SCIENTIFIC OPINION

Scientific Opinion on the safety of sucrose esters of fatty acids prepared from vinyl esters of fatty acids and on the extension of use of sucrose esters of fatty acids in flavourings[1]

EFSA Panel on Food Additives and Nutrient Sources added to Food (ANS)[2, 3]

European Food Safety Authority (EFSA), Parma, Italy

ABSTRACT

The Panel on Food Additives and Nutrient Sources added to Food provides a scientific opinion on the safety of sucrose esters of fatty acids produced by a new manufacturing method from sucrose and vinyl esters of fatty acids, and an evaluation of the extension of the use of this additive to flavoured fruit beverages. In 2004 EFSA established a group ADI of 40 mg/kg bw/day for sucrose esters of fatty acids, however this evaluation did not consider sucrose esters of lauric acid. The Panel considers that although the toxicological data on the sucrose ester of lauric acid are limited, they do not give rise to concerns since lauric acid is a natural constituent of a number of foods. The new manufacturing method results in residues of vinyl esters of fatty acids of <10-111 mg/kg and acetaldehyde of 20-48 mg/kg in the sucrose esters of fatty acids. *p*-Methoxyphenol was undetectable. The vinyl portion of the vinyl ester instantly tautomerises to acetaldehyde in the gastrointestinal tract. The Panel concludes that the additional average exposure of 1.4 µg acetaldehyde/kg bw/day resulting from the use of sucrose esters of fatty acids as a food additive would be negligible compared to the exposure from food and endogenous formation and not of safety concern. The Panel also concludes that since *p*-methoxyphenol was undetectable, this potential residue is not of safety concern. The Panel therefore concludes that sucrose esters of fatty acids produced by the new manufacturing method do not present any safety concern provided the overall exposure is within the ADI of 40 mg/kg bw/day. The Panel notes that the current intake of sucrose esters of fatty acids is high and for some individuals above the ADI but that an additional intake from fruit beverages only seems to contribute to a few percent of the ADI.

KEY WORDS

Sucrose monoesters of fatty acids, manufacturing method, vinyl esters of fatty acids, acetaldehyde, E473, food additive, emulsifier, stabiliser

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SUMMARY

Following a request from the European Commission to the European Food Safety Authority (EFSA), the Scientific Panel on Food Additives and Nutrient Sources added to Food (ANS) was asked to deliver a scientific opinion on the safety in use as food additive of sucrose esters of fatty acids produced from an alternative route by reacting sucrose and vinyl esters of fatty acids. In addition the applicant has requested an extension of the use of sucrose esters of fatty acids to allow the additives to be used in flavourings in order to improve solubility of the flavouring in water based beverages.

Sucrose esters of fatty acids (E 473) are authorised for use in a number of foods via Directive 95/2/EC of the European Parliament and Council on food additives other than colours and sweeteners. Sucrose esters of fatty acids were evaluated by the EC Scientific Committee for Food (SCF) in 1992. At that time the SCF established a group ADI of 0-20 mg/kg bw/day (expressed as sucrose monostearate) for sucrose esters of fatty acids and sucroglycerides derived from palm oil, lard and tallow fatty acids. In 2004, in light of new studies which had been provided, EFSA re-examined the safety of these food additives and established a group ADI of 40 mg/kg bw/day for sucrose esters of fatty acids (E 473) and sucroglycerides (E 474). However, sucrose ester of lauric acid were not considered in these evaluations.

Sucrose esters of fatty acids (and sucroglycerides) were evaluated by JECFA in 1992 and 1995. In the later evaluation JECFA allocated a temporary group ADI of 0-20 mg/kg bw/day (WHO, 1995). JECFA made the ADI temporary and requested the results of a well designed and conducted tolerance study for review in 1997 (WHO, 1995). This study was submitted and evaluated by JECFA in 1997 and a full group ADI of 0-30 mg/kg bw was established (WHO, 1998).

In 2009, JECFA established a group ADI of 0-30 mg/kg bw/day for sucrose esters of fatty acids, sucroglycerides and sucrose oligoesters type I and type II (JECFA, 2009).

The present opinion deals with the safety of sucrose esters of fatty acids (monoesters of lauric acid, myristic acid, palmitic acid, and stearic acid) produced by an alternative route by reacting sucrose and vinyl esters of fatty acids. The new manufacturing process results in residue levels of vinyl esters of fatty acid from <10-111 mg/kg, acetaldehyde (formed from the vinyl portion of the vinyl fatty acid esters) levels from 20-48 mg/kg, and not detectable (<0.1 mg/kg) levels of *p*-methoxyphenol (stabiliser) in the sucrose esters of fatty acids manufactured by this process.

In addition, the opinion has considered whether a requested extension of the use of sucrose esters of fatty acids in flavourings in water based beverages will increase the total intake of sucrose esters of fatty acids.

The Panel concludes that these monoesters are extensively hydrolysed in the gastrointestinal tract into the constituent fatty acids and sucrose prior to absorption. The Panel considers that there is no reason to believe that the sucrose monoesters of fatty acids *per se* produced by the new manufacturing process should in any way have biological or toxicological effects different from those of sucrose monoesters of fatty acids produced by the currently-used manufacturing methods.

The Panel notes that lauric acid is a natural dietary constituent found at relatively high concentrations in a number of foods, but that no specific toxicological data are available on the sucrose ester of lauric acid. The Panel considers that although the available data on the toxicological profile of lauric acid are limited, they do not give rise to specific concerns.

The maximum residual level of vinyl esters of fatty acids in sucrose esters of fatty acids, as reported by the petitioner, is around 111 mg/kg. The daily average and high level (95th percentile) exposure of Irish adults to vinyl fatty acid esters from all foodstuffs, in which sucrose esters of fatty acids are permitted, has been estimated by the Panel at 3.2 and 7.1 µg/kg bw/day. Clear soft drinks contribute insignificantly with 0.001 and 0.006 µg/kg bw/day, respectively. For children, exposure is estimated at 5.7 and 13 µg/kg bw/day for the average and high level (95th percentile) intakes, respectively. In

addition, according to the petitioner the vinyl esters of the fatty acids are hydrolysed in the gastrointestinal tract, the vinyl portion of the fatty acid vinyl ester instantly tautomerises to acetaldehyde and can only be detected in food in the form of acetaldehyde. The Panel concludes that the exposure to the vinyl portion of the vinyl esters of fatty acids, if present, will be very low.

The maximum residual level of acetaldehyde in sucrose esters of fatty acids, as reported by the petitioner, is 48.3 mg/kg. The daily average and high level (95th percentile) consumer exposure for Irish adults to acetaldehyde from all foodstuffs in which sucrose esters of fatty acids are permitted has been estimated by the Panel at 1.4 and 3.1 µg/kg bw/day, respectively. For children, exposure is estimated at 2.5 and 5.7 µg/kg bw/day for the average and high level (95th percentile) consumer intakes, respectively. Clear soft drinks among adults contribute marginally with 0.0005 and 0.003 µg/kg bw, respectively. Although the International Agency for Research on Cancer (IARC) recently concluded when assessing alcohol that acetaldehyde associated with alcohol consumption is carcinogenic to humans (Group 1), the Panel noted that the evaluation by IARC was mainly based on experimental data obtained from animals after inhalation exposure and on human epidemiological data considering polymorphisms of the enzymes involved in ethanol metabolism, i.e. alcohol dehydrogenase (ADH) and aldehyde dehydrogenase (ALDH), while in the single available carcinogenicity study in which the animals were orally exposed to acetaldehyde the effects were not dose-related and no clear conclusion could be drawn from this study. In the light that acetaldehyde occurs naturally in many fruits and vegetables and other food categories, e.g. up to 132 mg/kg in orange juice and up to 10 mg/kg in bread, and that it can occur endogenously in blood plasma resulting from metabolism of ethanol and carbohydrates, the Panel considered that an additional average exposure of 1.4 µg/kg bw/day resulting from the use of sucrose esters of fatty acids as food additive would be negligible and not of safety concern.

The Panel notes that the maximum residual level of *p*-methoxyphenol in sucrose esters of fatty acids as reported by the petitioner was <0.1 mg/kg and concludes that any exposure to this impurity resulting from the use of sucrose esters of fatty acids as food additive would be negligible and not of safety concern.

The Panel therefore concludes that sucrose esters of fatty acids produced by the new manufacturing method do not present any safety concern provided the exposure is within the ADI of 40 mg/kg bw/day for sucrose esters of fatty acids and sucroglycerides.

However, the Panel notes that the EC specifications for sucrose esters of fatty acids may need to be amended to include the sucrose ester of lauric acid and to permit supercritical carbon dioxide as an approved solvent to be used for their preparation.

The Panel additionally concludes that an additional use of sucrose esters of fatty acids in fruit beverages only contributes to a few percent of the group ADI of 40 mg/kg bw/day for sucrose esters of fatty acids (E 473) and sucroglycerides (E 474) established by EFSA in 2004. The Panel notes however that Tier 2 intake estimates calculated for Irish consumers give a mean dietary exposure to sucrose esters of fatty acids of 29.1 mg/kg bw/day, and of 64.2 mg/kg bw/day at the 95th percentile, the intake by high level adult consumers being above the ADI.

The Panel notes that the mean dietary exposure of Irish children aged 5-12 years was 51.6 mg/kg bw/day, and 117.3 mg/kg bw/day at the 95th percentile. For both groups (average intake and high level consumers), the estimated intakes were above the ADI.

The Panel noted that in the refined estimates the main contribution to total mean dietary exposure was from fruits (36% and 46% for adults and children, respectively), due to the use of sucrose esters of fatty acids as a surface glazing agent. For a more refined estimate, exact usage data of sucrose esters of fatty acids in fruit would have to be known, or in absence of the former, information on the exact depth of the application layer, the types of fruit which are treated with the glazing agent and the

market share of the glazing agent in comparison to other glazing agents/waxes would have to be provided.

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BACKGROUND AS PROVIDED BY THE EUROPEAN COMMISSION

Sucrose esters of fatty acids were evaluated by the EC Scientific Committee for Food (SCF) in 1992. At that time the SCF established a group ADI of 0-20 mg/kg bw (expressed as sucrose monostearate) for sucrose esters of fatty acids and sucroglycerides derived from palm oil, lard and tallow fatty acids. In 2004, in light of new studies which had been provided, the European Food Safety Authority (EFSA) re-examined the safety of these food additives and established a group ADI of 40 mg/kg bw/day for sucrose esters of fatty acids (E 473) and sucroglycerides (E 474).

Sucrose esters of fatty acids (E 473) are authorised for use in a number of foods via Directive 95/2/EC of the European Parliament and Council on food additives other than colours and sweeteners. The specific purity criteria for sucrose esters are laid down in Commission Directive 2008/84/EC which defines sucrose esters as 'essentially the mono-, di and triesters of sucrose with fatty acids occurring in food fats and oils. They may be prepared from sucrose and methyl and ethyl esters of food fatty acids. The European Commission has now received a request to additionally authorise sucrose esters which are produced from an alternative route by reacting sucrose and vinyl esters of food fatty acids.

In addition the applicant has requested an extension of use of sucrose esters to allow the additives to be used in flavourings in order to improve solubility of the flavouring in water based beverages.

TERMS OF REFERENCE AS PROVIDED BY THE EUROPEAN COMMISSION

In accordance with Article 29 (1) (a) of Regulation (EC) No 178/2002, the European Commission asks the European Food Safety Authority to provide a scientific opinion on the safety of sucrose esters of fatty acids prepared from vinyl esters of fatty acids. In addition, EFSA is asked to issue an opinion on the additional proposed use of sucrose esters of fatty acids in flavourings.

ASSESSMENT

1. Introduction

The present opinion deals with the safety in use as food additive of sucrose esters of fatty acids (lauric acid, myristic acid, palmitic acid and stearic acid) produced by reacting sucrose and vinyl esters of fatty acids. The sucrose esters of all of these fatty acids, other than that of lauric acid, have previously been evaluated by the European Food Safety Authority (EFSA) (EFSA, 2004). In addition to the existing uses for sucrose esters of fatty acids, the applicant is requesting an extended use as an emulsifier to enable flavouring oils to be added to water-based beverages. The opinion therefore also considers the impact of this extended use on the total intake of sucrose esters of fatty acids.

2. Technical data

2.1. Identity of the substance

Sucrose esters of fatty acids consist of a mixture of essentially mono-, di- and tri-esters of sucrose with food fatty acids. The fatty acids form esters with the hydroxyl groups in the sucrose molecule and in principle one sucrose molecule could accommodate a total of eight fatty acid molecules. Depending on the number of esterified fatty acids on a sucrose molecule, commercial products are classified in five groups as shown in Table 1.

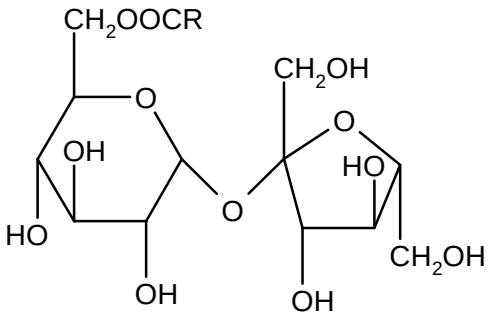
Table 1: Classification of sucrose esters of fatty acids

Group	Composition of esters %	Specifications
Sucroglycerides (E 474)	mono- to tri-esters 40-60% (contain residual mono-, di- and triglycerides)	Commission Directive 2008/84/EC[4]; JECFA, 1997
Sucrose esters of fatty acids (E 473)	mono- to tri-esters ≥ 80%	Commission Directive 2008/84/EC; JECFA, 2007
Sucrose oligoesters type II (INS 473a)	mono- to octa-esters 20-80%, hepta- and octa-esters ≤ 20%, octa-esters ≤ 10%	JECFA, 2009
Sucrose oligoesters type I (INS 473b)	tetra- to octa-esters 20-80%, hepta- and octa-esters ≤ 50%, octa-esters ≤ 20	JECFA, 2009
Olestra (authorised in USA as a fat substitute)	hexa-, hepta- and octa-esters ≥ 97%	FCC VI, 2008

Sucrose esters of fatty acids are non-ionic surfactants consisting of sucrose as a hydrophilic group and fatty acids as lipophilic groups. The lipophilic character increases with an increasing degree of esterification and the nature of the fatty acid in the ester group.

The chemical specifications of the fatty acids in the application specify the content to be not less than 80% of sucrose monolaurate (CAS No. 25339-99-5), sucrose monomyristate (CAS No 27216-47-3), sucrose monopalmitate (CAS No. 26446-38-8), and sucrose monostearate (CAS No. 25168-73-4), with the following structural formula.

[4] Commission Directive 2008/84/EC of 27 August 2008 laying down specific purity criteria on food additives other than colours and sweeteners. Official Journal of the European Communities, L 253, 20.9.2008, p. 107-108



$R = C_nH_{2n+1}$ (n = 11, 13, 15 or 17)

Figure 1: Structural formula of sucrose monoesters

2.2. Specifications

Specifications for sucrose esters of fatty acids and sucroglycerides are provided in the Commission Directive 2008/84/EC laying down specific purity criteria on food additives other than colours and sweeteners. The most recent specifications for sucrose esters of fatty acids (not less than 80% sucrose esters) have been prepared by the Joint FAO/WHO Expert Committee on Food Additives (JECFA) at its 68th meeting in 2007 (JECFA, 2007). According to the applicant, the purity criteria as set out in Directive 2008/84/EC and the specifications set out by JECFA for sucrose esters of fatty acids are achieved when the additive is produced by the new manufacturing process using vinyl esters of fatty acids. However, according to the submitted data for several lots of the commercial products, the manufacturing process results in low levels of vinyl fatty acid residues (from <10 mg/kg to 111.23 mg/kg, limit of quantification (LOQ) between 5 and 10 mg/kg), acetaldehyde (from 17.36 mg/kg to 48.29 mg/kg, LOQ 5 µg/kg) and *p*-methoxyphenol (<100 µg/kg, LOQ 100 µg/kg).

The petitioner proposed to include in the specifications an additional solvent, supercritical carbon dioxide, in the list of approved solvents to be used for the preparation of sucrose esters of fatty acids. The Panel notes that due to the high volatility of supercritical carbon dioxide, residues of this solvent in the final product will be extremely low. The Panel notes that the EC specifications for sucrose esters of fatty acids may need to be amended to include the sucrose ester of lauric acid and to permit supercritical carbon dioxide as an approved solvent to be used for their preparation.

2.3. Manufacturing process

According to the Commission Directive 96/77/EC[5], sucrose esters of fatty acids are either prepared from sucrose and the methyl and ethyl esters of food fatty acids or by extraction from sucroglycerides. No organic solvent other than dimethylsulphoxide, dimethylformamide, ethyl acetate, propane-2-ol, 2-methyl-1-propanol, propylene glycol and methyl ethyl ketone may be used for their preparation.

The new method of manufacturing sucrose esters of fatty acids is different from the existing production method. The starting fatty acid esters used are vinyl esters rather than the traditional methyl and ethyl esters of fatty acids. The initial starting material also contains a stabiliser, *p*-methoxyphenol. This change in manufacturing method results in trace levels of other residual chemicals, e.g. vinyl fatty acid residues, acetaldehyde (formed from the vinyl portion of the vinyl fatty acid esters) and *p*-methoxyphenol, not found in sucrose esters of fatty acids manufactured by the traditional methods. The reaction sequence involves the initial reaction of sucrose with the fatty acid esters followed by a series of purification steps to remove reaction solvents and the fatty acid vinyl ester starting materials.

[5] Commission Directive 96/77/EC of 2 December 1996 laying down specific purity criteria on food additives other than colours and sweeteners. Official Journal of the European Communities, L 339, 30.12.1996, p. 97

The solvent is removed by distillation and the residue mixed with water. The mixture is sprayed into supercritical CO_2 to remove solvent residues.

2.4. Methods of analysis in foods

2.4.1. Impurities in finished products

Residue levels of unreacted vinyl esters have been determined in the finished products by dissolution of the sugar esters in butanol or methanol and direct analysis by Gas Chromatography (GC) using a Flame Ionisation Detector (FID). The LOQs of this method were demonstrated to be 10, 5 and 5 mg/kg for vinyl laurate, vinyl palmitate and vinyl stearate, respectively.

Residue levels of acetaldehyde have been determined by reaction with 2,4-dinitrophenylhydrazine and High Performance Liquid Chromatography (HPLC) determination of the hydrazone product with Ultraviolet (UV) detection. This method was shown to have an LOQ of 0.005 mg/kg.

Residue levels of *p*-methoxyphenol polymerisation inhibitor have been determined by a non-specific activation test based on foaming with a claimed LOQ of 0.1 mg/kg.

2.4.2. Analysis of foods

A method has been published for estimating the total content of E 473 (sucrose esters of fatty acids) in foods (Scotter *et al.,* 2006). After selective solvent extraction of the food to recover the intact esters, they were hydrolysed to liberate sucrose, and then after acidic hydrolysis and silylation, gas chromatography/mass spectroscopy (GC/MS) was used to separately determine the glucose and fructose. The method determines the total sucrose esters content of a food sample and does not attempt to discriminate between individual sucrose esters when present as a mixture in a food sample. The method was applied to the analysis of eight different food types (including bakery wares, sugar confectionery, dairy product, margarine, meat pies and a sauce) and was shown to have a limit of quantification of around 50 mg/kg with an average recovery of 91%. The precision of the method (the relative standard deviation, RSD) averaged 11%.

2.5. Reaction and fate in food

The stability, reaction and fate in food of sucrose esters of fatty acids have been evaluated and described in previous evaluations by the SCF (1992), JECFA (1997) and EFSA (EFSA, 2004, modified on 25 January 2006). When stored at room temperature as dry powder, sucrose esters of fatty acids produced according to the new manufacturing process are expected to be stable for at least 2 years. The applicant is currently conducting a bulk stability test at 25 ºC for sucrose palmitate monoester where interim results after one year indicate an approximate 2% change in monoester content.

Under conditions of use in fruit flavoured beverages that have pHs in the 3.8 to 5.0 range, it is expected that some hydrolysis of the sucrose esters of fatty acids may occur resulting in the formation of small amounts of free sucrose and fatty acids. Potentially, sucrose may also hydrolyse further into glucose and fructose.

Surrogate stability studies have been performed and reported for sucrose monolaurate (Anderson and Polack, 1968). Buffer solutions at various pH values (2.1 to 9.3), containing approximately 10 mM sucrose monolaurate, were heated to 100 ºC for 20 hours and analysed for free lauric acid over time.

Maximum stability was observed between pH 4 to 5 where approximately 6.7% hydrolysis occurred after 20 hours at 100 ºC.

2.6. Case of need and proposed uses

Sucrose esters of fatty acids are approved food additives (E 473) allowed to be used in a wide range of food stuffs. The applicant wishes to market sucrose monoesters of lauric acid, myristic acid, palmitic acid and stearic acid for the currently authorised applications and in addition as emulsifiers in flavour concentrates for use in fruit flavoured beverages.

The new area of use is for solubilisation of essential oils without the need for processing of the oils. Without the addition of an emulsifier the flavour oil would not be soluble in water based beverages resulting in a less even dispersal of the flavouring, an increased exposure to oxygen and reduced organoleptic acceptability. The use of sucrose esters enables clear beverages with improved sensory properties to be obtained.

Table 2 provides an overview of the maximum permitted levels (MPLs) of sucrose esters of fatty acids as established by the Commission Directive 95/2/EC[6] on food additives other than colours and sweeteners.

Table 2: Maximum permitted levels of sucrose esters of fatty acids in foodstuffs

Food group	Maximum permitted level
Beverages (g/L)	
Canned liquid coffee	1
Non-alcoholic aniseed-based drinks	5
Non-alcoholic coconut and almond drinks	5
Spirituous beverages (excluding wine and beer)	5
Dairy-based drinks	5
Foodstuffs (g/kg)	
Heat-treated meat products	5 (on fat)
Fat emulsions for baking purposes	10
Fine bakery wares	10
Beverage whiteners	20
Edible ices	5
Sugar confectionery	5
Desserts	5
Sauces	10
Soups and broths	2
Fresh fruits, surface treatment	*quantum satis*
Powders for the preparation of hot beverages (g/L)	10
Food supplements as defined in Directive 2002/46/EC	*quantum satis*
Chewing gum	10
Cream analogues	5
Sterilised cream and sterilized cream with reduced fat content	5
Food for particular nutritional uses (PARNUTS)	
Infant formula and Follow on Formula for Children in good health containing hydrolysed proteins, peptides or amino acids	120 mg/L
Dietary foods for special medical purposes as defined in Commission Directive 1999/21/EC[7]; dietetic formulae for weight control intended to replace total daily food intake or an individual meal	5 g/kg

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

[7] Commission Directive 1999/21/EC of 25 March 1999 on dietary foods for special medical purposes. Official Journal of the European Communities, L 91, 7. 4. 1999, p. 29

2.7. Information on existing authorisations and evaluations

2.7.1. Sucrose esters of fatty acids

Sucrose esters of fatty acids (E 473) are approved food additives regulated by the European Parliament and Council Directive 95/2/EC[8] on food additives other than colours and sweeteners. They can be used *quantum satis* in food supplements and for surface treatment of fresh fruit and are authorised in a number of other foods via Maximum Permitted Levels (MPLs) varying from 1 to 20 g/kg. E 473 is authorised for use in infant formulae with a MPL of 120 mg/L in products containing hydrolysed proteins, peptides or amino acids. E 473 is authorised *quantum satis* for use as carrier for colours and for fat soluble antioxidants.

Sucrose esters of fatty acids (and sucroglycerides) were evaluated by the SCF in 1992 and a group ADI of 20 mg/kg bw/day (expressed as sucrose monostearate) was established for sucrose esters of fatty acids and sucroglycerides derived from palm oil, lard and tallow fatty acids, providing that specifications would limit the presence of tetra and higher esters to no more than 7%. The basis for establishing the numerical ADI was not specified by the SCF and no report was issued (SCF, 1992).

Sucrose esters of fatty acids (and sucroglycerides) were evaluated by JECFA in 1992 and 1995. In the later evaluation JECFA allocated a temporary group ADI of 0-20 mg/kg bw/day (WHO, 1995). JECFA made the ADI temporary and requested the results of a well designed and conducted tolerance study for review in 1997 (WHO, 1995). This study was submitted and evaluated by JECFA in 1997 and a full group ADI of 0-30 mg/kg bw/day was established (WHO, 1998).

In 2009, JECFA established a group ADI of 0-30 mg/kg bw/day for sucrose esters of fatty acids, sucroglycerides and sucrose oligoesters type I and type II (JECFA, 2009).

The EFSA Scientific Panel on Food Additives, Flavourings, Processing Aids and Materials in Contact with Food (AFC) issued an opinion on sucrose esters of fatty acid (E 473) and sucroglycerides (E 474) in 2004 (modified in 2006), establishing a group ADI of 40 mg/kg bw/day for sucrose esters of fatty acid and sucroglycerides (EFSA, 2004, modified on 25 January 2006).

The sucrose monoesters of lauric acid, palmitic acid and stearic acid, produced by the new manufacturing method, are according to the American Food and Drug Administration (FDA) Generally Recognized as Safe (GRAS) for the use as emulsifiers in flavour concentrates for use in fruit flavoured beverages (Federal Register, 2008).

2.7.2. Acetaldehyde

The Panel has included information on the existing evaluations and authorisations of acetaldehyde, as an impurity in sucrose esters of fatty acids produced by the new manufacturing method. Acetaldehyde originates from the vinyl alcohol portion of the vinyl esters of fatty acids, that is formed via hydrolysis upon reaction with sucrose.

Acetaldehyde [FL-no 05.001] may be used as a flavouring substance according to Commission Decision 1999/217/EC adopting a register of flavouring substances used in or on foodstuffs[9], last amended by Commission Decision 2009/163/EC[10],.

[8] European Parliament and Council Directive No 95/2/EC of 20 February 1995 on food additives other than colours and sweeteners. Official Journal of the European Communities, OJ L 61, 18.3.1995, p. 1

[9] Commission Decision 1999/217/EC of 23 February 1999 adopting a register of flavouring substances used in or on foodstuffs drawn up in application of Regulation (EC) No 2232/96 of the European Parliament and of the Council of 28 October 1996. Official Journal of the European Communities, L 84, 27.3.1999

The use of acetaldehyde as a flavouring substance was evaluated by JECFA in 1997. The Committee estimated that the intakes of acetaldehyde at levels of 9.7 and 11 mg per person per day in the USA and Europe, respectively would not present safety concern (WHO, 1998).

According to Commission Directive 2002/72/EC[11] acetaldehyde may be used as monomer or starting substance in the manufacture of plastic materials and articles intended to come into contact with foodstuffs. Its specific migration limit (SML) in food or in food simulant expressed as total of moiety or substance(s) indicated (SML(T)) is 6 mg/kg (Annex II of Directive 2002/72/EC). SML(T) in this specific case means that the restriction shall not be exceeded by the sum of the migration of the following substances mentioned as Ref. Nos: 10060 [acetaldehyde] and 23920 [Propionic acid, vinyl ester].

The SCF evaluated the use of acetaldehyde in the manufacture of plastic materials and articles intended to come into contact with foodstuffs and derived for acetaldehyde and vinyl propionate a group tolerable daily intake (TDI) of 0.1 mg/kg bw (SCF, 1998).

Acetaldehyde as a chemical was last evaluated by the IARC in 1999 and classified in Group 2B (IARC 1999). In 2009, IARC updated their assessments of several personal habits and household exposures that cause cancer, including consumption of alcoholic beverages and the resulting exposure to acetaldehyde. Based on studies showing a higher risk of alcohol related cancer of oesophagus and head and neck in East-Asian populations that accumulate acetaldehyde formed endogenously and after consumption of alcohol, due to a deficit (genetic polymorphism) in aldehyde dehydrogenase, it was concluded that acetaldehyde associated with alcohol consumption is carcinogenic to humans (Group 1) (IARC, 2009; Secretan *et al*., 2009).

2.8. Exposure

The exposure assessments presented in this opinion cover two aspects: (1) exposure to the sucrose esters of fatty acids themselves, from all permitted uses, including the additional use requested by the petitioner, for solubilisation of essential oils without the need for processing of the oils; (2) exposure to the potential by-products of the new manufacturing process, namely low levels of vinyl fatty acid residues, acetaldehyde (formed from the vinyl portion of the vinyl fatty acid esters) and *p*-methoxyphenol (stabiliser in the vinyl fatty acid starting material).

2.8.1. Exposure assessment for sucrose esters of fatty acids

2.8.1.1. Actual levels of use of sucrose esters of fatty acids

More information on current use levels was made available to the Panel for several food categories in finished products.

Beverages

Sucrose esters of fatty acids are permitted for use in non-alcoholic aniseed-based drinks, non-alcoholic coconut and almond drinks, spirituous beverages (excluding wine and beer), milk based drinks and canned liquid coffee. In France, a survey carried out by AFSSA (Bemrah *et al.*, 2008) on the occurrence of sucrose esters of fatty acids in a number of food categories included 13 samples of alcoholic beverages, none of which were found to contain the additive. For the new proposed application, a maximum usage level of 0.03 g/L in clear/colourless carbonated beverages (non fruit based beverages based on citrus oils, e.g. lemonades) has been indicated by the applicant. This is based on a maximum dosage in the flavouring concentrate of 1.5%. The flavouring is intended to be

[10] Commission Decision 2009/163/EC of 26 February 2009 amending Decision 1999/217/EC as regards the register of flavouring substances used in or on foodstuffs (notified under document number C(2009) 1222). Official Journal of the European Communities, L 55, 27.2.2009, p. 41

[11] Commission Directive 2002/72/EC of 6 August 2002 relating to plastic materials and articles intended to come into contact with foodstuffs. Journal of the European Communities, L 220, 15.8.2002, p. 18

incorporated into the beverage at 0.2%, giving a maximum level of sucrose esters of fatty acids in the beverage of 0.03 g/L.

No actual usage or concentration data was available for any of the remaining beverage categories.

Foodstuffs

For fine bakery wares, the Confederation of the Food and Drink Industries (CIAA) in the EU (2009) reported a range of typical use levels of sucrose esters of fatty acids ranging from 0.4-2.3 g/kg and extreme usage values of 5 g/kg. In France, a survey carried out by the French Food Safety Agency (AFSSA) (Bemrah *et al.*, 2008) on the occurrence of E473 in a number of food categories included 23 samples of fine bakery wares, none of which were found to contain the additive.

For sugar confectionery, the CIAA (2009) reported typical use levels of sucrose esters of fatty acids ranging from 0-5 g/kg.

For foods intended for special medical purposes, the CIAA (2009) reported typical use levels of sucrose esters of fatty acids ranging from 0.03-5 g/kg.

For the categories fat emulsions, beverage whiteners, sauces and edible ices the CIAA (2009) report indicated no use of sucrose esters of fatty acids in these products.

In France, a survey carried out by AFSSA (Bemrah *et al.*, 2008) on the occurrence of E473 in a number of food categories included milk based desserts (27), flavoured desserts (27), powdered hot beverages (16), and soups/broths (23), none of which were found to contain the additive.

Overall, there is little information on actual usage levels of sucrose esters of fatty acids in foods or beverages. However, studies conducted in France (Bemrah *et al.*, 2008) and the UK (Scotter *et al.*, 2006) indicate that application of the additive is very sparse. Also, in Ireland, a database on ingredients (National Food Ingredient Database - NFID) of more than 1800 foodstuffs only identified 4 foodstuffs containing the additive.

In order to refine the exposure assessment for children and adults to sucrose esters of fatty acids, *quantum satis* applications have to be quantified. No usage data or concentration data for the relevant two food groups (surface treatment of fresh fruits, food supplements) were however, available, and levels were estimated according to a number of assumptions.

For the surface treatment of fresh fruits, a level of 18 g/kg has been applied, based on the following assumptions:

The surface area of an apple amounts to approximately 113 cm^2 ($4\pi r^2$, r=3 cm). Assuming an application of 0.3 mm glazing agent onto the surface, the volume ($4/3\pi r^3$) of the glazing agent can be calculated as follows:

Volume of apple including glazing agent – volume of apple excluding glazing agent

$(4/3\times3.14159\times3.03^3) - (4/3\times3.14159\times3^3) = 116.5\text{-}113.1 = 3.4\ cm^3$

According to the applicant, the density of the powder is approximately 600 kg/m^3 (0.6 g/cm^3) and hence the applied amount of sucrose ester of fatty acids amounts to 2 g (per apple) following ($m=\rho\times v$; mass=density×volume). Based on the weight of a medium sized apple of 112 g (EC, 2004), a total concentration of 18 g/kg can be calculated.

The exposure estimates for fruit are very conservative, as it is assumed that all fruits (reported as being consumed including skin) are treated with sucrose esters of fatty acids as a glazing agent and that the calculated concentration based on apples is applicable to all fruits. The application layer of 0.3 mm is also an assumption. For a more refined estimate, exact usage data of sucrose esters of fatty acids in

fruit would have to be known, or in absence of the former, information on the exact thickness of the application layer, the types of fruit which are treated with the glazing agent and the market share of the glazing agent in comparison to other glazing agents/waxes would have to be provided.

Table 3: Maximum reported use levels of sucrose esters of fatty acids in beverages and foodstuffs used for the refined exposure assessment

Beverages	**Maximum reported use level (g/L)**
Non-alcoholic aniseed-based drinks	5
Non-alcoholic coconut and almond drinks	5
Spirituous beverages (excluding wine and beer)	5
Dairy-based drinks	5
Canned liquid coffee	1
Dairy-based drinks	5
Non alcoholic clear/colourless beverages	*0.03**
Foodstuffs	**Maximum reported use level (g/kg)**
Heat-treated meat products	5 (on fat)
Fat emulsions for baking purposes	10
Fine bakery wares	10
Beverage whiteners	20
Edible ices	5
Sugar confectionery	5
Desserts	5
Sauces	10
Soups and broths	2
Fresh fruits, surface treatment**	*18*
Powders for the preparation of hot beverages	10 g/L
Food supplements as defined in Directive 2002/46/EC **	*10*
Chewing gum	10
Cream analogues	5
Sterilised cream and sterilized cream with reduced fat content	5

* According to applicant's information
** Estimated usage in *quantum satis* application

For food supplements, which are marketed either as liquids or in powder form, a concentration of 10 g/kg was assumed based on the similarity of the product to the matrix "powders for the preparation of hot beverages".

To take into account the potential additional exposure due to the new use proposed by the applicant, a maximum level of sucrose ester of 0.03 g/L in accordance with the applicant's information has been allocated to clear/colourless carbonated beverages.

2.8.1.2. Exposure assessment

The Panel agreed to follow the principles of the stepwise approach, which were used in the report of the Scientific Co-operation (SCOOP) Task 4.2, to estimate additives' intakes (EC, 1997). In the tiered

approach, Tier 1 is based on theoretical food consumption data and maximum permitted use levels (MPLs) for additives as permitted by relevant Community legislation. The Second and Third tiers refer to assessment at the level of individual Member States, combining national data on food consumption with the maximum permitted usage levels for the additive (Tier 2) and with its actual usage patterns (Tier 3).

Crude estimates (Budget method)

The dietary exposure to sucrose esters of fatty acids from the MPLs was estimated using the Budget method (Tier 1), which is based on the fact that there is a physiological upper limit to the amount of food and drink (for beverages 100 mL/kg bw and for solids 25 g/kg bw), and thus of food additives, that can be consumed each day. A further assumption is that only a certain proportion of the diet is likely to contain food additives (25%). Full details on the budget method are described in the report of the SCOOP Task 4.2 (EC, 1997).

For adults, the maximum permitted use level of sucrose esters of fatty acids considered for beverages was 5 g/L. The maximum permitted level considered for solid foods was 20 g/kg (Table 2).

The default proportion (25%) of beverages and solid food that could contain the additive was considered adequate. In effect, even though sucrose esters of fatty acids may be used in a variety of solid foods that could represent more than 25% of processed foods, it is unlikely that a person would systematically choose all processed solid foods with the same emulsifier added. In the case of beverages, uses are reported for a limited number of beverages; however, some of these may constitute a significant proportion of liquid intake (i.e., dairy based drinks), with consumer loyalty to a single brand often being high for this category of product. The 25% proportion was therefore considered adequate also for beverages (EC, 1997). This assumes that a typical adult, weighing 60 kg, consumes daily 1.5 litres (it is assumed that only 25% of the daily consumption of 6 litres contain sucrose esters of fatty acids) of beverages and 375 g of solid foods, containing sucrose esters of fatty acids.

For children, the level of sucrose esters of fatty acids considered in beverages was 5 g/L (after exclusion of alcoholic drinks), and in solid food 10 g/kg as children are unlikely to consume beverage whiteners (the food group with the highest permitted level).

The default proportion of 25% in solid foods was considered adequate, however for beverages it was recognised to be inadequate, as the corresponding consumption rate of 375 mL/day could easily be exceeded by young children. This conclusion was derived from UK data on consumption of soft drinks by children aged less than 5 years, where the 97.5th percentile of consumption was between 70 and 80 mL/kg bw/day and a proportion factor of 100 % for beverages was recommended for children in the SCOOP Task 4.2 (EC, 1997). This assumes that a typical 3-year old child, weighing 15 kg, consumes daily 1.5 litres of beverages and 94 g of solid foods.

The theoretical maximum daily exposure for adults and children is summarised in Table 4.

Table 4: Theoretical maximum daily exposure for adults and children

	Daily upper physiological limit of intake per kg/bw		Amount of food/beverage assumed to contain additive (%)		Maximum permitted level of sucrose esters of fatty acids		Theoretical maximum intake of sucrose esters of fatty acids				
	Beverage mL/day	**Food g/day**	**Beverage mL (%)**	**Food g (%)**	**Beverage g/L**	**Food g/kg**	**Beverage g/day**	**Food g/day**	**Beverage mg/kg bw/day**	**Food mg/kg bw/day**	**Total mg/kg bw/day**
Adult (60 kg)	6000	1500	1500 (25)	375 (25)	5	20	7.5	7.5	125	125	250
Child (15 kg)	1500	375	1500 (100)	94 (25)	5	10	7.5	0.94	500	63	563

Combined exposure to sucrose esters of fatty acids from beverages and food (mg/kg bw/day):

Adult: ((6000×0.25)/1000×5)/60 + ((1500×0.25)/1000×20)/60 = 250 mg/kg bw/day

Child: (1500×1)/1000×5)/15 + ((375×0.25)/1000×10))/15 = 563 mg/kg bw/day

It was noted that sucrose esters of fatty acids may be used *quantum satis* in food supplements and for the surface treatment of fresh fruits.

Refined estimates

Refined exposure estimates have been performed for Tier 2 using MPLs presented in Table 2 and maximum practical use levels presented in Table 3 to deal with the specific cases of *quantum satis* authorisation for food supplements and surface treated fruits for children and adult populations. As available quantitative information on usage levels is in line with existing MPLs, no separate Tier 3 calculations were performed as baseline data are identical to those used in Tier 2 calculations.

As sucrose esters of fatty acids are permitted in a wide range of food groups, including very specific foodgroups, exposure estimates have been derived using detailed individual food consumption data available for Irish children 5-12 years old derived from the National Children's Food Survey (NCFS) (IUNA, 2005) and adults 18-65 years old (IUNA, 2001) for Tier 2/Tier 3. This approach was chosen, as no other suitable food consumption data for children were available to perform detailed intake assessment of sucrose esters of fatty acids. For adults, the EFSA Concise European Food Consumption Database, which gives access to aggregate food categories consumed in 15 European countries, was considered to provide insufficient details for the refined assessment of sucrose esters of fatty acids.

Table 5 summarises the anticipated exposure of children and adults to sucrose esters of fatty acids.

Total exposure to sucrose esters of fatty acids was calculated using Creme 2.0 probabilistic software (2005-2009 Creme Software Ltd) and a distributional exposure was derived for both the adult and children population in Ireland.

In the case of sucrose esters of fatty acids, when considering MPLs of use (Tier 2), the mean dietary exposure of Irish children (aged 5-12 years and weighing on average 33 kg) from all foods in which sucrose esters of fatty acids are permitted was 51.6 mg/kg bw/day, and 117.3 mg/kg bw/day at the 95th percentile. The main contributors to the total anticipated exposure to sucrose esters of fatty acids were fruit (46%), fine bakery wares (16.2%), and sauces (6.1%).

Estimates calculated for the Irish adult population give a mean dietary exposure to sucrose esters of fatty acids of 29.1 mg/kg bw/day, and of 64.2 mg/kg bw/day at the 95th percentile. The main contributors to the total anticipated exposure to sucrose esters of fatty acids were fruit (35.8%), fine bakery wares (15.0 %), and hot drinks prepared from powders (11.1%).

As the above assumptions incorporate a great degree of uncertainty, results should be interpreted with the necessary caution.

Refined intake estimates for the new application of sucrose esters of fatty acids to be used in flavourings in water based beverages have been estimated by the Panel based on Irish adult and children population and usage data provided by the applicant. For adults an average intake of 0.01 mg/kg bw/day and a 95th percentile of 0.06 mg/kg bw/day, contributing 0.03% to total mean intake of sucrose esters of fatty acids, were calculated. For children, a mean of 0.04 mg/kg bw/day and high intake (95th percentile) of 0.18 mg/kg bw/day contributing 0.1% to the total mean exposure of sucrose esters of fatty acids, was calculated.

Table 5: Summary of anticipated exposure to sucrose esters of fatty acids using tiered approach (EC, 2001) in children and adult populations

Tier 1. Budget method							
	Adult population				**Children population**		
	250 mg/kg bw/day				**562 mg/kg bw/day**		
Tier 2. Maximum permitted level/ Tier 3. Maximum reported use levels							
	(Total) Irish adult population (18-65)				**(Total) Irish children population (5-12)**		
	Mean	**P95**	**Contribution**		**Mean**	**P95**	**Contribution**
Food Group	**mg/kg bw/day**	**mg/kg bw/day**	**%**		**mg/kg bw/day**	**mg/kg bw/day**	**%**
Beverages (10%) (1)	0.92	5.37	3.2		2.55	11.07	4.9
Beverages clear (2)	0.01	0.06	0.03		0.04	0.18	0.1
Milk Based Beverages	0.06	0.00	0.2		0.62	5.49	1.2
Spirituous Beverages	0.46	2.66	1.6		0.0002	0.00	0.0004
Cream sterilised and UHT	0.003	0.00	0.01		0.001	0.00	0.0019
Desserts	1.48	6.03	5.1		1.97	9.20	3.8
Edible ices	0.50	2.40	1.7		2.41	8.76	4.7
Fat Emulsions	2.58	6.80	8.9		2.62	6.60	5.1
Fine Bakery Ware (5)	4.35	12.87	15.0		8.38	21.01	16.2
Fruit (3)	10.41	40.38	35.8		23.78	80.63	46.1
Fat from Processed meat	0.42	1.18	1.4		0.68	2.06	1.3
Sauces (4)	2.33	7.97	8.0		3.17	10.05	6.1
Soups (4)	0.69	3.06	2.4		0.73	4.45	1.4
Sugar Confectionery	0.10	0.65	0.3		2.02	7.54	3.9
Coffee Whitener	0.001	0.00	0.004		0.00	0.00	0.0
Hot Drink Powders (5)	3.23	3.77	11.1		1.52	9.33	2.9
Supplements (6)	1.50	4.00	5.2		1.00	2.00	1.9
Chewing Gum	0.01	0.00	0.0231		0.09	0.58	0.2
Total	29.1	64.2	100		51.6	117.3	100

(1) Sucrose esters of fatty acids are permitted only in non-alcoholic soft drinks based on aniseed, coconut or almond. No such products were found in the Irish Food Consumption Databases. Therefore and due to the specificity of these food categories, exposure was estimated assuming that 10% of non alcoholic beverages contain sucrose esters of fatty acids (10% presence probability).
(2) Clear beverages (e.g. lemonades, excluding all cola and fruit based beverages) for which a new application of sucrose esters of fatty acids has been applied for (0.03 g/L)
(3) Fruit which was reported as being consumed or used in a recipe as whole (e.g. unpeeled)
(4) Excluding homemade products
(5) As consumed (i.e. made up)
(6) Sucrose esters of fatty acids are permitted in supplements at *quantum satis*. An MPL of 10 g/kg has been assumed based on the comparability of the substrate with powders for the preparation of hot drinks. As consumption of food supplements is reported in units rather than in mass, exposure could not be calculated as part of the overall distributional exposure. The average unit weight of a typical food supplement is 100mg, therefore an additional exposure of 1 g per unit can be assumed. Mean and 95th percentile daily unit intake for adults was 1.5 and 4 units respectively and for children 1 and 2 units respectively. These were added to the distributional exposure figures.

Sucrose esters of fatty acids are authorised for use in infant formulae and follow on formulae for infants in good health with a maximum permitted level of 120 mg/L in products containing hydrolysed

proteins, peptides or amino acids. The maximum levels of use indicated refer to foodstuffs ready for consumption prepared following manufacturers' recommendations.

As no food consumption data are available for infants, exposure has been estimated based on manufacturer's feeding recommendations.

The Panel also noted that the petitioner has submitted data on the sucrose ester of fatty acids in foods for particular nutritional uses (PARNUTS). Based on the Terms of Reference provided to the Panel, this aspect is considered to be outside the scope of this evaluation..

2.8.2. Exposure assessment for vinyl fatty acid esters

The residual levels of vinyl fatty esters in sucrose esters of fatty acids have been measured and reported by the petitioner. The maximum vinyl fatty ester content reported was 111.23 mg/kg.

Exposure to residues of vinyl fatty esters has been calculated based on the estimated intake of sucrose esters of fatty acids from consumption of all food in which sucrose esters of fatty acids are permitted and from clear soft drinks alone (see Table 5, Tier 2 Calculations). Total mean and high intake (95th percentile) of sucrose esters of fatty acids was 29.1 and 64.2 mg/kg bw/day in adults and 51.6 and 117.3 mg/kg bw/day in children respectively. For clear soft drinks alone, mean and high intake (95th percentile) of sucrose esters of fatty acids intake was estimated at 0.01 and 0.06 mg/kg bw/day for adults and 0.04 and 0.18 mg/kg bw/day for children, respectively.

As also shown in Table 6, daily average and high level (95th percentile) exposure of Irish adults to vinyl fatty acid esters from all foodstuffs, in which sucrose esters of fatty acids are permitted, has been estimated at 3.2 and 7.1 µg/kg bw/day. Clear soft drinks contribute marginally with 0.001 and 0.006 µg/kg bw/day respectively.

For children, exposure is estimated at 5.7 and 13 µg/kg bw/day for the average and high level (95th percentile) intake, respectively (see Table 6).

2.8.3. Exposure assessment for acetaldehyde

The residual levels of acetaldehyde in sucrose fatty acid esters have been measured and reported by the petitioner. The maximum acetaldehyde content reported was 48.3 mg/kg.

Exposure to residual acetaldehyde has been calculated based on the estimated intake of sucrose esters of fatty acids from consumption of all food in which sucrose esters of fatty acids are permitted and from clear soft drinks alone (see Table 5, Tier 2 Calculations). Total mean and high intake (95th percentile) of sucrose esters of fatty acids was 29.1 and 64.2 mg/kg bw/day in adults and 51.6 and 117.3 mg/kg bw/day in children respectively. For clear soft drinks alone, mean and high intake (95th percentile) of sucrose esters of fatty acids intake was estimated at 0.01 and 0.06 mg/kg bw/day for adults and 0.04 and 0.18 mg/kg bw/day for children, respectively.

As also shown in Table 6, the daily average and high level (95th percentile) consumer exposure for Irish adults to acetaldehyde from all foodstuffs, in which sucrose esters of fatty acids are permitted, has been estimated by the Panel at 1.4 and 3.1 µg/kg bw/day, respectively. Clear soft drinks contribute marginally with 0.0005 and 0.003 µg/kg bw, respectively.

For children, exposure is estimated at 2.5 and 5.7 µg/kg bw/day for the average and high level (95th percentile) intake, respectively (see Table 6).

Acetaldehyde is reported to occur naturally in a variety of fruits and vegetables and other categories of food. According to the former Committee of Experts on Flavouring Substances of the Council of

Europe, acetaldehyde occurs naturally in grapefruit juice (0.3 – 50 mg/kg), other fruits (up to 10 mg/kg), peas (1.2 - 400 mg/kg), other vegetables (up to 22 mg/kg), bread (4.2 – 9.96 mg/kg), cereals (up to 3.5 mg/kg), yoghurt (0.7 - 76 mg/kg), other milk products (up to 8 mg/kg), wine (white) (7.3 - 142 mg/kg) (CoE, 2000). Acetaldehyde levels of up to 132 and 190 mg/kg were reported for orange juice and grapefruit juice, respectively (Lund *et al.,* 1981). The database "Volatile Compounds in Foods" (TNO, The Netherlands) contains data on the natural occurrence of acetaldehyde in many foods, e.g. carrot (0.45 - 16.9 mg/kg), tomato (0.015 - 9 mg/kg), fig (<1 - 40 mg/kg), grapefruit juice (40 - 230 mg/kg), wheaten bread (7 mg/kg), cheddar cheese (0.1 - 7.5 mg/kg), cheese (various types) (0.4 - 1.4 mg/kg), vinegar (20 - 1060 mg/kg), alcoholic beverages e.g. sherry (100 - 500 mg/kg) (VCF, 2009). For many other foods only qualitative data were given in this database.

2.8.4. Exposure assessment for *p*-methoxyphenol

The residual levels of *p*-methoxyphenol in sucrose fatty acid esters have been measured and reported by the petitioner. The maximum *p*-methoxyphenol content reported was <100 µg/kg.

Exposure to residual *p*-methoxyphenol has been calculated based on the estimated intake of sucrose esters of fatty acids from consumption of all food in which sucrose esters of fatty acids are permitted and from clear soft drinks alone (see Table 5, Tier 2 Calculations). Total mean and high intake (95th percentile) of sucrose esters of fatty acids was 29.1 and 64.2 mg/kg bw/day in adults and 51.3 and 117.3 mg/kg bw/day in children respectively. For clear soft drinks alone, mean and high intake (P95) of sucrose esters of fatty acids intake was estimated at 0.01 and 0.06 mg/kg bw/day for adults and 0.04 and 0.18 mg/kg bw/day for children, respectively.

As also shown in Table 6, daily average and high level (95th percentile) exposure for Irish adults to *p*-methoxyphenol from all foodstuffs, in which sucrose esters of fatty acids are permitted, has been estimated at 2.9 and 6.4 ng/kg bw. Clear soft drinks contribute marginally with 0.001 and 0.006 ng/kg/bw, respectively. For children, exposure is estimated at 5.2 and 11.7 ng/kg bw/day for the average and high level (95th percentile) intake, respectively (see Table 6).

Table 5: Estimated total exposure to residual vinyl fatty acid, acetaldehyde and *p*-methoxyphenol from consumption of foods and beverages containing sucrose esters of fatty acids and from clear soft drinks containing sucrose esters of fatty acids

Residue intake from consumption of food and beverages containing sucrose esters of fatty acids						
		Irish adults			**Irish children**	
		Mean	95th percentile		**Mean**	95th percentile
Vinyl fatty acid esters residue at 111.23 mg/kg	Total diet µg/kg bw/day	3.2	7.1		5.7	13
	Clear soft drinks µg/kg bw/day	0.001	0.006		0.0043	0.0197
Acetaldehyde residue at 48.29 mg/kg	Total diet µg/kg bw/day	1.4	3.1		2.5	5.7
	Clear soft drinks µg/kg bw/day	0.0005	0.003		0.0019	0.0085
***p*-Methoxyphenol residue at 100 µg/kg**	Total diet ng/kg bw/day	2.9	6.4		5.2	11.7
	Clear soft drinks ng/kg bw/day	0.001	0.006		0.0039	0.0177

3. Biological and toxicological data

Since the monoesters of sucrose esters of fatty acids are extensively hydrolysed in the gastrointestinal tract into their constituent fatty acids and sucrose prior to absorption, and there are no specific toxicological data on sucrose monolaurate, the Panel considered that the main issues to be addressed in this opinion, not previously considered by SCF (SCF, 1992) and EFSA (EFSA, 2004, modified on 25 January 2006), were any safety concerns related to lauric acid and the trace levels of residual chemicals (e.g. vinyl fatty acid residues, acetaldehyde and *p*-methoxyphenol), not found in sucrose esters of fatty acids produced by previously accepted methods The following text presents a summary of the toxicological data of the EFSA opinion on sucrose esters of fatty acids (EFSA, 2004, modified on 25 January 2006), and an evaluation of the available toxicological data on lauric acid and the residual impurities.

3.1. Summary of the toxicological data of the EFSA opinion on sucrose esters of fatty acids (EFSA, 2004, modified on 25 January 2006)

The biological and toxicological data on sucrose esters of fatty acids (E 473) have been previously evaluated by the SCF in 1992 (SCF 1992), by JECFA in 1997 (JECFA, 1997), and recently by EFSA in 2006 (EFSA, 2004; modified on 25 January 2006), in the light of new studies on short- and long-term toxicity in experimental animals, toxicokinetic studies in animals and humans, and human tolerance studies.

The test compound administered to rats in these studies (S-570) was a mixture consisting of 28% monoesters, 34% diesters, 21% triesters, and 10% tetra and higher esters, whereas the material given to dogs and humans (S-1170) was a mixture consisting of 57% monoesters, 28% diesters, 10% triesters, and 1% tetra and higher esters, both with a fatty acid composition containing about 70% stearic acid and 30% palmitic acid. These materials were of a slightly different composition than the test mixtures used in the previous evaluations.

Pharmacokinetic studies on sucrose esters of fatty acids in rats, dogs, and humans including studies using radioactively labelled sucrose monopalmitate (SMP), and mono- and distearate (SMS and SDS) (Mitsubishi, 1994 a, b) indicated that these esters were extensively hydrolysed in the gastrointestinal tract into well-known food constituents prior to absorption, that only small amounts of intact monoesters were absorbed, and that incompletely hydrolysed sucrose esters appeared to be excreted in the faeces. There was no evidence of tissue accumulation of the absorbed monoesters. They were completely metabolised to carbon dioxide or integrated into other endogenous constituents.

In agreement with other studies, sucrose esters of fatty acids did not cause significant toxicological effects, including short-term (Mitsubishi, 1991) and long-term toxicity and carcinogenicity (Mitsubishi 1994c; Takeda and Flood, 2002). From a 2-year chronic toxicity/carcinogenicity study in rats a NOAEL could be established at 5% sucrose esters of fatty acids (stearic: palmitic acids = 70:30, with a 10% content of tetra- and higher esters) in the diet, equal to 1970 mg/kg bw/day in males and 2440 mg/kg bw/day in females (Mitsubishi 1994c).

However, concern about a potential laxative effect in humans was raised by results from an inadequate study in which laxation and related abdominal symptoms were reported in humans ingesting doses of sucrose esters of fatty acids exceeding 2 g/day, equivalent to 33 mg/kg bw/day (Mitsubishi, 1994b). In a subsequent well designed and conducted human tolerance study no adverse effects were observed in men and women receiving divided daily doses of 1.5 g sucrose esters of fatty acids in bread for 5 days (equal to 27 mg/kg bw/day in men and 29 mg/kg bw/day in women) (Mitsubishi, 1996). However, this was the only dose level tested, and it was lower than the dose range (33 – 75 mg/kg bw/day) reported to produce gastrointestinal symptoms in the first study.

Taking into account toxicity data in rats with an overall NOAEL of 2000 mg/kg/day, data from a human tolerance study and with the application of an uncertainty factor of 50, a group ADI of 40 mg/kg bw/day was established for sucrose esters of fatty acids (E 473). However, in view of the human tolerance studies, the AFC Panel stressed that at daily doses higher than 2 g/day in adults these substances may cause gastrointestinal symptoms. This ADI covered products containing mono-, di- and triesters with a content of tetra and higher esters of no more than 10%.

3.2. Lauric acid

3.2.1. Absorption, distribution, metabolism and excretion (ADME)

3.2.1.1. *In vitro* studies

Rioux *et al*., (2003) showed that lauric acid is rapidly taken up (95% in 4 hours) in rat liver cells *in vitro* and is metabolised into other fatty acids. Due to a high rate of β-oxidation of lauric acid in the liver cells (39 %), its incorporation into cellular lipids was low (25% in 4 hours) and preferentially into triglycerides. Lauric acid was also rapidly converted to palmitic acid by two successive elongations. Studies using labelled (3H-) lauric acid showed radio labelling of several proteins as well as labelling of its elongation product, myristic acid. The authors concluded that, although rapidly metabolised in liver cells, exogenous lauric acid is a substrate for the acylation of proteins.

Adas *et al*., (1999) investigated the metabolic pathways for various fatty acids including lauric acid in liver microsomes from various mammalian species, i.e. rat, mouse, hamster, gerbil, dog, monkey and human. Cytochrome P450 2E1 was observed to catalyse (ω-1)-hydroxylation across all species and lauric acid ranked as the most efficient substrate (fatty acid) for hydroxylation.

3.2.1.2. Animal studies

A fat balance study in rats (n=3) fed a semipurified diet containing 2.5% of different sucrose esters of fatty acids showed, for example, a digestibility of 98% for the laurate monoester, 92% for the oleic acid, and 87% for the stearic acid monoesters (Ishizuka and Nakamura, 1974). However, currently there are no toxicological studies available on sucrose monolaurate and the safety evaluation therefore has to be based on data on lauric acid.

3.2.1.3. Human studies

11 healthy men were administered diets that contained 39% of energy from fat with 8% of the fat substituted across the diets with *trans* monoenes, oleic acid, saturated fatty acids (lauric, myristic and palmitic) or stearic acid (as triglycerides). Faeces were collected for 7 days following a 14-day adaptation period. Across all diets, stearic acid absorption was lower than that of palmitic acid (94% *vs*. 97%), and that of other fatty acids (lauric, myristic, oleic, linoleic and *trans* fatty acid, for which absorption was greater than 99%) (Baer *et al.*, 2003).

3.2.2. Toxicological data

According to the petitioner, no studies on reproduction and developmental toxicity, immunotoxicity, allergenicity, intolerance or neurotoxicity for lauric acid have been identified.

3.2.2.1. Acute toxicity

Based on a modified acute 3-day toxicity study in mice it was calculated that the lethal dose of lauric acid was >1238 mg/kg bw/day (Schafer and Bowles, 1985).

In another study, lauric acid was administered to 5 rats per group at doses up to 10 g/kg bw (CIR, 1987). One death occurred in the 10 g/kg group, showing at necropsy congested lungs and kidneys. Transient sign of toxicity was observed in rats at doses of 4.64 and 10 g/kg bw (i.e. oily fur, excessive salivation, mucoid diarrhea, discharge from the muzzle and eyes, and depressed righting and placement reflexes).

3.2.2.2. Subchronic toxicity

Fitzhugh *et al.,* (1960) administered lauric acid in the diet to Osborne-Mendel rats. Five male rats were fed lauric acid at 10 % (6000 mg/kg bw/day) of their diet for 18 weeks. There were no observable adverse, clinical or histopathological effects, no mortality, or effects on weight gain.

3.2.2.3. Genotoxicity

Lauric acid (99% pure) was negative in a *Salmonella typhimurium* mutagenicity assay in the test strains TA97, TA98, TA1535 and TA1537 (Zeiger *et al*., 1988). Tests were performed with and without metabolic activation in rat and hamster liver S-9. The test substance was evaluated up to 666 µg/plate.

Renner (1986) investigated the clastogenic potential of methyl esters of various fatty acids including lauric acid in an *in vivo* chromosome aberration study. The esters were administered by gavage at a dose of 100 mg/kg bw to Chinese hamsters (3/sex), followed by a dose of 50 mg/kg bw of the mutagen busulfan. It was reported that lauric acid methyl ester caused a statistically significant ($p<0.001$) decrease in the percentage of aberrant metaphases (excluding gaps), i.e. the percentage was reduced to approximately a third of the positive control (3.2% *vs* 9.4 %).

Based on the data available there is no indication of a genotoxic potential of lauric acid.

3.2.2.4. Chronic toxicity

Lauric acid glycerides (a mixture of mono-, di-, and tri-glycerides of lauric acid) were fed at 0 and 25 % in the diet to 24 Osborne-Mendel rats/group for 2 years (Fitzhugh *et al*., 1960). Apart from an increase in weight gain, the treatment did not cause any adverse effects. Histopathological examination indicated only a slight excess of hepatic cell fatty changes compared to the basal diet controls, but not more than in a similar group of rats fed hydrogenated vegetable oil at the same dose level. The authors concluded that the lauric moiety (from lauric acid or its glycerides) was not toxic when administered by the oral route. The Panel noted that this study was performed before OECD (Organisation for Economic Co-operation and Development) guidelines were established.

The Panel notes that no carcinogenicity studies on lauric acid are available.

3.2.2.5 Other studies

Immune-mediated effects

In vitro studies using the murine monocytic RAW 264.7 and the human embryonic kidney 293-T cell lines transfected with specific plasmids indicate that saturated and polyunsaturated fatty acids reciprocally modulate the activation of Toll-like Receptors 4 (TLR4) and their downstream signalling pathways. Polyunsaturated fatty acids inhibited, whereas lauric acid potentiated, the expression of cyclo-oxygenase 2 (COX 2) and inflammatory cytokines. Lauric acid (75 µM) affects innate immunity and subsequently nuclear factor κB activation, which according to the authors suggest that the risk for tumours and inflammatory diseases could be differently modulated by different fatty acids (Lee *et al*., 2003a). An effect on TLR 2 and 4 was also reported in bone marrow dendritic cells (Wheatherill *et al.*, 2005) and in macrophages (Lee *et al.*, 2003b). Lauric acid modulates TLR4 activation by regulation of the dimerization and recruitment of TLR4 into lipid rafts (Wong *et al.*, 2009).

The Panel noted that these *in vitro* studies used low concentrations of lauric acid and they provide a plausible mechanism for a possible pro-inflammatory effect of lauric acid. However, the biological significance of these data is not clear, and the findings are unlikely to be of major relevance for the safety assessment of sucrose esters of lauric acid as food additives given that lauric acid is a natural dietary constituent at relatively high concentrations in a number of foods

Irritancy

Several studies have according to the petitioner been conducted on the irritant effects of lauric acid (CIR, 1987; Kanaar, 1971). The Panel considered that these are not relevant to the evaluation of sucrose esters of lauric acid as food additives.

Effects on absorption of other compounds

Absorption-promoting activity has been reported for numerous compounds, including various fatty acids, but due to the potential local toxicity it has been difficult to apply them in practical use. This local toxicity seems to be the reason why only sodium caprate is used as an absorption-enhancer in drug products (Yata *et al*., 2001). Amino acids have however been shown to protect epithelial cells from local toxicity caused by sodium laurate, while the enhancement of drug absorption is maintained (Takayama *et al*., 2009; Yata *et al*., 2001). Studies in an *in situ* colon loop model showed that markers of local toxicity in the colon increased upon sodium laurate exposure (10 mM), i.e. phospholipids, total protein and lactate dehydrogenase (Yata *et al*., 2001). Furthermore, sodium laurate seems to increase the intracellular concentration of Ca^{2+} in rat intestinal epithelial cells and to cause a dose-dependent increase in the release of histamine from the cells (Endo *et al.,* 2002).

The Panel noted that these studies using ex vivo colon preparations have shown that lauric acid in the range of 10 mM may cause toxicological effects and increased absorption of marker substances, i.e. phenol red (Yata *et al.,* 2001). A high intake of the sucrose ester of lauric acid (e.g. the high percentile level intake of 64.2 mg/kg bw/day derived from the exposure estimates), could theoretically result in lauric acid concentrations in the gastrointestinal tract comparable to those causing adverse reactions in these studies. The Panel noted however that lauric acid is a natural constituent at relatively high concentrations in, for example, milk (11 mg/kg), butter (43 - 253 mg/kg), blue cheese (1 - 2458 mg/kg) (VCF, 2009), etc. Also, the high level intake of 64.2 mg/kg bw/day sucrose esters would have to be taken in one bolus, and possibly even in one food category, an exposure scenario which the Panel considered is extremely unlikely. The Panel also noted that these effects have only been demonstrated in ex vivo colon preparations, and considers that these findings are of little relevance for the safety assessment of sucrose esters of lauric acid as food additive.

3.3. Acetaldehyde and the vinyl portion of the vinyl fatty acid

Acetaldehyde originates from the vinyl alcohol portion of the vinyl esters of fatty acids, that is formed via hydrolysis upon reaction with sucrose. According to the petitioner, the likelihood of the vinyl portion of residual vinyl ester being present in the food is extremely low. The vinyl ester is unstable and instantly tautomerises to acetaldehyde.

3.3.1. Vinyl fatty acid esters

3.3.1.1. *In vitro* studies

In vitro studies regarding the hydrolysis of vinyl fatty acids, such as vinyl laurate, showed that they are hydrolysed by purified enzymes including guinea pig and human pancreatic lipase (Chahinian *et al.*, 2002). In addition, i*n vitro* incubation with human or rabbit blood led to the complete saponification of the fatty acid ester (Filov, 1959).

3.3.2. Acetaldehyde

There is only one oral carcinogenicity study available on acetaldehyde (Soffritti *et al*., 2002), in which acetaldehyde was administered in drinking water supplied ad libitum to 50 male and 50 female Sprague-Dawley rats beginning at six weeks of age at concentrations of 0, 50, 250, 500, 1500, or 2500

mg/L. Animals were kept under observation until spontaneous death. The study ended with the death of the last animal at 161 weeks of age. According to the authors acetaldehyde was found to produce an increase in total malignant tumours in the treated groups and showed specific carcinogenic effects on various organs and tissues. However, no dose related effects were observed in total malignant tumours and a significant ($p<0.05$) increase could only be shown at 50 mg/L in females and at 2500 mg/L in males and females. In addition, there was no treatment related increase in the number of rats bearing malignant tumours.

This study was evaluated in a draft Risk Assessment Report on vinyl acetate (ECB, 2005): "Soffritti and his colleagues (Soffritti *et al*., 2002) published the results of an oral carcinogenicity study that may correspond to the positive carcinogenicity bioassay that were announced by Maltoni *et al*., (1997). Acetaldehyde was administered to 50 male and 50 female Sprague-Dawley rats for 104 weeks in drinking water at concentrations of 0, 50, 250, 500, 1500, or 2500 mg/L. Increased rates of tumours at several organs were observed in treated groups. However, the effects were not dose-related and no clear conclusion could be drawn from this study.

The Panels agrees with this interpretation.

3.4. *p*-Methoxyphenol

The Panel considered that data on the carcinogenicity of methoxyphenol was the primary issue of concern in relation to its presence in sucrose esters of fatty acids produced by the new manufacturing route. Consequently, data on Absorption, Distribution, Metabolism and Excretion (ADME) and on short term toxicity and other toxicological properties have not been considered further in this opinion. *p*-Methoxyphenol is considered to be non-mutagenic as evaluated by the Ames test (Asakawa *et al*., 1994).

The petitioner reported three studies on the chronic toxicity/carcinogenicity of *p*-methoxyphenol.

In the first study, the chronic toxicity/carcinogenicity of *p*-methoxyphenol was investigated in 30 rats/sex/dose group administered 0 and 2% of the test compound in the diet for 104 weeks (Asakawa *et al*., 1994). Water and food were provided *ad libitum*. Body weights and food and water intake were measured weekly for the first 14 weeks and thereafter once every 4 weeks. Moribund rats and rats that died during the experimental period were autopsied and all surviving rats killed at the end of 104 weeks. All organs were removed for histopathological examination and the liver and kidneys weighed.

Food and water consumption was according to the authors slightly lower after *p*-methoxyphenol administration, and body weights were significantly decreased in treated animals. Survival decreased from week 70 in the treated groups, which was concluded to be caused by perforation of the stomach due to glandular stomach ulceration. The treatment significantly increased the relative weights of the liver and kidneys. The gross morphology of the forestomach showed multiple nodules or masses of ulceration in the mid region, Ulceration was also observed at early stages of the treatment. The incidence of hyperplasia in the forestomach was 100% in both sexes, whereas papillomas were found in 50 and 23% in males and females, respectively. The incidence of squamous cell carcinoma of the forestomach in treated rats was 77 and 20% in male and female rats, respectively, whereas no findings were observed in control males (females not reported). No other organs revealed increased incidences of tumour lesions.

In the second study, the chronic toxicity/carcinogenicity of *p*-methoxyphenol and other antioxidants were investigated in 30-31 male rats/dose group administered 0 and 0.4% of the test compounds in the diet for 104 weeks (Hirose *et al*., 1997). Water and food were provided *ad libitum*. Body weights and food and water intake were measured weekly for the first 14 weeks and thereafter once every 4 weeks. Moribund rats and rats that died during the experimental period were autopsied and all surviving rats

killed at the end of 104 weeks. All organs (complete autopsy) were removed and the liver and kidneys weighed.

Treatment with *p*-methoxyphenol resulted in lower body weight gain but no effects on relative liver and kidney weights. No carcinomas developed. However, incidences of forestomach papillary or nodular hyperplasia (forestomach hyperplasia and papilloma) were increased to 31% in treated rats compared to 4 % in control rats given the basal diet.

In a separate experiment with 13 to 15 rats per group fed diets containing 0, 0.08%, and 0.4% of *p*-methoxyphenol for 28 weeks, following treatment with the tumour initiators diethylnitrosamine (DEN), N-methylnitrosourea (MNU), 1,2-dimethylhydrazine (DMH), N-butyl-N-(4-hydroxybutyl)nitrosamine (BBN), and 2,2´-dihydroxy-di-n-propylnitrosamine (DHPN), there were no effects on body weights or on relative kidney and liver weights. At the low dose of *p*-methoxyphenol there were no effects in the forestomach, whereas at the high dose of *p*-methoxyphenol, in combination with pre-treatment with MNU, the incidence of hyperplasia and papillomas increased to 87% and 60%, respectively, compared to 13% in control rats given the basal diet. It was concluded that *p*-methoxyphenol likely acted as a promoter of MNU (forestomach target)-induced carcinogenicity because of the observed increase in forestomach tumours.

In the third study, the toxicity and promoting activity of *p*-methoxyphenol, subsequent to pre-treatment with N-methyl-N´-nitro-N-nitrosoguanidine (MNNG) were investigated in 10 rats/sex/dose group administered 0, 0.25, 0.5, 1.0, and 2.0 % of the test compound in the diet for 51 weeks (Wada *et al*., 1990). Doses corresponded to 0, 0.09, 0.2, 0.35, and 0.76 g/kg bw/day. Water and food were provided *ad libitum*. Body weights and food consumption were measured every 2 to 4 weeks. Moribund rats and rats that died during the experimental period were autopsied and all surviving rats killed at the end of 51 weeks. The liver and kidneys were weighed and histopathological examination performed on the stomach and oesophagus.

There was a dose related decrease in body weight, but no effects at the lowest dose. At the two lowest doses there were no effects on liver and kidney weights, but at higher doses there was a dose-related increase in tissue weights. Incidences of forestomach papillomas and carcinomas were not significantly different among the groups treated with MNNG and no tumours were observed in animals not receiving this carcinogen. The experiment clearly demonstrated that whereas treatment with 2% *p*-methoxyphenol is associated with toxic damage and cell proliferation in the rat forestomach epithelium, it does not promote tumorigenesis in this organ.

In addition, in a model of azoxymethane-induced colon cancer in rats it has been shown that *p*-methoxyphenol significantly inhibited the invasive adenocarcinoma incidence and multiplicity (Rao *et al.,* 1995).

4. Discussion

The present opinion deals with the safety of sucrose esters of fatty acids that are monoesters of lauric acid, myristic acid, palmitic acid, and stearic acid produced using an alternative route by reacting sucrose and vinyl esters of fatty acids. In addition, the opinion considers whether a requested extension of use of sucrose esters to be used in flavourings in water based beverages will increase the total intake of sucrose esters of fatty acids.

The Panel considered that there is no reason to assume that sucrose monoesters of fatty acids *per se* produced by the new manufacturing process should in any way have biological or toxicological effects different from those of the sucrose monoesters of fatty acids produced by the presently authorised manufacturing methods. However, the SCF and EFSA opinions did not specifically evaluate the sucrose ester of lauric acid.

Based on toxicokinetic studies on sucrose esters of fatty acids (e.g. sucrose monopalmitate and mono- and distearate) in rats, dogs and humans, the Panel concludes that these esters, including the monoesters of lauric and myristic acids, will be extensively hydrolysed in the gastrointestinal tract followed by rapid absorption of its constituent fatty acids and sucrose. The Panel noted that no toxicological information is available in the open literature or from the petitioner on the sucrose ester of lauric acid. However, lauric acid glycerides (a mixture of mono-, di-, and tri-glycerides of lauric acid) were without significant toxic effects when fed at 25 % in the diet to rats for 2 years. In addition, lauric acid (in the form of triglycerides) is a natural dietary constituent with relatively high concentrations in a number of foods. Moreover, although the available data on the toxicological profile of lauric acid itself is limited it does not give rise to specific concerns.

The Panel noted that free lauric acid has produced cytotoxicity in studies using ex vivo colon preparations and possibly had a pro-inflammatory effect in *in vitro* studies using the murine monocytic RAW 264.7 and the human embryonic kidney 293-T cell lines transfected with specific plasmids. However, as these studies may not properly reflect the toxicokinetics of lauric acid following ingestion in sucrose monolaurate, the biological significance of these data is not clear, and the findings are unlikely to be of major relevance for the safety assessment of the sucrose ester of lauric acid as food additives given that lauric acid glyceride is a natural dietary constituent at relatively high concentrations in a number of foods.

The new manufacturing process results in residues of vinyl fatty acid esters and acetaldehyde (formed from the vinyl portion of the vinyl fatty acid esters). *p*-Methoxyphenol is also a potential residue in the sucrose esters of fatty acids produced by the new manufacturing method since it is a stabiliser in the vinyl fatty acid starting material, although it was not detectable in the batches of sucrose esters of fatty acids analysed by the petitioner. The levels of these residues are submitted by the petitioner and the methods with detection limits for these residues in the sucrose ester fatty of acids preparations are described.

The maximum residual level of vinyl fatty acid esters in sucrose esters of fatty acids preparations, as reported by the petitioner, is around 111 mg/kg. The daily average and high level (95th percentile) exposure of Irish adults to vinyl fatty acid esters from all foodstuffs, in which sucrose esters of fatty acids are permitted, has by the Panel been estimated at 3.2 and 7.1 µg/kg bw. Clear soft drinks contribute insignificantly with 0.001 and 0.006 µg/kg bw, respectively. For children, exposure is estimated at 5.7 and 13 µg/kg bw/day for the average and high level (95th percentile) intakes, respectively. In addition, according to the petitioner the vinyl fatty acid esters are hydrolysed in the gastrointestinal tract and the vinyl portion of the fatty acid ester instantly tautomerises to acetaldehyde and can only be detected in food in the form of acetaldehyde. The Panel concludes that the exposure to the vinyl portion of these molecules, if present, will be very low.

The maximum residual level of acetaldehyde in sucrose esters of fatty acids, as reported by the petitioner, is 48.3 mg/kg. The daily average and high level (95th percentile) consumers exposure for Irish adults to acetaldehyde from all foodstuffs, in which sucrose esters of fatty acids are permitted, has been estimated by the Panel at 1.4 and 3.1 µg/kg bw/day, respectively. For children, exposure is estimated at 2.5 and 5.7 µg/kg bw/day for the average and high level (95th percentile) consumer's intakes, respectively. Clear soft drinks among adults contribute marginally with 0.0005 and 0.003 µg/kg bw, respectively.

IARC recently concluded, when assessing alcohol consumption as a personal habit, that acetaldehyde associated with alcohol consumption is carcinogenic to humans (Group 1). However, the Panel noted that the evaluation by IARC was mainly based on experimental data obtained from animals after inhalation exposure and on human epidemiological data, considering polymorphisms of the enzymes involved in ethanol metabolism, i.e. alcohol dehydrogenase (ADH) and aldehyde dehydrogenase (ALDH), while in the single available carcinogenicity study in which the animals were orally exposed to acetaldehyde the effects were not dose-related and no clear conclusion could be drawn from this study. In the light that acetaldehyde occurs naturally in many fruits and vegetables and other food

categories, e.g. up to 132 mg/kg in orange juice and up to 10 mg/kg in bread, and that it can occur endogenously in blood plasma resulting from metabolism of ethanol and carbohydrates, the Panel considered that an additional average exposure of 1.4 µg/kg bw/person/day resulting from the use of sucrose esters of fatty acids as food additive would be negligible and therefore not of safety concern.

The maximum residual levels of *p*-methoxyphenol in sucrose esters of fatty acids as reported by the petitioner was <0.1 mg/kg. The daily average and above average exposure for Irish adults to *p*-methoxyphenol from all foodstuffs, in which sucrose esters of fatty acids are permitted, has been estimated at 2.9 and 6.4 ng/kg bw. For children, exposure is estimated at 5.2 and 11.7 ng/kg bw/day for the average and the above average intake, respectively. Clear soft drinks among adults contribute marginally with 0.001 and 0.006 ng/kg/bw respectively.

Based on results from the toxicity studies in rats it seems that *p*-methoxyphenol administered daily in the diet at doses up 0.25 % (0.09 g/kg bw/day) does not cause effects of concern for human exposure. Squamous cell carcinomas were seen in one chronic toxicity/carcinogenicity study employing a single, high dose level of 2% *p*-methoxyphenol in the diet and in an initiation:promotion study in combination with MNU, but no such tumours were seen in a third study (Wada *et al*., 1990). Additionally, the Panel considered that forestomach tumours in the rat are of no relevance for human exposure, and noted that *p*-methoxyphenol is regarded to be non-mutagenic as evaluated by the Ames test (Asakawa *et al.,* 1994). The Panel therefore concluded that potential residues of *p*-methoxyphenol in sucrose esters of fatty acids were not of concern, and noted that these were undetectable in a number of samples of sucrose esters of fatty acids analysed by the petitioner.

An intake estimate calculated for foodstuffs in the Irish adult population give a mean dietary exposure to sucrose esters of fatty acids of 29.1 mg/kg bw/day, and of 64.2 mg/kg bw/day at the 95th percentile. The mean dietary exposure of Irish children aged 5-12 years was 51.6 mg/kg bw/day, and 117.3 mg/kg bw/day at the 95th percentile. For adults, the main contributors to the total anticipated exposure to sucrose esters of fatty acids were fruit (35.8%), fine bakery wares (15.0%), and hot drinks prepared from powders (11.1%). For children, fruits were also the highest contributor at 46% of total exposure. However, the Panel considered the anticipated exposure estimates for fruit as being very conservative, as it is assumed that all fruit (reported as being consumed including skin) are treated with sucrose esters of fatty acids as a glazing agent and that the calculated concentration based on apple is applicable to all fruits. The application layer of 0.3 mm is also an assumption. Refined intake estimates for the new application of sucrose esters of fatty acids to be used in flavourings in water based beverages have been calculated by the Panel based on Irish adult and children populations and usage data provided by the applicant. For adults an average intake of 0.01 mg/kg bw/day and a 95th percentile of 0.06 mg/kg bw/day, contributing 0.03% to total mean intake of sucrose esters of fatty acids, were calculated. For children, this calculation resulted in a mean of 0.04 mg/kg bw/day and above average of 0.18 mg/kg bw/day contributing to 0.1% of the total mean exposure of sucrose esters of fatty acids. The Panel considers that the minor additional exposure to sucrose esters of fatty acids from fruit flavoured beverages does not have an impact on the total exposures from the current use of sucrose fatty acid esters in food.

The petitioner proposed to include in the specifications an additional solvent, supercritical carbon dioxide, in the list of approved solvents to be used for the preparation of sucrose esters of fatty acids. The Panel notes that due to the high volatility of supercritical carbon dioxide, residues of this solvent in the final product will be extremely low. The Panel notes that the EC specifications for sucrose esters of fatty acids may need to be amended to include the sucrose ester of lauric acid and to permit supercritical carbon dioxide as an approved solvent to be used for their preparation.

CONCLUSIONS

The Panel concludes that the lauric acid ester of sucrose should be included in the group ADI of 40 mg/kg bw/day for sucrose esters of fatty acids (E473) and sucroglycerides (E474).

The Panel notes that the vinyl fatty acid esters, present in only mg/kg levels in the sucrose esters of fatty acids, are hydrolysed in the gastrointestinal tract and the vinyl portion of the fatty acid instantly tautomerises to acetaldehyde. The Panel concludes that any exposure to the vinyl part of the vinyl fatty acid molecule will be very low and not of toxicological concern.

Acetaldehyde is similarly only present in mg/kg levels in the sucrose esters of fatty acids, and the additional average exposure of 1.4 µg acetaldehyde/kg bw/day resulting from the use of sucrose esters of fatty acids as food additive would be negligible compared to the exposure from food and endogenous formation and not of safety concern.

The Panel notes that the maximum residual level of *p*-methoxyphenol in sucrose fatty acid esters as reported by the petitioner was <0.1 mg/kg and concludes that any exposure to this impurity resulting from the use of sucrose esters of fatty acids as food additive would be negligible and not of safety concern.

The Panel therefore concludes that sucrose esters of fatty acids produced by the new manufacturing method do not present any safety concern provided the overall exposure is within the ADI of 40 mg/kg bw/day for sucrose esters of fatty acids and sucroglycerides.

However, the Panel notes that the EC specifications for sucrose esters of fatty acids may need to be amended to include the sucrose ester of lauric acid and to permit supercritical carbon dioxide as an approved solvent to be used for their preparation.

The Panel additionally concludes that an additional use of sucrose esters of fatty acids in fruit beverages would only contribute a few percent to the group ADI of 40 mg/kg bw/day for sucrose esters of fatty acids (E 473) and sucroglycerides (E 474) established by EFSA in 2006.

The Panel notes however that refined estimates calculated for Irish consumers give a mean dietary exposure to sucrose esters of fatty acids of 29.1 mg/kg bw/day, and of 64.2 mg/kg bw/day at the 95th percentile, the intake by high level adult consumers being above the ADI.

The Panel notes that the mean dietary exposure of Irish children aged 5-12 years was 51.6 mg/kg bw/day, and 117.3 mg/kg bw/day at the 95th percentile. For both groups (average intake and high level consumers), the intakes were above the ADI.

The Panel notes that in the refined estimates the main contribution to total mean dietary exposure was from fruits treated with suctose esters of fatty acids as a glazing agent (36% and 46% for adults and children, respectively) for a more refined estimate, exact usage data of sucrose esters of fatty acids in fruit would have to be known, or in absence of the former, information on the exact depth of the application layer, the types of fruit which are treated with the glazing agent and the market share of the glazing agent in comparison to other glazing agents/waxes would have to be provided.

DOCUMENTATION PROVIDED TO EFSA

1. The dossier ADD 2008-014 “Sucrose esters of fatty acids (Lauric acid, Palmitic acid and Stearic acid)” was submitted on July 2008 and updated on the 15 of December 2008. Submitted by Compass Foods Pte, Ltd., Singapore. Additional data submitted October and November 2009.

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GLOSSARY AND ABBREVIATIONS

ADI	Acceptable Daily Intake
ADH	Alcohol dehydrogenase
ADME	Absorption, Distribution, Metabolism and Excretion
AFC	Scientific Panel on Food Additives, Flavourings, Processing Aids and Materials in Contact with Food
AFSSA	French Food Safety Agency (Agence française de sécurité sanitaire des aliments)
ALDH	Aldehyde dehydrogenase
ANS	Scientific Panel on Food Additives and Nutrient Sources added to Food
BBN	N-butyl-N-(4-hydroxybutyl)nitrosamine
CIAA	Confederation of the Food and Drink Industries in the EU
COX	Cyclo-oxygenase
DEN	Diethylnitrosamine
DHPN	2,2´-dihydroxy-di-n-propylnitrosamine
DMH	1,2-dimethylhydrazine
EFSA	European Food Safety Authority
FAO	Food and Agriculture Organisation of the United Nations
FCC	Food Chemicals Codex
FDA	American Food and Drug Administration
FID	Flame Ionisation Detector
GC	Gas Chromatography
GC/MS	Gas chromatography/mass spectroscopy
GRAS	American Food and Drug Administration
HPLC	High performance liquid chromatography
IARC	International Agency for Research on Cancer
JECFA	Joint FAO/WHO Expert Committee on Food Additives
LOQ	Limit of quantification
MPL	Maximum permitted use level
MNNG	N-methyl-N´-nitro-N-nitrosoguanidine

MNU	N-methylnitrosourea
NCFS	National Children's Food Survey
NFID	National Food Ingredient Database
NOAEL	No observed adverse effect level
NOEL	No observed effect level
OECD	Organisation for Economic Co-operation and Development (OECD)
PARNUTS	Foods for particular nutritional purposes
RSD	Relative standard deviation
SCF	Scientific Committee on Food
SCOOP	Scientific Co-operation
SDS	Sistearate
SML	Specific migration limit
SMP	Sucrose monopalmitate
SMS	Monodistearate
TDI	Total daily intake
TNO	Netherlands Organisation for Applied Scientific Research
TLR	Toll-like receptors
UHT	Ultra High Temperature
UV	Ultraviolet
WHO	World Health Organization