of microcrystalline wax E 905. Based on the results of these studies the EFSA in 2009 concluded that no carcinogenic effects were observed in any of the studies in F344 rats. Non-neoplastic effects were limited to infiltration of histiocytes in mesenteric lymph nodes and oil deposition in the liver. These effects are considered to be an indication of white oil exposure rather than an adverse effect. There were no adverse effects on survival, body weight, food consumption, clinical signs, clinical chemistry, haematology, and no treatment-related changes were seen at gross necropsy.

Based on the observed NOAEL of 1200 mg/kg bw/day of the study, EFSA (EFSA Panel on Food Additives and Nutrient Sources added to Food (ANS), 2009) derived an ADI of 12 mg/kg bw/day for high viscosity mineral oils.

The Panel noted that the Scientific Panel on Contaminants in the Food Chain (CONTAM) evaluated the range of mineral oil hydrocarbons that have been detected in food rather than specific products (EFSA Panel on Contaminants in the Food Chain (CONTAM), 2012). The CONTAM Panel also evaluated the results of the Trimmer et al. (2004) study and acknowledged that no hepatic microgranulomas were observed in this study. At the same time the CONTAM Panel stated that it would be prudent to assume that liver microgranulomas observed in studies with various mineral oil saturated hydrocarbons (MOSH) in the Fischer 344 rats could be relevant to humans. This endpoint was therefore used by the CONTAM Panel for the risk assessment of mineral oil saturated hydrocarbons in food.

The CONTAM Panel observed that all mineral oil products accumulated in tissues in a dose- and time-dependent manner with the exception, however, of microcrystalline waxes.

Based on this the CONTAM Panel concluded that with respect to microcrystalline waxes, high-viscosity mineral oils and medium- and low-viscosity class I mineral oils, the existing ADIs are of low priority for revision, although they are based on products with a poor chemical characterisation.

No studies on reproductive and developmental toxicity on microcrystalline wax were available. However, chronic toxicity studies on various mineral oils, as evaluated by EFSA (EFSA Panel on Food Additives and Nutrient Sources added to Food (ANS), 2009), did not show treatment related histopathological changes on female and male reproductive organs (i.e. ovaries, oviducts, uterus (corpus, cervix), vagina, testes, prostate, or seminal vesicles).

In addition, several reproductive and developmental toxicity studies using low viscosity mineral oils as a solvent control are available (Schreiner et al., 1997; McKee et al., 1987a; McKee et al., 1987b). In 2009, EFSA reviewing these studies concluded that, although there are no specific reproductive or developmental toxicity studies of high viscosity mineral oils, the studies performed with low viscosity white mineral oils are useful in providing evidence of the lack of reproductive or developmental effects of white mineral oils.

The Panel also considered that the studies performed with low viscosity white mineral oils are useful in providing evidence for the lack of reproductive or developmental effects for high viscosity mineral oils and microcrystalline wax (E 905).

As regards observations in humans, the SCF (1997) stated that some mineral hydrocarbons have accumulated in humans, but no further details were provided.

JECFA (1995) stated that the limited data on mineral hydrocarbons available from human studies indicate that mineral-oil-induced lesions similar to those seen in rats, have been identified in human tissues, but that it was not possible to assess the level of intake of mineral oil associated with hydrocarbon accumulation in humans.

EFSA (EFSA Panel on Food Additives and Nutrient Sources added to Food (ANS), 2009) indicated that mineral hydrocarbons have been found visually, chemically and analytically in a number of human tissues at autopsy and biopsy. For decades, the presence of mineral hydrocarbon oils has been observed in human liver, spleen, lymph nodes and other tissues, and it is believed to occur from both natural and man-made sources of mineral hydrocarbons in the diet.

The Panel considered that the generalised conclusion, from the literature of human mineral oil tissue deposition and concurrent histopathological changes, is that none of the investigations have clearly demonstrated any clinical significance due to the observed pathological changes and the presence of oil.

In 2001, a group of medical and veterinary pathologists (Carlton et al., 2001) reviewed published and unpublished reports dealing with studies of various white mineral oils (including high viscosity and Class 1 medium viscosity white oils) and waxes in both F344 and SD rats. The overall conclusions drawn by the pathologists were that granulomatous lesions are produced in rats by mineral hydrocarbon-feeding, especially in the livers of the F344 rat with certain mineral hydrocarbons but these lesions are generally not found in human tissues. The pathologists considered that this finding suggests a heightened and perhaps different type of toxic response in the rat compared to humans. The mineral hydrocarbons-associated alterations in humans are present after a certain age in most, if not all cases, and consist of intra-and-extra-cellular oil droplets with a minimal macrophage (including giant cells) response. These mineral hydrocarbon-induced lesions were considered by the authors as incidental and inconsequential.

Exposure estimates derived using the maximum permitted levels (following *quantum satis* rules), showed that the mean intake of microcrystalline wax from use as food additive ranged from 0.3-1.4 mg/kg bw/day in toddlers, 0.5-1.8 mg/kg bw/day in children, 0.2-1.3 mg/kg bw/day in adolescents, 0.03-0.6 mg/kg bw/day in adults and 0.05-0.2 mg/kg bw/day in the elderly. High intake for estimates derived using the maximum permitted levels ranged from 1.8-6.7 mg/kg bw/day in toddlers, 1.1-5.5 mg/kg bw/day in children, 0.5-4.4 mg/kg bw/day in adolescents, 0.3-11 mg/kg bw/day in adults and 0.3-1.8 mg/kg bw/day in the elderly.

For the highest consumers (95th percentile), given the NOAEL of 1 200 mg/kg bw/day for the closely related high viscosity mineral oils, these exposures would result in a margin of safety of approximately 177 for toddlers and of approximately 108 for adults.

CONCLUSIONS

Microcrystalline wax (E 905) is authorised, *quantum satis*, as a surface treatment agent on confectionery, decorations and coatings and chewing gum. It is also permitted as a surface treatment agent on melons, papaya, mango and avocado.

The substance was evaluated previously by the Scientific Committee on Food (SCF) in 1990 and 1995 and by the Joint FAO/WHO Expert Committee on Food Additives (JECFA), the latest in 1995. The JECFA established a group ADI of 20 mg/kg bw/day for mineral oils, paraffins and microcrystalline waxes.

The Panel concluded that there is no concern for genotoxicity for microcrystalline wax (E 905).

The Panel also considered that the available toxicity studies with mineral hydrocarbons, which are closely related from a chemical point of view with microcrystalline waxes, consistently reported no effects of concern associated with the intake of microcrystalline wax.

However, the Panel concluded that since no long-term toxicity and carcinogenicity studies with microcrystalline wax E 905 were available, no ADI could be established.

The Panel also concluded that the conservative exposure estimates to microcrystalline wax (E 905) from its use at maximum permitted level (following *quantum satis* rules), resulted in a sufficient margin of safety compared to the NOAEL identified by the Panel for the closely related high viscosity mineral oils, and therefore the use of microcrystalline wax (E 905) as a food additive with the currently authorised uses would not be of safety concern.

DOCUMENTATION PROVIDED TO EFSA

1. Pre-evaluation document prepared by the Technical University of Denmark (DTU). December 2010.
2. European Wax Federation. Data on waxes permitted as food additives. October 2012.
3. CONCAWE (Conservation of Clean Air and Water in Europe), 2012. Additional data [reply to EFSA letter Ref. CH/KP/mp (2012) out 6980523] submitted by CONCAWE to EFSA on December 27, 2012.

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APPENDIX

A. RULES DEFINED BY THE PANEL TO DEAL WITH QUANTUM SATIS (QS) AUTHORISATION, USAGE DATA OR OBSERVED ANALYTICAL DATA FOR ALL REGULATED FOOD ADDITIVES TO BE RE-EVALUATED

Figure 1: Rules defined by the Panel to deal with usage data or observed analytical data for all regulated food additives to be re-evaluated and procedures for estimating intakes using these rules.



GLOSSARY AND ABBREVIATIONS

ADME	Absorption, Distribution, Metabolism or Excretion
ADI	Acceptable Daily Intake
ANS	Scientific Panel on Food Additives and Nutrient Sources added to Food
CAS	Chemical Abstracts Service
CONTAM	Scientific Panel on Contaminants in the Food Chain
DSC	Differential Scanning Calorimetry
EC	European Commission
EFSA	European Food Safety Authority
EU	European Union
FAO	Food and Agriculture Organization of the United Nations
GC/MS	Gas Chromatography-Mass Spectrometry
GLP	Good Laboratory Practice
GMP	Good Manufacturing Practice
HMPW	High Melting Point microcrystalline Wax
HSW	High Sulphur microcrystalline Wax
JECFA	Joint Expert Committee on Food Additives
LMPW	Low Melting Point Wax
MOSH	Mineral Oil Saturated Hydrocarbons
MPL	Maximum Permitted Level
NOAEL	No-Observed-Adverse-Effect Level
OECD	The Organisation for Economic Co-operation and Development
SCF	Scientific Committee on Food
SML	Specific Migration Limit
TATCA	Trialkoxytricarbaldehyde
THM	Thermally assisted hydrolysis and methylation
WHO	World Health Organization