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SCIENTIFIC OPINION

Scientific Opinion on the re-evaluation of ascorbyl palmitate (E 304(i)) and ascorbyl stearate (E 304(ii)) as food additives[1]

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

European Food Safety Authority (EFSA), Parma, Italy

ABSTRACT

The EFSA Panel on Food Additives and Nutrient Sources added to Food provides a scientific opinion re-evaluating the safety of ascorbyl palmitate (E 304(i)) and ascorbyl stearate (E 304(ii)) as food additives. The use of these food additives was evaluated by the Joint FAO/WHO Expert Committee on Food Additives and by the Scientific Committee on Food. Biological data on ascorbyl palmitate and stearate are sparse and the safety assessment of them for use as food additives is mainly based on the assumption that ascorbyl palmitate and ascorbyl stearate fully hydrolyse pre-systemically to ascorbic acid and their respective fatty acids. This was supported by an *in vitro* study reporting near-complete hydrolysis of ascorbyl palmitate in simulated intestinal fluid and by human data. The Panel considered that the toxicity of ascorbyl palmitate can be extrapolated from data describing the toxicity of ascorbic acid and palmitic acid and further considered that this assumption is also valid for ascorbyl stearate. The Panel concluded that the available toxicological data were too limited to establish an ADI for ascorbyl palmitate (E 304(i)) or ascorbyl stearate (E 304(ii)). Exposure estimates based on the high percentile for the maximum level exposure scenario range from 0.4 to 10.8 mg/kg bw/day across all population groups and from 0.3 to 9.9 mg/kg bw/day for the refined brand-loyal scenario. Considering the available data, the Panel concluded that there is no safety concern for the use of ascorbyl palmitate (E 304(i)) and ascorbyl stearate (E 304(ii)) as food additives at the reported uses and use levels.

KEY WORDS

ascorbyl palmitate, E 304(i), CAS No 137-66-6, ascorbyl stearate, E 304(ii), CAS No 2340231-5, ascorbyl esters, E 304

[1] On request from European Commission, Question No EFSA-Q-2011-00474 and EFSA-Q-2011-00473, adopted on 27 October 2011.

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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 re-evaluating the safety of ascorbyl palmitate (E 304(i)) and ascorbyl stearate (E 304(ii)) as food additives.

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

Fatty acid esters of ascorbic acid (E 304) are authorised in the European Union (EU) as food additives in accordance with Annex II and Annex III of Regulation (EC) No 1333/2008 and specific purity criteria have been defined in the Commission Regulation (EU) No 231/2012 for ascorbyl palmitate (E 304(i)) and ascorbyl stearate (E 304(ii))

Ascorbyl palmitate was considered acceptable for food additive use by the Scientific Committee on Food (SCF, 1989b). The Joint Food and Agriculture Organization of the United Nations (FAO)/World Health Organization (WHO) Expert Committee on Food Additives (JECFA) evaluated ascorbyl palmitate and ascorbyl stearate as food additives in 1973 and established an acceptable daily intake (ADI) of 1.25 mg/kg bw/day for ascorbyl palmitate or ascorbyl stearate or the sum of both (JECFA, 1974).

Based on the confidential information on the maximum levels for the residual solvents in ascorbyl palmitate, as provided by industry, the Panel considered that there is not a safety concern. However, the Panel considered that the level of residual solvents used in the manufacturing process should be kept under the levels that could raise a safety concern. Therefore, the Panel considered that limits for residual solvents used in the manufacturing process should be included in the EC specifications.

The Panel also considered that the maximum limits for lead, mercury and arsenic in the EC specification for ascorbyl palmitate (E 304(i)) and ascorbyl stearate (E 304(ii)) should be revised in order to ensure that ascorbyl palmitate (E 304(i)) and ascorbyl stearate (E 304(ii)) as food additives will not be a significant source of exposure to these toxic elements in food. In addition, the Panel considered that the current European Inventory of Existing Commercial chemical Substances (EINECS) Number in the EC specifications for ascorbyl stearate (E 304(ii)) should be substituted by 234-231-5

Absorption, distribution, metabolism and excretion (ADME) data on ascorbyl palmitate (E 304(i)) and ascorbyl stearate (E 304(ii)) are sparse and the safety assessment for their use as food additives is based on the assumption that ascorbyl palmitate and ascorbyl stearate fully hydrolyse pre-systemically to ascorbic acid and their respective fatty acids. This assumption was supported by an *in vitro* study reporting near-complete hydrolysis of ascorbyl palmitate in simulated intestinal fluid (Beck et al., 2014) and by human data. Additional information can be gathered by read-across between palmitate and stearate. Both compounds are saturated fatty acids of the same structure, with stearate having 18 C-atoms and palmitate having 16 C-atoms. In the first catabolic step, stearate is metabolised to palmitate and undergoes the same catabolic pathway of β-oxidation as other endogenous fatty acids. Therefore, the Panel considered that the toxicity of ascorbyl palmitate can be extrapolated from the data describing the toxicity of ascorbic acid and palmitic acid. The Panel further considered that this assumption is also valid for ascorbyl stearate. The Panel noted that it cannot exclude the possibility that some absorption of the parent compounds may take place before hydrolysis in the gut. However, the Panel considered that any absorbed intact ascorbyl palmitate or ascorbyl stearate would be completely hydrolysed in the hepatic portal plasma and/or liver and therefore would not be systemically available.

Ascorbyl palmitate and stearate have a very low acute toxicity. The only chronic and carcinogenicity studiy available was performed on ascorbyl palmitate. The Panel considered the study not adequate for the re-evaluation of ascorbyl palmitate as a food additive because the group sizes were too small, only one sex was used, histopathological examination was limited and only two dose levels were tested.

There was only one *in vitro* mutagenicity study on ascorbyl palmitate available, in which ascorbyl palmitate did not show any mutagenic activity. No genotoxicity studies were available for ascorbyl stearate. No studies on reproductive and developmental toxicity on ascorbyl palmitate or ascorbyl stearate were available.

Maximum levels of the available use levels provided by industry were used to provide a conservative combined exposure estimate scenario—*maximum level exposure assessment* scenario—because it was not possible to carry out an exposure assessment scenario based on maximum permitted levels (MPLs) as set out in the EU legislation, as, for most of the food categories, these food additives are authorised according to *quantum satis* (*QS*). In addition, it is considered unlikely that more than one antioxidant is used in any food items, for all scenarios, the Panel estimated the combined exposure to ascorbyl palmitate (E 304(i)) and ascorbyl stearate (E 304(ii)) using the highest concentration reported from any of them for each food category. Mean estimates ranged from 0.2 to 3.2 mg/kg body weight (bw)/day across all population groups. Estimates based on the high percentile ranged from 0.4 to 10.8 mg/kg bw/day across all population groups.

Based on the available dataset, the Panel calculated combined exposure estimates for fatty acid esters of ascorbic acid (E 304) following two refined exposure scenarios based on different assumptions: a *brand-loyal consumer scenario*, where it is assumed that a consumer is exposed over a long time to the food additive present at the maximum reported use levels for one food category and at the mean levels for the remaining food categories; and a *non-brand-loyal scenario*, where it is assumed that a consumer is exposed over a long time to the food additive present at the mean reported use levels in all food. The high exposure to fatty acid esters of ascorbic acid (E 304) ranged from 0.3 mg/kg bw/day in adults and the elderly to 9.9 mg/kg bw/day in children considering the *brand-loyal consumer scenario*.

The Panel noted that intake of palmitic and stearic acids from the use of ascorbyl palmitate and ascorbyl stearate as food additives represents only a limited fraction (around 3 %) of their daily intake from the regular diet.

The Panel concluded that the available toxicological data were too limited to establish an ADI for ascorbyl palmitate (E 304(i)) or ascorbyl stearate (E 304(ii)). The Panel also concluded that ascorbyl palmitate and ascorbyl stearate are hydrolysed and not systemically available and therefore their toxicity can be extrapolated from the data available for ascorbic acid, palmitic acid and stearic acid.

Considering the available data, the Panel concluded that there is no safety concern for the use of ascorbyl palmitate (E 304(i)) and ascorbyl stearate (E 304(ii)) as food additives at the reported uses and use levels.

The Panel recommended that:

- limits for residual solvents should be included in the EC specifications;
- the maximum limits for the impurities of toxic elements (lead, mercury and arsenic) in the EC specification for ascorbyl palmitate (E 304(i)) and ascorbyl stearate (E 304(ii)) should be revised in order to ensure that ascorbyl palmitate (E 304(i)) and ascorbyl stearate (E 304(ii)) as food additives will not be a significant source of exposure to those toxic elements in food;
- the current EINECS Number in the EC specifications for ascorbyl stearate (E 304(ii)) should be substituted by 234-231-5.

TABLE OF CONTENTS

BACKGROUND AS PROVIDED BY AS PROVIDED BY THE EUROPEAN COMMISSION

Regulation (EC) No 1333/2008 of the European Parliament and of the Council on food additives requires that food additives are subject to a safety evaluation by the European Food Safety Authority (EFSA) before they are permitted for use in the European Union. In addition, it is foreseen that food additives must be kept under continuous observation and must be re-evaluated by EFSA.

For this purpose, a programme for the re-evaluation of food additives that were already permitted in the European Union before 20 January 2009 has been set up under the Regulation (EU) No 257/2010[4]. This Regulation also foresees that food additives are re-evaluated whenever necessary in light of changing conditions of use and new scientific information. For efficiency and practical purposes, the re-evaluation should, as far as possible, be conducted by group of food additives according to the main functional class to which they belong.

The order of priorities for the re-evaluation of the currently approved food additives should be set on the basis of the following criteria: the time since the last evaluation of a food additive by the Scientific Committee on Food (SCF) or by EFSA, the availability of new scientific evidence, the extent of use of a food additive in food and the human exposure to the food additive taking also into account the outcome of the Report from the Commission on Dietary Food Additive Intake in the EU[5] of 2001. The report "Food additives in Europe 2000[6]" submitted by the Nordic Council of Ministers to the Commission, provides additional information for the prioritisation of additives for re-evaluation. As colours were among the first additives to be evaluated, these food additives should be re-evaluated with a highest priority.

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

TERMS OF REFERENCE AS PROVIDED BY THE EUROPEAN COMMISSION

The Commission asks the European Food Safety Authority to re-evaluate the safety of food additives already permitted in the Union before 2009 and to issue scientific opinions on these additives, taking especially into account the priorities, procedures and deadlines that are enshrined in the Regulation (EU) No 257/2010 of 25 March 2010 setting up a programme for the re-evaluation of approved food additives in accordance with the Regulation (EC) No 1333/2008[7] of the European Parliament and of the Council on food additives.

INTERPRETATION OF THE TERMS OF REFERENCE AS PROVIDED BY THE EUROPEAN COMMISSION

The ANS Panel described its risk assessment paradigm in its Guidance for submission for food additive evaluations in 2012 (EFSA ANS Panel, 2012). This Guidance states, that in carrying out its risk assessments, the Panel sought to define a health-based guidance value e.g. an Acceptable Daily Intake (ADI) (IPCS, 2004) applicable to the general population. According to the definition above, the ADI as established for the general population does not apply to infants below 12 weeks of age (JECFA, 1978; SCF, 1998b). In this context, the re-evaluation of the use of food additives, such as thickening agents and certain emulsifiers, in food for infants below 12 weeks represents a special case for which specific recommendations were given by the Joint FAO/WHO Expert Committee on Food

[4] Commission Regulation (EU) No 257/2010 of 25 March 2010 setting up a programme for the re-evaluation of approved food additives in accordance with Regulation (EC) No 1333/2008 of the European Parliament and of the Council on food additives. OJ L 80, 26.3.2010, p. 19–27.

[5] COM(2001) 542 final.

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

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

Additives (JECFA) (JECFA, 1972, 1978) and by the SCF (SCF, 1996, 1998). The Panel endorsed these recommendations.

In the current EU legislation (Annex II of Regulation (EC) No 1333/2008) use levels of additives in food for infants under the age of 12 weeks are included in categories 13.1.1, 13.1.5.1 and 13.1.5.2[8]. The Panel considers that these uses would require a specific risk assessment in line with the recommendations given by JECFA and SCF and endorsed by the Panel by the Panel in its current Guidance for submission for food additives evaluations (EFSA ANS Panel, 2012). Therefore, a risk assessment as for the general population is not considered to be applicable for infants under the age of 12 weeks and will be performed separately.

[8] Food of category 13.1.1: Infant formulae as defined by Directive 2006/141/EC; Food of category 13.1.5.1: Dietary foods for infants for special medical purposes and special formulae for infants. This interpretation also applies to those food additives in food category 13.1.5.2 (Dietary foods for babies and young children for special medical purposes as defined in Directive 1999/21/EC) for which exceptional uses in food for infants under the age of 12 weeks are indicated.

ASSESSMENT

1. Introduction

The present opinion deals with the re-evaluation of the safety of ascorbyl palmitate (E 304(i)) and ascorbyl stearate (E 304(ii)) as food additives.

According to Annex II and Annex III of Regulation (EC) No 1333/2008,[9] fatty acid esters of ascorbic acid (E 304) are authorised as food additives in the European Union (EU). Ascorbyl palmitate was previously considered on several occasions by the EU Scientific Committee on Food (SCF) in 1983, 1989, 1991, 1997 and 1998 (SCF, 1983, 1989a,b, 1991, 1997, 1998a). The Joint Food and Agriculture Organization of the United Nations (FAO)/World Health Organization (WHO) Expert Committee on Food Additives (JECFA) evaluated ascorbyl palmitate and ascorbyl stearate as food additives in 1973 (JECFA, 1974).

The Panel on Food Additives and Nutrient Sources added to Food (ANS) was not provided with a newly submitted dossier and based its evaluation on previous evaluations, additional literature that became available since the previous evaluations and the data available following EFSA public calls for scientific data[10,11,12].

2. Technical data

2.1. Identity of the substance

2.1.1. Ascorbyl palmitate (E 304(i))

Ascorbyl palmitate (E 304(i)) is a synthetic organic compound. It is an ester formed from the reaction of the primary alcohol group of ascorbic acid (vitamin C) and the carboxylic group of palmitic acid. It has the molecular formula $C_{22}H_{38}O_7$ and the molecular weight 414.55 g/mol (from which 42 % corresponds to the ascorbic acid moiety). It has the Chemical Abstracts Service (CAS) Registry Number 137-66-6 and the European Inventory of Existing Commercial chemical Substances (EINECS) Number 205-305-4. Its chemical name is [(*2S*)-2-[(*2R*)-3,4-dihydroxy-5-oxo-2*H*-furan-2-yl]-2-hydroxy-ethyl]hexadecanoate. Synonyms include ascorbyl monopalmitate, L-ascorbic acid 6-palmitate, L-ascorbic acid 6-hexadecanoate, 2,3-didehydro-L-threo-hexono-1,4-lactone-6-palmitate, 6-palmityl-L-ascorbic acid, 6-*O*-palmitoyl-L-ascorbic acid, 6-monopalmitoyl-L-ascorbate and many others (SciFinder software[13]).

Ascorbyl palmitate is a white or yellowish-white powder with a citrus-like odour, which is very slightly soluble in water and freely soluble in ethanol (JECFA, 2006; Commission Regulation (EU) No 231/2012[14]). The structural formula can be seen in Figure 1.

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

[10] Call for scientific data on food additives permitted in the EU and belonging to the functional classes of preservatives and antioxidants. Published: 23 November 2009. Available from: http://www.efsa.europa.eu/en/dataclosed/call/ans091123a.htm

[11] Call for food additives usages level and/or concentration data in food and beverages intended to human consumption. Published: 27 March 2013. Available online: http://www.efsa.europa.eu/en/dataclosed/call/130327.htm

[12] Call for scientific data on selected food additives permitted in the EU—Extended deadline: 1 September 2014 (batch A), 1 November 2014 (batch B) Available online: http://www.efsa.europa.eu/en/dataclosed/call/140324.htm

[13] SciFinder® the choice for chemistry researchTM.

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

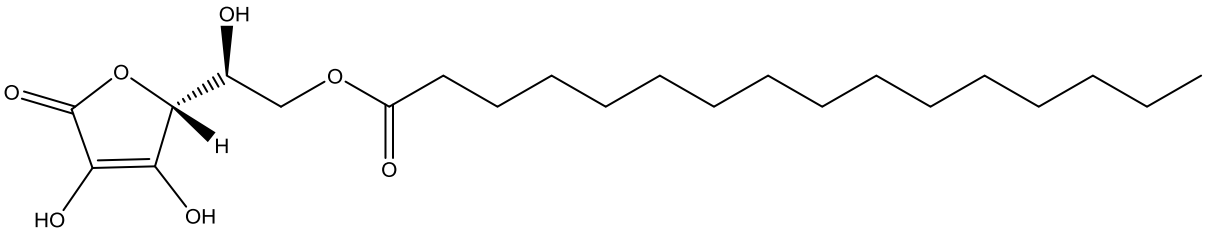

Figure 1: Structural formula of ascorbyl palmitate.

2.1.2. Ascorbyl stearate (E 304(ii))

Ascorbyl stearate (E 304(ii)) is a synthetic organic compound. It is an ester formed from the reaction of the primary alcohol group of ascorbic acid (vitamin C) and the carboxylic group of stearic acid. It has the molecular formula $C_{24}H_{42}O_7$ and a molecular weight of 442.6 g/mol (from which 40 % corresponds to the ascorbic acid moiety). According to Commission Regulation (EU) No 231/2012 the EINECS Number is 246-944-9, which corresponds to the CAS Registry Number 25395-66-8 (EC Inventory, online); however, the CAS Number 25395-66-8 corresponds to ascorbyl stearate ester where the position of the ester is not defined (SciFinder software). The CAS Number 10605-09-1 corresponds to the EINECS Number 234-231-5, which is 6-(stearoyloxy)-L-ascorbic acid (EC Inventory, online). Therefore, the Panel considered that the EINECS Number in the EC specifications should be substituted by 234-231-5.

Its chemical name is [(*2S*)-2-[(*2R*)-3,4-dihydroxy-5-oxo-2*H*-furan-2-yl]-2-hydroxy-ethyl] octadecanoate. Synonyms include L-ascorbic acid monostearate, L-ascorbic acid 6-stearate, L-ascorbic acid 6-octadecanoate, 6-*O*-stearylascorbic acid, among others (SciFinder software).

Ascorbyl stearate is a white or yellowish-white powder with a citrus-like odour, which is insoluble in water and soluble in ethanol (JECFA 2006; Commission Regulation (EU) No 231/2012). The chemical structure can be seen in Figure 2.

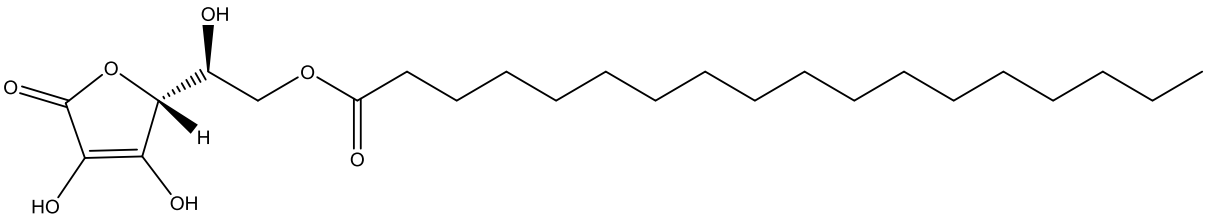

Figure 2: Structural formula of ascorbyl stearate

2.2. Specifications

Specifications for ascorbyl palmitate (E 304(i)) and ascorbyl stearate (E 304(ii)) have been defined in Commission Regulation (EU) No 231/2012 and by JECFA (2006) (Tables 1 and 2).

Table 1: Specifications established for ascorbyl palmitate (E 304i) according to Commission Regulation (EU) No 231/2012 and JECFA (2006)

	Commission Regulation (EU) No 231/2012	**JECFA (2006)**
Definition		
Chemical names	Ascorbyl palmitate; L-ascorbyl palmitate; 2,3-didehydro-L-threo-hexono-1,4-lactone-6-palmitate; 6-palmitoyl-3-keto-L-gulofuranolactone	Ascorbyl palmitate; L-ascorbyl palmitate; 2,3-didehydro-L-threo-hexono-1,4-lactone-6-palmitate; 6-palmitoyl-3-keto-L-gulofuranolactone
CAS number	–	–
EINECS number	205-305-4	–
Chemical formula	$C_{22}H_{38}O_7$	$C_{22}H_{38}O_7$
Molecular weight (g/mol)	414.55	414.55
Assay	Content not less than 98 % on the dried basis	Not less than 95 % on the dried basis
Description	White or yellowish-white powder with a citrus-like odour	White or yellowish-white solid, with a citrus-like odour
Identification		
Melting point	107–117 °C	107 –117 °C
Specific rotation	$[\alpha]_D^{20}$ between +21° and +24° (5 % w/v in methanol solution)	$[\alpha]_D^{20}$: Between +21° and +24° (10 % (w/v) solution)
Solubility	–	Very slightly soluble in water; freely soluble in ethanol
Reducing reaction	–	A solution of the sample in ethanol will decolorise a solution of 2,6-dichlorophenol-indophenol TS
Purity		
Loss on drying	Not more than 2 % (vacuum oven, 56–60 °C, 1 hour)	Not more than 2 % (vacuum oven, 56–60 °C, 1 hour)
Sulphated ash	Not more than 0.1 %	Not more than 0.1 %
Arsenic	Not more than 3 mg/kg	–
Lead	Not more than 2 mg/kg	Not more than 2 mg/kg
Mercury	Not more than 1 mg/kg	–

Table 2: Specifications established for ascorbyl stearate (E 304ii) according to Commission Regulation (EU) No 231/2012 and JECFA (2006)

	Commission Regulation (EU) No 231/2012	**JECFA (2006)**
Definition		
Chemical names	Ascorbyl stearate; L-ascorbyl stearate; 2,3-didehydro-L-threo-hexono-1,4-lactone-6-stearate; 6-stearoyl-3-keto-L-gulofuranolactone	Ascorbyl stearate; L-ascorbyl stearate; 2,3-didehydro-L-threo-hexono-1,4-lactone-6-stearate; 6-stearoyl-3-keto-L-gulofuranolactone
CAS number	–	25395-66-8
EINECS number	246-944-9	–
Chemical formula	$C_{24}H_{42}O_7$	$C_{24}H_{42}O_7$
Molecular weight (g/mol)	442.6	442.6
Assay	Content not less than 98 %	Not less than 95 %
Description	White or yellowish-white powder with a citrus-like odour	White or yellowish-white solid, with a citrus-like odour
Identification		
Melting point	About 116 °C	About 116 °C
Solubility	–	Insoluble in water; soluble in ethanol
Reducing reaction	–	A solution of the sample in ethanol will decolorise a solution of 2,6-dichlorophenol-indophenol TS
Purity		
Loss on drying	Not more than 2 % (vacuum oven, at 56–60 °C 1 hour)	Not more than 2 % (vacuum oven, 56–60 °C, 1 hour)
Sulphated ash	Not more than 0.1 %	Not more than 0.1 %
Arsenic	Not more than 3 mg/kg	–
Lead	Not more than 2 mg/kg	Not more than 2 mg/kg
Mercury	Not more than 1 mg/kg	–

The Panel considered that residual solvent's limits for solvents used in the manufacturing process (see section 2.3) should be included in the EC specifications.

The Panel noted that, according to the EC specifications for ascorbyl palmitate and ascorbyl stearate, impurities of the toxic elements lead, mercury and arsenic are accepted up to concentrations of 2, 1 and 3 mg/kg, respectively. Contamination at those levels could have a significant impact on the exposure to these metals, for which the intake is already close to the health-based guidance values established by EFSA (EFSA CONTAM Panel, 2009, 2010, 2012).

2.3. Manufacturing process

Neither the SCF nor JECFA give any information concerning the manufacture of the ascorbyl esters of fatty acids.

According to data in literature, the ascorbyl esters of fatty acids are synthesised, chemically, by the catalysed esterification of ascorbic acid with concentrated sulphuric acid in the presence of a specific fatty acid (e.g. palmitic, stearic acid) (Swern et al., 1943; Swern and Wells, 1944; Cousins et al., 1977; Nickels and Hackenberger, 1987). It is indicated that this chemical synthesis is an energy-intensive process and results in the formation of a mixture of products with a preponderance of *O*-6 substitution. It is also indicated that this process involves cumbersome downstream processing of the final product.

Enzymatic synthesis has been described as an alternative method of synthesis, claimed to be more region-selective, involving milder reaction conditions and that the use of immobilised enzyme simplified the downstream processing and made the process more economical.

Sakashita et al. (1992) described a process in which ascorbyl palmitate and ascorbyl stearate are produced by reacting ascorbic acid with an organic acid enol ester in the presence of an active lipase, using an organic solvent with a solubility of ascorbic acid of more than 0.3 % at 25 °C. Among a group of solvents, pyridine (solubility of ascorbic acid: > 6 %), t-butanol (solubility of ascorbic acid: > 0.62 %), dioxane (solubility of ascorbic acid: > 0.57 %) or tetrahydrofuran (solubility of ascorbic acid: > 1.1 %) were preferred.

Bradoo et al. (1999) described a process in which high yields of ascorbyl palmitate were obtained by lipase-mediated esterification using *Bacillus stearothermophilus* SB 1 lipase.

According to information provided by the manufacturer (DSM, 2014), ascorbyl palmitate as food additive is produced in accordance with current Good Manufacturing Practices (GMP). In the presence of sulphuric acid, palmitic acid is esterified with ascorbic acid at slightly elevated temperature. After completion of the ester reaction, the ascorbyl palmitate formed is extracted from the reaction mixture and purified by recrystallisation.

According to industry, petroleum ether, mesityl oxide and acetone are the solvents used during the manufacturing process (DSM, 2010).

2.4. Methods of analysis in foods

The analysis of ascorbyl palmitate in various foods using high-performance liquid chromatography (HPLC) has been described in the literature (Melton et al., 1981; Vicente et al., 1985; Shiroma and Ohshiro, 1993; Perrin and Meyer, 2003).

The rapid method using amperometric flow injection analysis for the evaluation of ascorbyl 6-palmitate in foods is described. Under optimised conditions, the calibration curve was linear in the range from 0 to 20 mg/L and the detection limit was 0.2 mg/L (Buratti et al., 2001).

Titrimetric and colorimetric methods were applied for the detection of ascorbic acid monostearate in food. With the colorimetric method, 89 % recovery of ascorbyl stearate was obtained in chocolate and margarine (Ikegami et al., 1968).

2.5. Reaction and fate in food

No information on reaction products of ascorbyl palmitate and stearate in food has been identified, but as the esters are in the 6-position of ascorbic acid, leaving the enediol structure of ascorbic acid free, it may be assumed that ascorbyl palmitate will react with other compounds similarly to ascorbic acid (Saltmarsh, 2013). Information on the reaction and fate in food of ascorbic acid has been revised by the Panel (EFSA ANS Panel, 2015).

The effect of ascorbyl palmitate on oxidative stability of fats and oils measured by peroxide value and by analysis of volatile secondary oxidation products has been reported as lower than the effects of tocopherols, but higher than the effects of butylated hydroxyanisole, butylated hydroxytoluene and β-carotene (Cort, 1974; Madhavi et al., 1995). The prooxidant effect was observed in fish oil-enriched salad dressing at a concentration of 300 mg/kg (Let et al., 2007). Karabulut (2010) performed tests on antioxidative activity of various antioxidants in butter oil by measuring peroxide value and *p*-anisidine value and concluded that ternary combinations of α-tocopherol, β-carotene and ascorbyl palmitate were significantly better at retarding oxidation than binary blends of α-tocopherol with β-carotene or ascorbyl palmitate. However, a prooxidant effect was observed, especially when β-carotene and ascorbyl palmitate were used individually or in binary combination.

2.6. Case of needs and proposed uses

Maximum permitted levels (MPLs) of fatty acid esters of ascorbic acid (E 304) have been defined in Annex II to Regulation (EC) No 1333/2008 on food additives, as amended.

Currently, fatty acid esters of ascorbic acid (E 304) are authorised food additives in the EU, mostly according to *quantum satis* (*QS*) except for foods for infants and young children (Food Categorisation System (FCS) 13.1.1, 13.1.2, 13.1.3, 13.1.4, 13.1.5.1 and 13.1.5.2). For certain food categories, the MPL is expressed on fat basis. Fatty acid esters of ascorbic acid (E 304) are included in Group I food additives.

Table 3 summarises the food categories in which fatty acid esters of ascorbic acid (E 304) are permitted and the corresponding MPLs as set by Annex II to Regulation (EC) No 1333/2008.

Table 3: MPLs of fatty acid esters of ascorbic acid (E 304) in foods according to Annex II of Regulation (EC) No 1333/2008

FCS category number [(a)]	FCS food category	E-number/ group	Name	MPL (mg/L or mg/kg as appropriate)	Restrictions/exceptions
01.3	Unflavoured fermented products, heat-treated after fermentation	Group I	Additives	*Quantum satis*	
01.4	Flavoured fermented milk products, including heat-treated products	Group I	Additives	*Quantum satis*	
01.5	Dehydrated milk as defined by Directive 2001/114/EC	E 304	Fatty acid esters of ascorbic acid	*Quantum satis*	
01.6.3	Other creams	Group I	Additives	*Quantum satis*	
01.7.1	Unripened cheese, excluding products falling in category 16	Group I	Additives	*Quantum satis*	Except *mozzarella*
01.7.5	Processed cheese	Group I	Additives	*Quantum satis*	
01.7.6	Cheese products (excluding products falling in category 16)	Group I	Additives	*Quantum satis*	
01.8	Dairy analogues, including beverage whiteners	Group I	Additives	*Quantum satis*	
02.1	Fats and oils essentially free from water (excluding anhydrous milk fat)	E 304	Fatty acid esters of ascorbic acid	*Quantum satis*	Except virgin oils and olive oils
02.2.2	Other fat and oil emulsions, including spreads as defined by Council Regulation (EC) No 1234/2007 and liquid emulsions	Group I	Additives	*Quantum satis*	
02.3	Vegetable oil pan spray	Group I	Additives	*Quantum satis*	
03	Edible ices	Group I	Additives	*Quantum satis*	
04.2.1	Dried fruit and vegetables	Group I	Additives	*Quantum satis*	
04.2.2	Fruit and vegetables in vinegar, oil or brine	Group I	Additives	*Quantum satis*	
04.2.4.1	Fruit and vegetable preparations, excluding compote	Group I	Additives	*Quantum satis*	
04.2.5.4	Nut butters and nut spreads	Group I	Additives	*Quantum satis*	

FCS category number [a]	FCS food category	E-number/ group	Name	MPL (mg/L or mg/kg as appropriate)	Restrictions/exceptions
04.2.6	Processed potato products	Group I	Additives	*Quantum satis*	
05.1	Cocoa and chocolate products as covered by Directive 2000/36/EC	Group I	Additives	*Quantum satis*	Only energy-reduced or with no added sugars
05.2	Other confectionery, including breath refreshening microsweets	Group I	Additives	*Quantum satis*	
05.3	Chewing gum	Group I	Additives	*Quantum satis*	
05.4	Decorations, coatings and fillings, except fruit-based fillings covered by category 4.2.4	Group I	Additives	*Quantum satis*	
06.2.2	Starches	Group I	Additives	*Quantum satis*	
06.3	Breakfast cereals	Group I	Additives	*Quantum satis*	
06.4.2	Dry pasta	Group I	Additives	*Quantum satis*	Only gluten free and/or pasta intended for hypoproteic diets in accordance with Directive 2009/39/EC
06.4.4	Potato gnocchi	Group I	Additives	*Quantum satis*	Only fresh refrigerated potato gnocchi
06.4.5	Fillings of stuffed pasta (ravioli and similar)	Group I	Additives	*Quantum satis*	
06.5	Noodles	Group I	Additives	*Quantum satis*	
06.6	Batters	Group I	Additives	*Quantum satis*	
06.7	Pre-cooked or processed cereals	Group I	Additives	*Quantum satis*	
07.1.1	Bread prepared solely with the following ingredients: wheat flour, water, yeast or leaven, salt	E 304	Fatty acid esters of ascorbic acid	*Quantum satis*	
07.1.2	Pain courant francais; Friss búzakenyér, fehér és félbarna kenyerek	E 304	Fatty acid esters of ascorbic acid	*Quantum satis*	Only *Friss búzakenyér, fehér és félbarna kenyerek*
07.1	Bread and rolls	Group I	Additives	*Quantum satis*	Except products in categories 7.1.1 and 7.1.2
07.2	Fine bakery wares	Group I	Additives	*Quantum satis*	
08.2.1	Non-heat-treated processed meat	Group I	Additives	*Quantum satis*	
08.3.2	Heat-treated processed meat	Group I	Additives	*Quantum satis*	Except foie gras, foie gras entier, blocs de foie gras, Libamáj, libamáj egészben, libamáj tömbben
08.3.3	Casings and coatings and decorations for meat	Group I	Additives	*Quantum satis*	
09.2	Processed fish and fishery products, including molluscs and crustaceans	Group I	Additives	*Quantum satis*	

FCS category number [a]	FCS food category	E-number/ group	Name	MPL (mg/L or mg/kg as appropriate)	Restrictions/exceptions
09.3	Fish roe	Group I	Additives	*Quantum satis*	Only processed fish roe
10.2	Processed eggs and egg products	Group I	Additives	*Quantum satis*	
11.2	Other sugars and syrups	Group I	Additives	*Quantum satis*	
12.1.2	Salt substitutes	Group I	Additives	*Quantum satis*	
12.2.2	Seasonings and condiments	Group I	Additives	*Quantum satis*	
12.3	Vinegars	Group I	Additives	*Quantum satis*	
12.4	Mustard	Group I	Additives	*Quantum satis*	
12.5	Soups and broths	Group I	Additives	*Quantum satis*	
12.6	Sauces	Group I	Additives	*Quantum satis*	
12.7	Salads and savoury-based sandwich spreads	Group I	Additives	*Quantum satis*	
12.8	Yeast and yeast products	Group I	Additives	*Quantum satis*	
12.9	Protein products, excluding products covered in category 1.8	Group I	Additives	*Quantum satis*	
13.1.1	Infant formulae as defined by Directive 2006/141/EC	E 304(i)	Ascorbyl palmitate	10	
13.1.2	Follow-on formulae as defined by Directive 2006/141/EC	E 304(i)	Ascorbyl palmitate	10	
13.1.3	Processed cereal-based foods and baby foods for infants and young children as defined by Directive 2006/125/EC	E 304(i)	Ascorbyl palmitate	100	Only fat-containing cereal-based foods, including biscuits and rusks and baby foods
13.1.4	Other foods for young children	E 304(i)	Ascorbyl palmitate	100	
13.1.5.1	Dietary foods for infants for special medical purposes and special formulae for infants	E 304(i)	Ascorbyl palmitate	100	
13.1.5.2	Dietary foods for babies and young children for special medical purposes as defined in Directive 1999/21/EC	E 304(i)	Ascorbyl palmitate	100	
13.2	Dietary foods for special medical purposes defined in Directive 1999/21/EC (excluding products from food category 13.1.5)	Group I	Additives	*Quantum satis*	
13.3	Dietary foods for weight control diets intended to replace total daily food intake or an individual meal (the whole or part of the total daily diet)	Group I	Additives	*Quantum satis*	
13.4	Foods suitable for people intolerant to gluten as defined by Regulation (EC) 41/2009	Group I	Additives	*Quantum satis*	Including dry pasta

FCS category number [(a)]	FCS food category	E-number/ group	Name	MPL (mg/L or mg/kg as appropriate)	Restrictions/exceptions
14.1.2	Fruit juices as defined by Council Directive 2001/112/EC and vegetable juices	Group I	Additives	*Quantum satis*	Only vegetable juices
14.1.3	Fruit nectars as defined by Council Directive 2001/112/EC and vegetable nectars and similar products	Group I	Additives	*Quantum satis*	Only vegetable nectars,
14.1.4	Flavoured drinks	Group I	Additives	*Quantum satis*	
14.1.5.2	Other	Group I	Additives	*Quantum satis*	Excluding unflavoured leaf tea; including flavoured instant coffee
14.2.3	Cider and perry	Group I	Additives	*Quantum satis*	
14.2.4	Fruit wine and made wine	Group I	Additives	*Quantum satis*	
14.2.5	Mead	Group I	Additives	*Quantum satis*	
14.2.6	Spirit drinks as defined in Regulation (EC) No 110/2008	Group I	Additives	*Quantum satis*	Except whisky or whiskey
14.2.7.1	Aromatised wines	Group I	Additives	*Quantum satis*	
14.2.7.2	Aromatised wine-based drinks	Group I	Additives	*Quantum satis*	
14.2.7.3	Aromatised wine-product cocktails	Group I	Additives	*Quantum satis*	
14.2.8	Other alcoholic drinks, including mixtures of alcoholic drinks with non-alcoholic drinks and spirits with less than 15 % of alcohol	Group I	Additives	*Quantum satis*	
15.1	Potato-, cereal-, flour- or starch-based snacks	Group I	Additives	*Quantum satis*	
15.2	Processed nuts	Group I	Additives	*Quantum satis*	
16	Desserts, excluding products covered in category 1, 3 and 4	Group I	Additives	*Quantum satis*	
17.1	Food supplements supplied in a solid form, including capsules and tablets and similar forms, excluding chewable forms	Group I	Additives	*Quantum satis*	
17.2	Food supplements supplied in a liquid form	Group I	Additives	*Quantum satis*	
17.3	Food supplements supplied in a syrup-type or chewable form	Group I	Additives	*Quantum satis*	
18	Processed foods not covered by categories 1 to 17, excluding foods for infants and young children	Group I	Additives	*Quantum satis*	

(a): FCS, Food Categorisation System (food nomenclature) presented in the Annex II to Regulation (EC) No 1333/2008.

According to Annex III, Part 3 of Regulation (EC) No 1333/2008, fatty acid esters of ascorbic acid (E 304) are also authorised as food additives in food enzymes with a maximum level in the final food products (beverages or not) at *QS*.

According to Annex III, Parts 2 and 4, fatty acid esters of ascorbic acid (E 304) are authorised, respectively, in all food additives preparations at *QS* and all flavourings at *QS*.

In addition, according to Annex III, Part 5, Section A of Regulation (EC) No 1333/2008, fatty acid esters of ascorbic acid (E 304) are also authorised as food additives added in nutrients, except nutrients intended to be used in foodstuffs for infants and young children listed in point 13.1 of Part E of Annex II, at *QS* in all nutrients. In addition, according to Annex III, Part 5, Section B of Regulation (EC) No 1333/2008, ascorbyl palmitate (E 304(i)) is authorised as a food additive added in all nutrients intended to be used in foodstuff for infants and young children in point 13.1 of Part E of Annex II.

2.7. Reported use levels or data on analytical levels of fatty acid esters of ascorbic acid (E 304) in food

Most food additives in the EU are authorised at a specific MPL. However, a food additive may be used at a lower level than the MPL. Therefore, information on actual use levels is required for performing a more realistic exposure assessment, especially for those food additives for which no MPL is set and which are authorised according to *QS*.

In the framework of Regulation (EC) No 1333/2008 on food additives and of Commission Regulation (EU) No 257/2010[15] regarding the re-evaluation of approved food additives, EFSA issued a public call[16] for concentration data (usage and/or analytical data) on fatty acid esters of ascorbic acid (E 304).

In response to this public call, updated information on the actual use levels of fatty acid esters of ascorbic acid (E 304) in foods was made available to EFSA by industry. No analytical data have been provided by the Member States.

2.7.1. Summarised data on reported use levels in foods provided by industry

Industry provided EFSA with data on use levels (n = 216) of fatty acid esters of ascorbic acid (E 304) in foods for 71 out of the 77 food categories in which fatty acid esters of ascorbic acid (E 304) are authorised. Data were received on ascorbyl palmitate (E 304(i)) (n = 145) and ascorbyl stearate (E 304(ii)) (n = 71). Some data were reported in whole weight but others in fat weight. The data were provided by the Food Chemical Risk Analyses (FCRA), FoodDrinkEurope (FDE), the International Chewing Gum Association (ICGA) and Specialised Nutrition Europe (SNE).

Some reported use levels in fat weight related to foods with no fat (FCS 11.2/12.3/14.1.4/…). EFSA received the information that "*the presence of ascorbyl palmitate could be explained by the addition of essential oils and/or flavour oils (e.g. orange oil) to a very small number of products. The reported ascorbyl palmitate concentrations would correspond to the levels required in the oils and not the whole food*". The Panel decided not to take these food categories into account in the present exposure estimates.

A report linked to the reported use levels of fatty acid esters of ascorbic acid (E 304) was also provided to EFSA by FCRA (Tennant, 2014).

Appendix A provides data on the use levels of fatty acid esters of ascorbic acid (E 304) in foods as reported by industry.

[15] Commission Regulation (EU) No 257/2010 of 25 March 2010 setting up a programme for the re-evaluation of approved food additives in accordance with Regulation (EC) No 1333/2008 of the European Parliament and of the Council on food additives. OJ L 80, 26.3.2010, p. 19.
[16] Available online: http://www.efsa.europa.eu/en/dataclosed/call/130327

2.8. Information on existing authorisations and evaluations

Fatty acid of ascorbic acid (E 304) are authorised as food additives in the EU in accordance with Annexes II and III to Regulation (EC) No 1333/2008 on food additives. Specific purity criteria on ascorbyl palmitate (E 304i) and ascorbyl stearate (E304ii) have been defined in Commission Regulation (EU) No 231/2012.

At its 17th meeting in 1973, JECFA allocated an Acceptable Daily Intake (ADI) of 1.25 mg/kg body weight (bw)/day to ascorbyl palmitate based on a long-term study in male rats with up to 0.25 % (w/w) L-ascorbyl palmitate in the diet (equivalent to 125 mg/kg bw/day) (Fitzhugh and Nelson, 1946) (see section 3.2.2). No diet-related effects were noted and the JEFCA applied a safety factor of 100 to the highest dose level tested. JEFCA noted that although no studies had been performed on ascorbyl stearate, commercial products of ascorbyl palmitate, including the one used in the Fitzhugh and Nelson (1946) study, would contain between 5 and 20 % of the total as the stearate and, therefore, extended the ADI to cover ascorbyl stearate or ascorbyl palmitate or the sum of both (JECFA, 1974).

The SCF evaluated ascorbyl palmitate in 1983 and found the substance acceptable as a source of vitamin C and as a technological additive (antioxidant) in infant formulae and "*follow-up milks based on cows' milk proteins*". No scientific data or explanation were given (SCF, 1983). The use of ascorbyl palmitate in other types of foods for infants and small children was endorsed in later opinions, (SCF, 1989a, 1991, 1997, 1998). In its opinion on additives in nutrient preparations for use in infant formulae, follow-on formulae and weaning foods, the SCF stated that the use of ascorbyl palmitate and tocopherols for infant formulae and follow-on formulae is acceptable if the total level of the substances (as nutrients and as antioxidants) is less than 1.5 mg/100 kcal (SCF, 1997). In 1998, the SCF stated "*The Committee considers ascorbyl palmitate to be acceptable as an antioxidant up to 10 mg/l in infant formulae and follow-on for infants and young children in good health and at corresponding levels in FSMP for the same age group*" (SCF, 1998a). In its opinion on antioxidants used as food additives the SCF did not allocate an ADI, but argued that "*Ascorbyl palmitate is presumed to yield ascorbic acid during digestion*" and therefore concluded that the "*ascorbyl palmitate was acceptable, with ascorbic acid and its salts, for food additive use*". The evaluation also covered ascorbyl stearate as the commercial material tested was thought to contain 5–10 % (w/w) ascorbyl stearate (SCF, 1989b).

TemaNord (2002) concluded that an absence of safety data is acceptable if the ascorbyl esters are fully hydrolysed in the digestive tract before absorption in the body, but they note that hydrolysis has not been demonstrated and therefore recommended further investigations, in the first instance on bioavailability and biotransformation. If complete hydrolysis does not occur in the digestive tract, TemaNord recommended that ascorbyl esters be examined for any adverse effects on reproduction.

EFSA Panel on Additives and Products or Substances used in Animal Feed (FEEDAP) has issued opinions on the safety and efficacy of vitamin C (ascorbic acid, sodium ascorbate, calcium ascorbate, ascorbyl palmitate, sodium calcium ascorbyl phosphate and sodium ascorbyl phosphate) as a feed additive for all animal species and concluded that vitamin C, being essential for primates, guinea pigs and fish, in the form of ascorbic acid and its calcium and sodium salts, ascorbyl palmitate, sodium calcium ascorbyl phosphate and sodium ascorbyl phosphate, is safe for all animal species (EFSA FEEDAP Panel 2013a, b).

The US Food and Drug Administration (FDA) considered ascorbyl palmitate to be "Generally Recognized as Safe" (GRAS) based on a report by the Federation of American Societies for Experimental Biology (FASEB, 1979).

Ascorbyl palmitate (PM Reference 36080) and ascorbyl stearate (PM Reference 36160) are included in the EU list of authorised substances that may be intentionally used in the manufacture of plastic

layers in plastic materials and articles (Annex I to Commission Regulation (EU) No 10/2011[17]). Ascorbyl palmitate and ascorbyl stearate are permitted as antioxidants in cosmetic products (European Commission database-CosIng[18]). Furthermore, ascorbyl palmitate (but not ascorbyl stearate) is listed as a permitted source of vitamin C in Directive 2002/46/EC[19], Regulation (EC) No 1925/2006[20], Commission Directive 2006/141/EC[21] and Commission Directive 2006/125/EC[22].

In its opinion on the tolerable upper intake level of vitamin C, the EFSA Scientific Panel on Dietetic Products, Nutrition and Allergies (NDA Panel) included ascorbyl palmitate as a source of vitamin C. The NDA Panel concluded that intakes of vitamin C above 1 g/day would be associated with negligible increased uptake and tissue levels, but may lead to an increased risk of adverse gastrointestinal effects. However, the Panel also recognised that there are no data on the gastrointestinal absorption or tolerability of esterified forms of vitamin C, such as ascorbyl palmitate, but such esters might be expected to show similar properties, and therefore this conclusion applies to these forms as well as ascorbic acid and its salts (EFSA, 2004).

The EFSA NDA Panel (2013) also considered several health outcomes that may be associated with vitamin C intake; however, the available data were considered insufficient for the setting of Dietary Reference Values (DRVs).

Ascorbic acid and its salts (E 300–302) have been re-evaluated by the Panel (EFSA ANS Panel, 2015). It was concluded that the available data for ascorbic acid and its salts did not report any adverse effects in animal studies, even at the highest doses tested.

2.9. Exposure assessment

2.9.1. Food consumption data used for exposure assessment

2.9.1.1. EFSA Comprehensive European Food Consumption Database

Since 2010, the EFSA Comprehensive European Food Consumption Database (Comprehensive Database) has been populated with national data on food consumption at a detailed level. Competent authorities in the European countries provide EFSA with data on the level of food consumption by the individual consumer from the most recent national dietary survey in their country (cf. Guidance of EFSA on the "Use of the EFSA Comprehensive European Food Consumption Database in Exposure Assessment" (EFSA, 2011a)). New consumption surveys recently added in the Comprehensive database (end 2014) were also taken into account in this assessment[23].

The food consumption data gathered by EFSA were collected by different methodologies and thus direct country-to-country comparisons should be interpreted with caution. Depending on the food category and the level of detail used for exposure calculations, uncertainties could be introduced owing to possible underreporting by subjects and/or misreporting of the consumption amounts. Nevertheless, the EFSA Comprehensive Database represents the best available source of food consumption data across Europe at present.

[17] Commission Regulation (EU) No 10/2011 of 14 January 2011 on plastic materials and articles intended to come into contact with food. OJ L 12, 15.1.2011, p. 1–89.
[18] Available online: http://ec.europa.eu/consumers/cosmetics/cosing/index.cfm?fuseaction=search.simple
[19] Directive 2002/46/EC of the European Parliament and the Council of 10 June 2002 on the approximation of the laws of the Member States relating to food supplements. OJ L 183 12.7.2002, p. 51–57.
[20] Regulation (EC) No 1925/2006 of the European Parliament and the Council of 20 December 2006 on the addition of vitamins and minerals and of certain other substances to foods. OJ L 404, 30.12.2006, p. 26–38.
[21] Commission Directive 2006/141/EC of 22 December 2006 on infant formulae and follow-on formulae and amending Directive 1999/21/EC.OJ L401 30.1.2006, p. 1–33
[22] Commission Directive 2006/125/EC of 5 December 2006 on processed cereal-based foods and baby foods for infants and young children. OJ L 339, 6.12.2006, p. 16–35.
[23] Available online: http://www.efsa.europa.eu/en/datexfoodcdb/datexfooddb.htm

Food consumption data were available for the exposure assessment for the following population groups: infants, toddlers, children, adolescents, adults and the elderly. For the present assessment, food consumption data were available from 33 different dietary surveys carried out in 19 European countries (Table 4).

Table 4: Population groups considered for the exposure estimates of fatty acid esters of ascorbic acid (E 304)

Population	Age range	Countries with food consumption surveys covering more than one day
Infants	From 4 months up to and including 11 months of age	Bulgaria, Denmark, Finland, Germany, Italy, UK
Toddlers	From 12 months up to and including 35 months of age	Belgium, Bulgaria, Denmark, Finland, Germany, Italy, Netherlands, Spain, UK
Children [(a)]	From 36 months up to and including 9 years of age	Austria, Belgium, Bulgaria, Czech Republic, Denmark, Finland, France, Germany, Greece, Italy, Latvia, Netherlands, Spain, Sweden, UK
Adolescents	From 10 years up to and including 17 years of age	Austria, Belgium, Cyprus, Czech Republic, Denmark, Finland, France, Germany, Italy, Latvia, Spain, Sweden, UK
Adults	From 18 years up to and including 64 years of age	Austria, Belgium, Czech Republic, Denmark, Finland, France, Germany, Hungary, Ireland, Italy, Latvia, Netherlands, Romania, Spain, Sweden, UK
The elderly [(a)]	From 65 years of age and older	Austria, Belgium, Denmark, Finland, France, Germany, Hungary, Ireland, Italy, Romania, Sweden, UK

(a): The terms "children" and "the elderly" correspond, respectively, to "other children" and the merge of "elderly" and "very elderly" in the Guidance of EFSA on the "Use of the EFSA Comprehensive European Food Consumption Database in Exposure Assessment" (EFSA, 2011a).

Consumption records were codified according to the FoodEx classification system (EFSA, 2011b). Nomenclature from the FoodEx classification system has been linked to the FCS as presented in Annex II of Regulation (EC) No 1333/2008, part D, to perform exposure estimates. In practice, FoodEx food codes were matched to the FCS food categories.

2.9.1.2. Food categories selected for the exposure assessment of fatty acid esters of ascorbic acid (E 304)

The food categories in which the use of fatty acid esters of ascorbic acid (E 304) is authorised were selected from the nomenclature of the EFSA Comprehensive Database (FoodEx classification system food codes), at the most detailed level possible (up to FoodEx level 4) (EFSA, 2011b).

Some food categories are not referenced in the EFSA Comprehensive Database, therefore no consumption data are available for them. They were not taken into account in the present estimate. This may have resulted in an underestimation of the exposure. The food categories that were not taken into account are described below (in ascending order of FCS code):

- 01.7.6 Cheese products (excluding products falling in category 16)
- 02.3 Vegetable oil pan spray
- 05.4 Decorations, coatings and fillings, except fruit-based fillings covered by category 04.2.4
- 06.4.4 Potato gnocchi
- 06.6 Batters
- 06.7 Pre-cooked or processed cereals

- 08.3.3 Casings and coatings and decorations for meat
- 12.1.2 Salt substitutes
- 14.2.4 Fruit wine and made wine
- 14.2.5 Mead.

For the following food categories (in ascending order of FCS code), the restrictions that apply to the use of fatty acid esters of ascorbic acid (E 304) could not be taken into account and, therefore, the whole food category was considered in the exposure assessment. This resulted in an overestimation of the exposure:

- 01.7.1 Unripened cheese, excluding products falling in category 16, except mozzarella
- 02.1 Fats and oil essentially free from water (excluding anhydrous milk fat), except virgin oils and olive oils
- 05.1 Cocoa and chocolate products as covered by Directive 2000/36/EC, only energy-reduced or with no added sugars
- 06.4.2 Dry pasta, only gluten free and/or pasta intended for hypoproteic diets in accordance with Directive 2009/39/EC
- 07.1.2 Pain courant français, friss buzakenyer, feher es felbarna kenyerek, only friss buzakenyer, feher es felbarna kenyerek
- 08.3.2 Heat-treated processed meat, except or only foie gras, foie gras entier, blocs de foie gras/*Libamaj*, *libamaj egészben*, *labamaj tömbben*
- 09.3 Fish roe, only processed fish roe
- 13.1.3 Processed cereal-based foods and baby foods for infants and young children as defined by Directive 2006/12/EC, only fat-containing cereal-based foods, including biscuits and rusk and baby foods
- 17.1/17.2/17.3 Food supplements, in liquid, syrup-type or chewable form and solid form, cannot be differentiated and are therefore all assigned the mean level of all samples of food supplements.

The food category "Other cream" (FCS 01.6.3) could not be differentiated from the parental food category "Cream and cream powder" (FCS 01.6) in FoodEx. Therefore, the food category "Cream and cream powder" (FCS 01.6) was used in the exposure assessment.

Overall, 10 food categories were not taken into account in the exposure assessment because they are not referenced in the EFSA Comprehensive Database, whereas 11 food categories were included without considering the restrictions as set in Annex II of Regulation (EC) No 1333/2008. Added to that, as mentioned above, for some food categories usage levels were reported in fat weight when there is no fat content (FCS 11.2 "Other sugar and syrups", 14.1.2, 14.1.3, 14.1.4 "Flavoured drinks", …). Owing to this, 14 added food categories were not taken into account. Thus, in the current exposure estimate, 24 food categories out of 77 are not taken into account.

2.9.2. Exposure to fatty acid esters of ascorbic acid (E 304) from its use as a food additive

The Panel estimated chronic exposure to fatty acid esters of ascorbic acid (E 304). According to Tennant (2014), "*it is unlikely that more than one antioxidant will be used in any given food item […]. The antioxidants considered in this report are mutually exclusive*". Therefore, the Panel estimated the combined exposure to ascorbyl palmitate (E 304(i)) and ascorbyl stearate (E 304(ii)) using the highest concentration reported from any of them for each food category.

Dietary exposure was calculated by multiplying fatty acid esters of ascorbic acid (E 304) concentrations reported in Appendix B for each food category with their respective consumption amount per kilogram of body weight for each individual in the Comprehensive Database. The exposure per food category was subsequently added to derive an individual total exposure per day. These exposure estimates were averaged over the number of survey days, resulting in an individual average exposure per day for the survey period. Surveys with only one day per subject were excluded as they were not considered adequate to assess chronic dietary exposure.

This was carried out for all individuals per survey and per population group, resulting in distributions of individual average exposure per survey and population group (Table 4). Based on these distributions, the mean and 95th percentile of exposures were calculated per survey for the total population and per population group. High percentile exposure was calculated for only those population groups where the sample size was sufficiently large to allow calculation of the 95th percentile of exposure (EFSA, 2011a). Therefore, in the present assessment, high levels of exposure for infants from Italy and for toddlers from Belgium, Italy and Spain were not included. Thus, for the present assessment, food consumption data were available from 33 different dietary surveys carried out in 19 European countries.

Two exposure scenarios are defined and carried out by the ANS Panel regarding the concentration data of fatty acid esters of ascorbic acid (E 304) used: (1) MPLs as set down in the EU legislation (defined as the *regulatory maximum level exposure assessment scenario*); and (2) the reported use levels (defined as the *refined exposure assessment scenario*). These two scenarios are discussed in detail below.

2.9.2.1. Regulatory maximum level exposure assessment scenario

The regulatory maximum level exposure assessment scenario is based on the MPLs as set in Annex II to Regulation (EC) No 1333/2008. As fatty acid esters of ascorbic acid (E 304) are authorised according to *QS* in almost all food categories, a "maximum level exposure assessment" scenario was estimated based on the maximum reported use levels as provided by industry (EFSA ANS Panel, 2014). Some reported use levels expressed for fatty acid esters of ascorbic acid (E 304) on fat basis were converted to whole weight based on fat content information obtained from the Comprehensive Database (see Appendix B).

The exposure estimates derived following this scenario should be considered as the most conservative, as this scenario assumes that a consumer will be continuously exposed to fatty acid esters of ascorbic acid (E 304) present in food at the maximum reported use levels.

2.9.2.2. Refined exposure assessment scenario

The refined exposure assessment scenario is based on use levels reported by industry. This exposure scenario can consider only food categories where these data were available to the Panel.

Appendix B summarises the concentration levels of fatty acid esters of ascorbic acid (E 304) used in the refined exposure assessment scenario. Based on the available dataset, the Panel calculated two refined exposure estimates based on different model populations:

- The brand-loyal consumer scenario: It was assumed that a consumer is exposed long-term to the fatty acid esters of ascorbic acid (E 304) present at the maximum reported use for one food category. This exposure estimate is calculated as follows:
  - Combining food consumption with the maximum reported use for the main contributing food category at the individual level.
  - Using the mean of the typical reported use for the remaining food categories.

- The non-brand-loyal consumer scenario: It was assumed that a consumer is exposed long-term to fatty acid esters of ascorbic acid (E 304) present at the mean reported use in food. This exposure estimate is calculated using the mean of the typical reported use levels for all food categories.

No data were reported for the food categories authorised according to Annex III to Regulation (EC) No 1333/2008. In these food categories fatty acid esters of ascorbic acid (E 304) can be present as food additives in food additive preparations, food enzymes, food flavourings or nutrients. These food categories were not taken into account in the present estimates, and may therefore have resulted in an underestimation of the exposure.

2.9.2.3. Anticipated exposure to fatty acid esters of ascorbic acid (E 304)

Table 5 summarises the estimated exposure to fatty acid esters of ascorbic acid (E 304) from their use as food additives in six population groups (Table 4) according to the different exposure scenarios (section 2.9.2.2). Detailed results per population group and survey are presented in Appendix C.

Table 5: Summary of anticipated exposure to fatty acid esters of ascorbic acid (E 304) from their use as food additives in the maximum level exposure assessment scenario and in the refined exposure scenarios, in six population groups (minimum–maximum across the dietary surveys in mg/kg bw/day)

	Infants (4–11 months)	Toddlers (12–35 months)	Children (3–9 years)	Adolescents (10–17 years)	Adults (18–64 years)	The elderly (≥ 65 years)
Maximum level exposure assessment scenario						
Mean	0.5–2.8	0.8–3.0	0.9–3.2	0.5–1.8	0.3–1.1	0.2–1.0
High level	1.9–5.7	1.7–6.8	1.5–10.8	1.2–6.0	0.5–4.0	0.4–2.2
Refined estimated exposure scenario						
Brand-loyal scenario						
Mean	0.4–2.1	0.6–2.4	0.7–2.6	0.3–1.5	0.2–1.0	0.2–0.9
High level	1.9–4.6	1.4–5.9	1.3–9.9	1.0–5.6	0.3–3.7	0.3–1.7
Non-brand-loyal scenario						
Mean	0.3–0.9	0.5–1.1	0.5–1.8	0.2–1.0	0.1–0.6	0.1–0.4
High level	1.1–1.8	0.9–4.1	0.9–7.3	0.4–4.1	0.2–2.7	0.2–0.8

2.9.3. Main food categories contributing to exposure to fatty acid esters of ascorbic acid (E 304) using the maximum level exposure assessment scenario

Table 6: Main food categories contributing to exposure to fatty acid esters of ascorbic acid (E 304) using maximum usage levels (> 5 % to the total mean exposure) and number of surveys in which each food category is contributing

FCS category number	FCS food category	Infants	Toddlers	Children	Adolescents	Adults	The elderly
		Range of % contribution to the total exposure (number of surveys) [a]					
01.5	Dehydrated milk as defined by Directive 2001/114/EC			11.6 (1)			
01.6	Cream and cream powder					5.3 (1)	6.1 (1)
01.7.5	Processed cheese	5.0 (1)					
02.1	Fats and oils essentially free from water (excluding anhydrous milk fat)	5.0–32.4 (3)	5.7–34.3 (4)	6.8–35.9 (7)	5.2–31.2 (7)	8.2–46.3 (7)	9.3–49.0 (4)
03	Edible ices		5.6 (1)	7.2–12.0 (3)	7.7 (1)	6.9 (1)	
04.2	Processed fruit and vegetables	9.5–71.7 (6)	11.5–69.0 (10)	21.5–60.2 (16)	19.3–63.3 (15)	22.3–67.7 (13)	18.4–75.1 (13)
05.3	Chewing gum		5.2–28.1 (3)	8.4–52.2 (11)	7.2–59.5 (13)	6.0–47.3 (6)	9.8–23.7 (2)
06.3	Breakfast cereals	8.0–15.6 (4)	5.1–18.1 (6)	5.2–15.3 (11)	5.8–12.0 (7)	5.8–20.4 (7)	5.6–35.4 (6)
07.2	Fine bakery wares	8.0 (1)	6.0–21.2 (3)	5.4–22.2 (12)	5.0–13.9 (11)	5.5–14.6 (7)	5.4–13.6 (6)
08.3	Processed meat		5.6–9.9 (4)	5.0–9.0 (9)	6.1–12.7 (7)	5.1–25.8 (9)	5.6–23 (5)
12.6	Sauces				5.9 (1)	5.0–5.1 (2)	
12.7	Salads and savoury-based sandwich spreads					6.1–7.1 (3)	8.7 (1)
13.1	Foods for infants and young children	8.3–65 (5)	6.0 (1)				
15.1	Potato-, cereal-, flour- or starch-based snacks		6.8 (1)		6.0 (1)		
15.2	Processed nuts					5.3 (1)	
16	Desserts, excluding products covered in categories 1, 3 and 4		5.8–13.5 (4)	7.1–10.4 (3)		5.1 (1)	5.4–6.7 (2)
18	Processed foods not covered by categories 1 to 17, excluding foods for infants and young children	16.5–25.2 (3)	5.0–6.2 (2)	5.4–6.0 (2)	5.5–11.2 (3)	6.6–7.6 (2)	

(a): The total number of surveys may be greater than the total number of countries as listed in Table 3, as some countries submitted more than one survey for a specific population.

2.9.4. Main food categories contributing to exposure to fatty acid esters of ascorbic acid (E 304) using the refined exposure assessment scenario

Table 7: Main food categories contributing to exposure to fatty acid esters of ascorbic acid (E 304) using the brand-loyal refined exposure scenario (> 5 % to the total mean exposure) and number of surveys in which each food category is contributing

FCS category number	FCS Food category	Infants	Toddlers	Children	Adolescents	Adults	The elderly
		Range of % contribution to the total exposure (number of surveys) [(a)]					
01.5	Dehydrated milk as defined by Directive 2001/114/EC			10.4 (1)			
02.1	Fats and oils essentially free from water (excluding anhydrous milk fat)	9.2–31.8 (2)	5.8–38.1 (4)	6.4–42.5 (7)	8.2–37.0 (6)	7.3–62.5 (7)	7.6–66.8 (4)
03	Edible ices			6.4–10.0 (2)	7.3 (1)		
04.2	Processed fruit and vegetables	10–83.3 (6)	14.2–83.8 (10)	5.1–78.1 (17)	21.6–81.5 (15)	27–84.8 (13)	22.7–87.3 (13)
05.3	Chewing gum		6.9–35.7 (3)	5.5–63.5 (12)	5.4–71.0 (14)	7.7–54.4 (6)	12.4–26.6 (2)
06.3	Breakfast cereals	6.7–13.8 (2)	5.9–13.5 (5)	5.4–10.1 (4)	5.1–7.8 (3)	6.8–16.6 (4)	7.9–38.4 (4)
07.2	Fine bakery wares	8.4 (1)	5.3–26.2 (7)	5.3–28.9 (15)	5.0–18.0 (15)	5.3–20.1 (13)	5.1–18.4 (10)
08.3	Processed meat				6–6 (1)	15.8–18.3 (2)	10.8 (1)
12.7	Salads and savoury-based sandwich spreads						6.3 (1)
13.1	Foods for infants and young children	7.2–67.7 (5)					
15.1	Potato-, cereal-, flour- or starch-based snacks		6.1 (1)		6.1 (1)		
15.2	Processed foods not covered by categories 1 to 17, excluding foods for infants and young children	14.3–23.2 (3)			6.4 (1)	8.3 (1)	
15.2	Processed nuts					5.8 (1)	5.3 (1)
16	Desserts excluding products covered in category 1, 3 and 4		5.7–10.3 (2)	5.1–7.8 (2)			

(a): The total number of surveys may be greater than the total number of countries as listed in Table 3, as some countries submitted more than one survey for a specific population.

Table 8: Main food categories contributing to exposure to fatty acid esters of ascorbic acid (E 304) using the non-brand-loyal refined exposure scenario (> 5 % to the total mean exposure) and number of surveys in which each food category is contributing

FCS category number	FCS food category	Infants	Toddlers	Children	Adolescents	Adults	The elderly
		Range of % contribution to the total exposure (number of surveys) [(a)]					
01.5	Dehydrated milk as defined by Directive 2001/114/EC			17.0 (1)			
02.1	Fats and oils essentially free from water (excluding anhydrous milk fat)	8.1–44.7 (5)	8.6–39.1 (5)	5.7–41.6 (9)	5.5–37.2 (9)	5.4–70.2 (9)	7.2–69.7 (5)
04.2	Processed fruit and vegetables	6.0–66.4 (6)	6.9–69.0 (10)	13.7–60.4 (16)	12.5–64.1 (15)	17.7–70.3 (13)	15.5–72.9 (13)
05.1	Cocoa and chocolate products as covered by Directive 2000/36/EC		6.3–7.8 (2)	5.3–8.2 (6)	5.5–8.2 (5)	5.1 (1)	
05.3	Chewing gum	5.7 (1)	9.3–43.5 (3)	8.8–67.5 (12)	7.9–74.6 (14)	5.2–64.3 (10)	20.0–38.8 (2)
06.3	Breakfast cereals	6.5–11.5 (3)	8.7–10.7 (4)	5.0–8.6 (2)	5.6–6.6 (2)	5.2–11.7 (4)	8.6–20.2 (4)
07.2	Fine bakery wares	6.3–14.3 (2)	9.4–36.2 (8)	7–38.5 (16)	8.6–26.1 (15)	6.2–31.6 (15)	8.1–34.6 (12)
13.1	Foods for infants and young children	15.1–64.3 (5)	9.5 (1)				
15.1	Potato-, cereal-, flour- or starch-based snacks		7.0 (1)	6.0 (1)	6.5–7.4 (3)		
15.2	Processed nuts				5.7 (1)	5.0–7.2 (3)	6.1 (1)
16	Desserts, excluding products covered in categories 1, 3 and 4	5.2 (1)	6.3–12.5 (4)	5.1–8.5 (4)			5.2–6.6 (2)

(a): The total number of surveys may be greater than the total number of countries as listed in Table 3, as some countries submitted more than one survey for a specific population.

2.10. Uncertainty analysis

Uncertainties in the exposure assessment of fatty acid esters of ascorbic acid (E 304) have been discussed above. In accordance with the guidance provided in the EFSA opinion related to uncertainties in dietary exposure assessment (EFSA, 2006), the following sources of uncertainties have been considered and summarised in Table 9.

Table 9: Qualitative evaluation of influence of uncertainties on the dietary exposure estimate

Sources of uncertainties	Direction [(a)]
Consumption data: different methodologies/representativeness/underreporting/misreporting/no portion size standard	+/–
Use of data from food consumption survey of only a few days to estimate long-term (chronic) exposure for high percentiles (95th percentile)	+
Correspondence of reported use levels to the food items in the EFSA Comprehensive Food Consumption Database: uncertainties regarding which types of food the levels refer to	+/–
Food categories selected for the exposure assessment: exclusion of food categories due to missing FoodEx linkage (n = 10)	–
Food categories selected for the exposure assessment: inclusion of food categories without considering the restriction/exception (n = 11)	+
Food categories selected for the exposure assessment: use levels reported in fat weight for certain food categories which were then excluded from the exposure estimates (n = 14)	–
Reported use levels: levels considered applicable for all items within the entire food category	+
Exposure assessment scenarios: food categories authorised according to Annex III to Regulation (EC) No 1333/2008 not considered	–
Maximum exposure assessment scenario: food categories authorised at the maximum reported use levels	+
Refined exposure assessment scenarios: exposure calculations based on the maximum or mean levels (reported use from industries)	+/–
Uncertainty in possible national differences in use levels of food categories	+/–

(a): A "+" indicates uncertainty with potential to cause overestimation of exposure; a "–" indicates uncertainty with potential to cause underestimation of exposure.

Overall, the Panel considered that the uncertainties identified would, in general, result in an overestimation of the real exposure to fatty acid esters of ascorbic acid (E 304) as a food additive in European countries.

3. Biological and toxicological data

The present opinion briefly reports the major studies on the ascorbyl esters of fatty acids evaluated previously by the SCF (1989b) and JECFA (1974), and additional information has been identified from the literature and the calls for data.

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

No information on the metabolic fate of ascorbyl esters of fatty acids is reported in the SCF and JECFA evaluations (JECFA, 1974; SCF, 1989b).

3.1.1. *In vitro* studies

Using combined homogenates of guinea pig small intestine and pancreas, and with the addition of purified bacterial lipase, Inagaki and Kawaguchi (1966) showed that 80 % of L-ascorbyl palmitate was hydrolysed to ascorbic acid after incubation for 1 hour at 37 °C.

A new *in vitro* study report on the hydrolysis of L-ascorbyl palmitate in simulated intestinal fluid was recently provided by an interested party (Beck et al., 2014). ^{14}C-labelled L-ascorbyl palmitate (labelled on the 1-C position in the ascorbyl moiety) was incubated in simulated intestinal fluid containing bile acids and pancreatic enzymes prepared as described in EFSA Note for Guidance for Food Contact materials (EFSA, 2008) at concentrations of 0.1 mM and 0.2 mM ascorbyl palmitate. At various times, aliquots were removed and analysed for parent compound and its radiolabelled metabolic products by HPLC with radiodetection. The concentration of ^{14}C-ascorbyl palmitate decreased with incubation time and was virtually complete by 5–6 hours, while concomitantly ^{14}C-ascorbic acid as well as two further radiolabelled hydrolysis products (P1 and P2)—tentatively identified by liquid chromatography/mass spectrometry analysis to be dehydroascorbic acid and 2,3-diketogulonic acid—were formed (Beck et al., 2014). Both substances are known from the literature as degradation

products of ascorbic acid (Rubin et al., 2006; Nemet and Monnier, 2011). Half-lives of ascorbyl palmitate break down and of formation of ascorbic acid and its degradation products were estimated to be 15–45 minutes and 20–30 minutes, respectively. It was concluded by the authors, that ascorbyl palmitate was rapidly and completely hydrolysed to ascorbic acid and palmitic acid in simulated intestinal fluid and that a similar behaviour can be expected to occur in the intestine (Beck et al., 2014).

3.1.2. Animal studies

Guinea pigs were administered 20 mg L-ascorbic acid or L-ascorbyl palmitate, equivalent to 20 mg of ascorbic acid, orally, and daily urine was collected for up to 26 days. The levels of ascorbic acid in urine fell more rapidly in guinea pigs administered L-ascorbic acid (Inagaki and Kawaguchi, 1966). The Panel considered that these alterations were likely associated with differences in absorption, distribution and/or metabolism of L-ascorbic acid and L-ascorbyl palmitate.

Two groups of five male albino guinea pigs on a scorbutogenic diet were given equimolar amounts of ascorbic acid and ascorbyl palmitate (0.015 mmol/kg bw, equivalent[24] to 2.6 mg and 6.2 mg/kg bw of ascorbic acid and ascorbyl palmitate, respectively). There was no significant difference in food intake, gain in body weight or final body weight between the two groups. After 45 days, ascorbic acid levels were determined in the adrenals, brain, liver and spleen and no significant differences between the two groups were observed, except that the total ascorbic acid in the adrenal glands was significantly greater in the ascorbyl palmitate group than in the ascorbic acid group (Hughes and Jones, 1986).

Thirty mature male guinea pigs were fed a scorbutogenic diet until symptoms of scurvy were apparent. Animals were then randomly repleted over 9 days with equimolar concentrations (28 µmole/kg bw/day, equivalent[24] to 4.9 and 11.6 mg/kg bw/day of L-ascorbic acid and L-ascorbyl palmitate, respectively) and compared with placebo controls. Daily mean weight loss during repletion in control animals receiving placebo was significantly greater than that for both L-ascorbic acid- and L-ascorbyl palmitate-treated animals for days 3–10 of repletion. Daily mean weight loss for L-ascorbyl palmitate-treated animals was significantly greater than that of L-ascorbic acid-treated animals on days 5 and 6 of repletion. By comparing areas of the weight time curve during repletion, the authors concluded that L-ascorbyl palmitate appeared to be about 50 % as effective as L-ascorbic acid in reversing scurvy. However, mean plasma, liver, spleen and adrenal L-ascorbic acid levels did not differ significantly between L-ascorbic acid- and L-ascorbyl palmitate-treated animals at the end of repletion, and these values were significantly higher than those of control animals (Johnston et al., 1994).

3.1.3. Human studies

In a crossover experiment in seven subjects, L-ascorbic acid excretion was compared between intake of L-ascorbic acid and ascorbyl palmitate, given in doses equivalent to 300 mg ascorbic acid (L-ascorbic acid) and 285 mg ascorbic acid (ascorbyl palmitate). The amount excreted did not differ indicating a similar bioavailability of ascorbate from ascorbyl palmitate (DeRitter et al., 1951).

Johnston et al. (1994) compared the urinary excretion and plasma levels of vitamin C after dosing six human volunteers (one male, five females) for two weeks with equimolar amounts (2 g ascorbic acid or 4.7 g ascorbyl palmitate/day) following a diet not including foods known to contain high amounts of vitamin C (background intake through the diet was equivalent to 64 mg/day of ascorbic acid). They found that 24 hours after the first dose the mean plasma concentration of vitamin C was very similar for the two substances. They also found that after the repeated dosing, the urinary excretion was lower (not statistically significant) and plasma vitamin C levels higher (not statistically significant) after intake of ascorbyl palmitate compared with intake of ascorbic acid. The area under the curve 0–8 hours was 354 ± 188 µmol/L × hour and 440 ± 152 µmol/L × hour for ascorbic acid and ascorbyl palmitate, respectively, the 20 % difference was not statistically significantly different.

[24] Calculated by the Panel according to JECFA (2000).

3.1.4. Conclusion

Animal and human data suggested that ascorbyl palmitate is completely hydrolysed to ascorbic acid and palmitic acid in the gastrointestinal tract. This was further supported by an *in vitro* study reporting near complete hydrolysis of ascorbyl palmitate in simulated intestinal fluid. Considering the close relationship with ascorbyl stearate, the results of the studies on ascorbyl palmitate could be used for read-across.

Accordingly, the Panel considered that, in addition to the data obtained in the study with ascorbyl palmitate, the toxicity of ascorbyl palmitate and ascorbyl stearate could be evaluated by considering the toxicity of ascorbic, palmitic and stearic acids resulting from the hydrolysis of the ester.

3.2. Toxicological data

3.2.1. Acute toxicity

Ascorbyl palmitate showed a median lethal dose (LD_{50}) in mice from 4 700 to > 20 000 mg/kg bw and in rats from 5 150 to > 10 000 mg/kg bw and ascorbyl stearate showed a LD_{50} in mice from 6 250 to > 20 000 mg/kg bw and in rats from 7 300 to > 10 000 mg/kg bw (Bächtold, 1972, 1973a, b). From these studies, it appears that ascorbyl palmitate and stearate had a very low acute toxicity.

LD_{50} in mice of 2 000 mg/kg bw and in rats of > 5 000 mg/kg bw for ascorbyl palmitate was reported by the Scientific Committee on Cosmetology (SCC, 1993). No adverse effects were observed when rats were fed 100–3 000 mg/kg ascorbyl stearate. However, no further details were available (SCC, 1993).

3.2.2. Short-term and subchronic toxicity

No short-term or subchronic toxicity studies on ascorbyl palmitate or ascorbyl stearate were available.

3.2.3. Genotoxicity

The only study on genotoxicity of ascorbyl palmitate was a single bacterial mutation assay by Prival et al. (1991). In this study, ascorbyl palmitate at dose levels ranging from 0.033 to 3.3 mg per plate were assayed for mutagenicity in the standard *Salmonella typhimurium* plate-incorporation assay using the *Salmonella typhimurium* strains TA 98, TA 100, TA 1535, TA 1537 and TA 1538 and the tryptophan-requiring *Escherichia coli* strain WP2, both in the absence and presence of S9 metabolic activation. Higher doses than 3.3 mg per plate were not tested because of the cytotoxicity of the test substance. Under the reported experimental condition, ascorbyl palmitate did not show any mutagenic activity. The study met the requirements of Organisation of Economic Co-operation and Development (OECD) Guideline 471 for bacterial reverse mutation assay (OECD, 1997), with the exception that the negative results obtained were not confirmed in an additional experiment using different test conditions.

No genotoxicity studies were available for ascorbyl stearate.

3.2.4. Chronic toxicity and carcinogenicity

Six groups of 10 male Osborne–Mendel rats were fed a diet containing 2 % or 5 % L-ascorbyl palmitate, 2 % or 5 % D-isoascorbyl palmitate or 1 % D-isoascorbic acid. The sixth group received the control diet (Fitzhugh and Nelson, 1946). The study was terminated after 36 weeks. With the exception of the 1 % D-isoascorbic acid group, which showed no mortality, all groups of rats on the palmitate diet had fewer survivors than the control group, but the difference was not statistically significant and considered not treatment-related by the authors. All rats were autopsied and from 37 animals, the lungs, heart, liver, spleen, pancreas, stomach, small intestines, kidneys, adrenals and testes were sectioned, while the colon, lymph node, bone with bone marrow, thyroid and parathyroids were sectioned occasionally (no further details given). Microscopically, there was no difference among the four palmitate groups and the controls, except for two rats of the 5 % L-ascorbyl palmitate, which exhibited urinary bladders containing numerous white mulberry stones up to 5 mm in diameter,

one of which was found to consist of calcium oxalate. The authors considered this rarely observed lesion to be spontaneous and not related to treatment. The Panel agreed with their conclusion.

In another study performed by the same authors (Fitzhugh and Nelson, 1946), six groups of 10 male Osborne–Mendel rats were fed a diet containing 5 % non-treated lard or heated lard containing 1 % or 5 % L-ascorbyl palmitate or 1 % or 5 % D-isoascorbyl palmitate, heated lard without palmitate or fresh lard. The L-ascorbyl palmitate content of the diet was 0.05 % and 0.25 %, equivalent[25] to 25 mg and 125 mg L-ascorbyl palmitate/kg bw/day, respectively. There was no significant difference between the treated groups and the controls on weight gain and mortality. Haematological examinations made at intervals during the first year of the study (no further details given) showed no adverse effects. Histopathological examinations of the same organs and tissues as in the 36-month study, demonstrated no differences among the groups. The Panel, however, noted that this study was of limited relevance for risk assessment due to the low number of animals per group, the use of males only, only two doses were tested, the limited organs and tissues examined histopathologically and the limited reporting.

No chronic toxicity studies or carcinogenicity studies on ascorbyl stearate were available.

3.2.5. Reproductive and developmental toxicity

No reproductive and developmental toxicological studies on ascorbyl palmitate or ascorbyl stearate were available.

3.2.6. Hypersensitivity, allergenicity and intolerance

In a Cosmetic Ingredient Review (CIR), it was concluded that ascorbyl palmitate and ascorbyl stearate, which are also used in dermal products, are not irritating to the intact skin of albino rabbits and not irritating to the eyes of rabbits. Similarly, it was concluded that ascorbyl palmitate produced no signs of dermal irritation or sensitization in clinical studies (Lanigan, 1999).

3.2.7. Other studies

In its opinion on the tolerable upper intake level of vitamin C, EFSA (2004) included two studies investigating the possible effect of dietary ascorbyl palmitate on the promotion of colon tumours using known inducers (Huang et al., 1992; Rao et al., 1995). The authors of these studies concluded that there was no promoting effect of dietary ascorbyl palmitate.

4. Discussion

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

Fatty acid esters of ascorbic acid (E 304) are authorised as food additives in the EU in accordance with Annexes II and III to Regulation (EC) No 1333/2008 and specific purity criteria have been defined in the Commission Regulation (EU) No 231/2012 for ascorbyl palmitate (E 304(i)) and ascorbyl stearate (E 304(ii)).

Ascorbyl palmitate was considered as acceptable for food additive use by the SCF (1989b). The JECFA evaluated ascorbyl palmitate and ascorbyl stearate as food additives in 1973 and established an ADI of 1.25 mg/kg bw/day for ascorbyl palmitate or ascorbyl stearate or the sum of both (JECFA, 1974).

Based on the confidential information on the maximum levels for the residual solvents in ascorbyl palmitate as provided by industry (DMS, 2010), the Panel considered that there is not a safety concern.

[25] Calculated by the Panel according to JECFA (2000).

However, the Panel considered that the levels of residual solvents used in the manufacturing process should be kept under the levels that could raise a safety concern. Therefore, the Panel considered that limits for residual solvents used in the manufacturing process should be included in the EC specifications.

The Panel also considered that the maximum limits for lead, mercury and arsenic in the EC specification for ascorbyl palmitate (E 304(i)) and ascorbyl stearate (E 304(ii)) should be revised in order to ensure that ascorbyl palmitate (E 304(i)) and ascorbyl stearate (E 304(ii)) as food additives will not be a significant source of exposure to these toxic elements in food. In addition, the Panel considered that the current EINECS Number in the EC specifications for ascorbyl stearate (E 304(ii)) should be substituted with 234-231-5.

ADME data on ascorbyl palmitate (E 304(i)) and ascorbyl stearate (E 304(ii)) are sparse and the safety assessment for their use as food additives is based on the assumption that ascorbyl palmitate and ascorbyl stearate fully hydrolyse pre-systemically to ascorbic acid and their respective fatty acids. This assumption was supported by an *in vitro* study reporting near-complete hydrolysis of ascorbyl palmitate in simulated intestinal fluid (Beck et al., 2014) and by human data. Additional information can be gathered by read-across between palmitate and stearate. Both compounds are saturated fatty acids of the same structure, with stearate having 18 C-atoms and palmitate having 16 C-atoms. In the first catabolic step, stearate is metabolised to palmitate and undergoes the same catabolic pathway of β-oxidation as for other endogenous fatty acids. Therefore, the Panel considered that the toxicity of ascorbyl palmitate can be extrapolated from the data describing the toxicity of ascorbic acid and palmitic acid. The Panel further considered that this assumption is also valid for ascorbyl stearate. The Panel noted that it cannot exclude the possibility that some absorption of the parent compounds may take place before hydrolysis in the gut. However, the Panel considered that any absorbed intact ascorbyl palmitate or ascorbyl stearate would be completely hydrolysed in the hepatic portal plasma and/or liver and therefore would not be systemically available.

From the acute toxicity studies (Bächtold, 1972, 1973a, b), it appears that ascorbyl palmitate and stearate have very low acute toxicity.

The only chronic and carcinogenicity study available was performed with ascorbyl palmitate (Fitzhugh and Nelson, 1946). It was not performed according to current standards. The Panel considered the study not adequate for the re-evaluation of ascorbyl palmitate as a food additive because the group sizes were too small, only one sex was used, histopathological examination was limited and only two doses were tested.

There was only one *in vitro* mutagenicity study on ascorbyl palmitate available, from which ascorbyl palmitate did not show any mutagenic activity. No genotoxicity studies were available for ascorbyl stearate.

No studies on reproductive and developmental toxicity on ascorbyl palmitate or ascorbyl stearate were available.

The Panel considered that, in addition to the data obtained in studies with ascorbyl palmitate, the toxicity of ascorbyl palmitate and ascorbyl stearate could be evaluated by considering the toxicity of ascorbic, palmitic and stearic acids resulting from the hydrolysis of the ester. The Panel noted that stearic and palmitic acids are natural components of the regular human diet and that the safety of ascorbic acid has recently been evaluated by the Panel (EFSA ANS Panel, 2015).

JECFA established ADIs "not specified" for myristic, palmitic, stearic, capric, caprylic, lauric and oleic fatty acids and stated that "*Their safety is based on their occurrence in edible fats and oils that have a long history of use as foods or food components. In addition, the even-chain fatty acids from C_4 to C_{18} have been shown to undergo oxidation to give acetoacetic acid and ketone bodies. The metabolic products are utilized and excreted*" (JECFA, 1986). The Panel agreed with JECFA

conclusion for palmitic and stearic acids. In addition, the Panel considered the recent opinion on the re-evaluation of ascorbic acid and its salts (EFSA ANS Panel, 2015) where it was concluded that the available data for ascorbic acid and its salts did not report any adverse effects in animal studies, even at the highest dose tested (3 000 mg/kg bw/day).

The Panel considered that the available toxicological data were too limited to establish an ADI for ascorbyl palmitate (E 304(i)) or ascorbyl stearate (E 304(ii)).

For ascorbyl palmitate (E 304(i)) and ascorbyl stearate (E 304(ii)), it was not possible to carry out an exposure assessment scenario based on MPLs as set out in the EU legislation, as, for most of the food categories, these food additives are authorised according to *QS*. Therefore, maximum levels of the available use levels provided by industry were used to provide a conservative combined exposure estimate scenario (noted as *maximum level exposure assessment* scenario). As it is considered unlikely that more than one antioxidant is used in any food items, for all scenarios, the Panel estimated the combined exposure to ascorbyl palmitate (E 304(i)) and ascorbyl stearate (E 304(ii)) using the highest concentration reported from any of them for each food category.

Based on the available dataset, the Panel calculated combined exposure estimates for fatty acid esters of ascorbic acid (E 304) following two refined exposure scenarios based on different assumptions: a "brand-loyal consumer scenario", where it is assumed that a consumer is exposed over a long time to the food additive present at the maximum reported use levels for one food category and at the mean levels for the remaining food categories; and a "non-brand-loyal scenario", where it is assumed that a consumer is exposed over a long time to the food additive present at the mean reported use levels in all food.

From the *maximum level exposure assessment*, mean estimates ranged from 0.2 to 3.2 mg/kg bw/day across all population groups. Estimates based on the high percentile (95th percentile) ranged from 0.4 to 10.8 mg/kg bw/day across all population groups.

From the *refined estimated exposure scenario* in the *brand-loyal scenario*, mean exposure fatty acid esters of ascorbic acid (E 304) from their use as food additives ranged from 0.2 mg/kg bw/day, for adults and the elderly, to 2.6 mg/kg bw/day, in children. The high exposure to fatty acid esters of ascorbic acid (E 304) ranged from 0.3 mg/kg bw/day, for adults and the elderly, to 9.9 mg/kg bw/day, in children. The main contributing food categories for all groups were processed fruit and vegetables. In the *non-brand-loyal scenario*, mean exposure to fatty acid esters of ascorbic acid (E 304) ranged from 0.1 mg/kg bw/day, for adults and the elderly, to 1.8 mg/kg bw/day, in children. The high exposure ranged from 0.2 mg/kg bw/day, for adults and the elderly, to 7.3 mg/kg bw/day, in children. The main contributing food category for all groups was processed fruit and vegetables, and for infants, foods for infants and young children was also an important contributor.

The Panel noted that from the literature (Nkondjock et al., 2003; Ramirez-Silva et al., 2011; Huang et al., 2012) the daily intake of stearic acid from the regular diet ranged from 3 100 to 6 500 mg/person/day with a mean of 5 500 mg/person/day. In addition, the intake of palmitic acid ranged from 8 400 to 14 200 mg/person/day with a mean of 12 200 mg/person/day. The Panel noted that intake of palmitic and stearic acids from the use of ascorbyl palmitate and ascorbyl stearate as food additives represents only a limited fraction (around 3 %) of their daily intake from the regular diet.

The Panel noted that the refined exposure estimates will not cover future changes in the level of use of these food additives.

The Panel noted that in Annex II of Regulation (EC) No 1333/2008 use levels of ascorbyl palmitate (E 304(i)) in food for infants under the age of 12 weeks are included in categories 13.1.1, 13.1.5.1 and 13.1.5.2. The Panel considered that these uses would require a specific risk assessment in line with the recommendations given by JECFA (1978) and SCF (1998b) and endorsed by the Panel (EFSA ANS

Panel, 2012). Therefore the current re-evaluation of ascorbyl palmitate (E 304(i)) as a food additive is not considered to be applicable for infants under the age of 12 weeks.

CONCLUSIONS

The Panel concluded that the available toxicological data were too limited to establish an ADI for ascorbyl palmitate (E 304(i)) or ascorbyl stearate (E 304(ii)).

The Panel concluded that ascorbyl palmitate and ascorbyl stearate are hydrolysed and not systemically available and therefore their toxicity can be extrapolated from the data available for ascorbic acid, palmitic acid and stearic acid.

Considering the available data, the Panel concluded that there is no safety concern for the use of ascorbyl palmitate (E 304(i)) and ascorbyl stearate (E 304(ii)) as food additives at the reported uses and use levels.

RECOMMENDATIONS

The Panel recommended that:

- limits for residual solvents should be included in the EC specifications;
- the maximum limits for the impurities of toxic elements (lead, mercury and arsenic) in the EC specification for ascorbyl palmitate (E 304(i)) and ascorbyl stearate (E 304(ii)) should be revised in order to ensure that ascorbyl palmitate (E 304(i)) and ascorbyl stearate (E 304(ii)) as food additives will not be a significant source of exposure to those toxic elements in food.
- the current EINECS Number in the EC specifications for ascorbyl stearate (E 304(ii)) should be substituted with 234-231-5.

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APPENDICES

Appendix A. Summary of the reported use levels (mg/kg or mg/L as appropriate) of fatty acid esters of ascorbic acid (E 304) provided by industry

FCS category number	FCS food category	paramCode_text	exprRes	MPL	Restrictions	n	Reported use levels	
							Typical mean	Highest maximum level
1.3	Unflavoured fermented products, heat-treated after fermentation	Ascorbyl palmitate	Fat weight	*QS*		1	100.0	250.0
1.3	Unflavoured fermented products, heat-treated after fermentation	Ascorbyl stearate	Fat weight	*QS*		1	100.0	250.0
1.4	Flavoured fermented milk products, including heat-treated products	Ascorbyl palmitate	Fat weight	*QS*		1	100.0	250.0
1.4	Flavoured fermented milk products, including heat-treated products	Ascorbyl stearate	Fat weight	*QS*		1	100.0	250.0
1.5	Dehydrated milk as defined by Directive 2001/114/EC	Ascorbyl palmitate	Fat weight	*quantum satis*		1	300.0	500.0
1.5	Dehydrated milk as defined by Directive 2001/114/EC	Ascorbyl stearate	Fat weight	*quantum satis*		1	300.0	500.0
1.6.3	Other creams	Ascorbyl palmitate	Whole weight	*QS*		1	11.2	53.8
1.6.3	Other creams	Ascorbyl palmitate	Fat weight	*QS*		1	100.0	250.0
1.6.3	Other creams	Ascorbyl stearate	Fat weight	*QS*		1	100.0	250.0
1.7.1	Unripened cheese, excluding products falling in category 16	Ascorbyl palmitate	Fat weight	*QS*	Except mozzarella	1	100.0	250.0
1.7.1	Unripened cheese, excluding products falling in category 16	Ascorbyl stearate	Fat weight	*QS*	Except mozzarella	1	100.0	250.0
1.7.5	Processed cheese	Ascorbyl palmitate	Fat weight	*QS*		1	100.0	250.0
1.7.5	Processed cheese	Ascorbyl stearate	Fat weight	*QS*		1	100.0	250.0
1.7.6	Cheese products (excluding products falling in category 16)	Ascorbyl palmitate	Fat weight	*QS*		1	0.0	0.0
1.7.6	Cheese products (excluding products falling in category 16)	Ascorbyl stearate	Fat weight	*QS*		1	0.0	0.0
1.8	Dairy analogues, including beverage	Ascorbyl	Fat weight	*QS*		1	100.0	250.0

FCS category number	FCS food category	paramCode_text	exprRes	MPL	Restrictions	n	Reported use levels	
							Typical mean	Highest maximum level
	whiteners	palmitate						
1.8	Dairy analogues, including beverage whiteners	Ascorbyl stearate	Fat weight	*QS*		1	100.0	250.0
2.1	Fats and oils essentially free from water (excluding anhydrous milk fat)	Ascorbyl palmitate	Fat weight	*QS*		1	200.0	300.0
2.1	Fats and oils essentially free from water (excluding anhydrous milk fat)	Ascorbyl stearate	Fat weight	*QS*		1	200.0	300.0
2.2.2	Other fat and oil emulsions, including spreads as defined by Council Regulation (EC) No 1234/2007 and liquid emulsions	Ascorbyl palmitate	Fat weight	*QS*		1	200.0	300.0
2.2.2	Other fat and oil emulsions, including spreads as defined by Council Regulation (EC) No 1234/2007 and liquid emulsions	Ascorbyl stearate	Fat weight	*QS*		1	200.0	300.0
2.2.2	Other fat and oil emulsions, including spreads as defined by Council Regulation (EC) No 1234/2007 and liquid emulsions	Ascorbyl palmitate	Whole weight	*QS*		2	0.5	0.8
2.3	Vegetable oil pan spray	Ascorbyl palmitate	Fat weight	*QS*		1	200.0	300.0
2.3	Vegetable oil pan spray	Ascorbyl stearate	Fat weight	*QS*		1	200.0	300.0
3	Edible ices	Ascorbyl palmitate	Fat weight	*QS*		1	0.0	0.0
3	Edible ices	Ascorbyl palmitate	Whole weight	*QS*		7	15.9	100.0
3	Edible ices	Ascorbyl stearate	Fat weight	*QS*		1	0.0	0.0
4.2.1	Dried fruit and vegetables	Ascorbyl palmitate	Fat weight	*QS*		1	300.0	500.0
4.2.1	Dried fruit and vegetables	Ascorbyl stearate	Fat weight	*QS*		1	300.0	500.0
4.2.2	Fruit and vegetables in vinegar, oil or brine	Ascorbyl palmitate	Fat weight	*QS*		1	300.0	500.0

FCS category number	FCS food category	paramCode_text	exprRes	MPL	Restrictions	n	Reported use levels	
							Typical mean	Highest maximum level
4.2.2	Fruit and vegetables in vinegar, oil or brine	Ascorbyl stearate	Fat weight	*QS*		1	300.0	500.0
4.2.4.1	Fruit and vegetable preparations, excluding compote	Ascorbyl palmitate	Fat weight	*QS*		1	300.0	500.0
4.2.4.1	Fruit and vegetable preparations, excluding compote	Ascorbyl stearate	Fat weight	*QS*		1	300.0	500.0
4.2.5.4	Nut butters and nut spreads	Ascorbyl palmitate	Fat weight	*QS*		1	200.0	300.0
4.2.5.4	Nut butters and nut spreads	Ascorbyl stearate	Fat weight	*QS*		1	200.0	300.0
4.2.6	Processed potato products	Ascorbyl palmitate	Fat weight	*QS*		1	100.0	1000.0
4.2.6	Processed potato products	Ascorbyl stearate	Fat weight	*QS*		1	100.0	1000.0
4.2.6	Processed potato products	Ascorbyl palmitate	Whole weight	*QS*		3	122.3	349.0
5.2	Other confectionery, including breath refreshening microsweets	Ascorbyl palmitate	Fat weight	*QS*		1	300.0	500.0
5.2	Other confectionery, including breath refreshening microsweets	Ascorbyl stearate	Fat weight	*QS*		1	300.0	500.0
5.3	Chewing gum	Ascorbyl palmitate	Fat weight	*QS*		1	300.0	500.0
5.3	Chewing gum	Ascorbyl palmitate	Whole weight	*QS*		1	25 000.0	35 000.0
5.3	Chewing gum	Ascorbyl stearate	Fat weight	*QS*		1	300.0	500.0
5.3	Chewing gum	Ascorbyl stearate	Whole weight	*QS*		1	25000.0	35000.0
5.4	Decorations, coatings and fillings, except fruit-based fillings covered by category 4.2.4	Ascorbyl palmitate	Fat weight	*QS*		2	175.0	350.0
5.4	Decorations, coatings and fillings, except fruit-based fillings covered by category 4.2.4	Ascorbyl stearate	Fat weight	*QS*		2	175.0	350.0
		Ascorbyl palmitate	Whole weight	*QS*		1	0.0	0.0
6.3	Breakfast cereals	Ascorbyl	Whole	*QS*		4	48.1	192.0

FCS category number	FCS food category	paramCode_text	exprRes	MPL	Restrictions	n	Reported use levels Typical mean	Reported use levels Highest maximum level
		palmitate	weight					
6.4.4	Potato gnocchi	Ascorbyl palmitate	Fat weight	*QS*	Only fresh refrigerated potato gnocchi	1	0.0	250.0
6.4.4	Potato gnocchi	Ascorbyl stearate	Fat weight	*QS*	Only fresh refrigerated potato gnocchi	1	0.0	250.0
6.4.5	Fillings of stuffed pasta (ravioli and similar)	Ascorbyl palmitate	Fat weight	*QS*		1	0.0	250.0
6.4.5	Fillings of stuffed pasta (ravioli and similar)	Ascorbyl stearate	Fat weight	*QS*		1	0.0	250.0
6.5	Noodles	Ascorbyl palmitate	Fat weight	*QS*		1	0.0	250.0
6.5	Noodles	Ascorbyl stearate	Fat weight	*QS*		1	0.0	250.0
6.7	Pre-cooked or processed cereals	Ascorbyl palmitate	Fat weight	*QS*		1	0.0	250.0
6.7	Pre-cooked or processed cereals	Ascorbyl stearate	Fat weight	*QS*		1	0.0	250.0
7.1	Bread and rolls	Ascorbyl palmitate	Fat weight	*QS*	Except products in categories 7.1.1 and 7.1.2	1	50.0	150.0
7.1	Bread and rolls	Ascorbyl stearate	Fat weight	*QS*	Except products in categories 7.1.1 and 7.1.2	1	50.0	150.0
7.2	Fine bakery wares	Ascorbyl palmitate	Fat weight	*QS*		1	50.0	150.0
7.2	Fine bakery wares	Ascorbyl palmitate	Whole weight	*QS*		1	54.5	54.5
7.2	Fine bakery wares	Ascorbyl stearate	Fat weight	*QS*		1	50.0	150.0
8.3	Processed meat	Ascorbyl palmitate	Whole weight	*QS*		1	1 500.0	1 500.0
8.3	Processed meat	Ascorbyl stearate	Whole weight	*QS*		1	1 500.0	1 500.0
8.3.1	Non-heat-treated processed meat	Ascorbyl palmitate	Fat weight	*QS*		1	0.0	300.0
8.3.1	Non-heat-treated processed meat	Ascorbyl stearate	Fat weight	*QS*		1	0.0	300.0
8.3.3	Casings and coatings and decorations for meat	Ascorbyl palmitate	Fat weight	*QS*		1	0.0	300.0
8.3.3	Casings and coatings and	Ascorbyl stearate	Fat weight	*QS*		1	0.0	300.0

FCS category number	FCS food category	paramCode_text	exprRes	MPL	Restrictions	n	Reported use levels Typical mean	Reported use levels Highest maximum level
	decorations for meat							
9.2	Processed fish and fishery products, including molluscs and crustaceans	Ascorbyl palmitate	Fat weight	*QS*		1	100.0	250.0
9.2	Processed fish and fishery products including molluscs and crustaceans	Ascorbyl stearate	Fat weight	*QS*		1	100.0	250.0
9.3	Fish roe	Ascorbyl palmitate	Fat weight	*QS*	Only processed fish roe	1	100.0	250.0
9.3	Fish roe	Ascorbyl stearate	Fat weight	*QS*	Only processed fish roe	1	100.0	250.0
10.2	Processed eggs and egg products	Ascorbyl palmitate	Fat weight	*QS*		1	100.0	250.0
10.2	Processed eggs and egg products	Ascorbyl stearate	Fat weight	*QS*		1	100.0	250.0
11.2	Other sugars and syrups	Ascorbyl palmitate	Fat weight	*QS*		1	300.0	500.0
11.2	Other sugars and syrups	Ascorbyl stearate	Fat weight	*QS*		1	300.0	500.0
12.1.2	Salt substitutes	Ascorbyl palmitate	Fat weight	*QS*		1	300.0	500.0
12.1.2	Salt substitutes	Ascorbyl stearate	Fat weight	*QS*		1	300.0	500.0
12.2.2	Seasonings and condiments	Ascorbyl palmitate	Whole weight	*QS*		5	8.9	33.8
12.2.2	Seasonings and condiments	Ascorbyl palmitate	Fat weight	*QS*		1	300.0	500.0
12.2.2	Seasonings and condiments	Ascorbyl stearate	Fat weight	*QS*		1	300.0	500.0
12.3	Vinegars	Ascorbyl palmitate	Fat weight	*QS*		1	300.0	500.0
12.3	Vinegars	Ascorbyl stearate	Fat weight	*QS*		1	300.0	500.0
12.4	Mustard	Ascorbyl palmitate	Fat weight	*QS*		1	100.0	250.0
12.4	Mustard	Ascorbyl palmitate	Whole weight	*QS*		1	0.9	0.9
12.4	Mustard	Ascorbyl stearate	Fat weight	*QS*		1	100.0	250.0
12.5	Soups and broths	Ascorbyl palmitate	Fat weight	*QS*		1	100.0	250.0
12.5	Soups and broths	Ascorbyl	Whole	*QS*		13	2.3	10.2

FCS category number	FCS food category	paramCode_text	exprRes	MPL	Restrictions	n	Reported use levels Typical mean	Reported use levels Highest maximum level
		palmitate	weight					
12.5	Soups and broths	Ascorbyl stearate	Fat weight	*QS*		1	100.0	250.0
12.6	Sauces	Ascorbyl palmitate	Fat weight	*QS*		1	100.0	250.0
12.6	Sauces	Ascorbyl palmitate	Whole weight	*QS*		13	5.8	64.2
12.6	Sauces	Ascorbyl stearate	Fat weight	*QS*		1	100.0	250.0
12.7	Salads and savoury-based sandwich spreads	Ascorbyl palmitate	Fat weight	*QS*		1	100.0	250.0
12.7	Salads and savoury-based sandwich spreads	Ascorbyl stearate	Fat weight	*QS*		1	100.0	250.0
12.8	Yeast and yeast products	Ascorbyl palmitate	Fat weight	*QS*		1	100.0	250.0
12.8	Yeast and yeast products	Ascorbyl stearate	Fat weight	*QS*		1	100.0	250.0
12.9	Protein products, excluding products covered in category 1.8	Ascorbyl palmitate	Fat weight	*QS*		1	100.0	250.0
12.9	Protein products, excluding products covered in category 1.8	Ascorbyl stearate	Fat weight	*QS*		1	100.0	250.0
13.1.1	Infant formulae as defined by Directive 2006/141/EC	Ascorbyl palmitate	Whole weight	10		5	5.5	10.0
13.1.1	Infant formulae as defined by Directive 2006/141/EC	Ascorbyl stearate	Whole weight	10		2	0.0	10.0
13.1.2	Follow-on formulae as defined by Directive 2006/141/EC	Ascorbyl palmitate	Whole weight	10		5	5.1	10.0
13.1.2	Follow-on formulae as defined by Directive 2006/141/EC	Ascorbyl stearate	Whole weight	10		2	0.0	10.0
13.1.3	Processed cereal-based foods and baby foods for infants and young children as defined by Directive 2006/125/EC	Ascorbyl palmitate	Whole weight	100		4	14.3	100.0
13.1.3	Processed cereal-based foods and baby foods for infants and young children as defined by Directive 2006/125/EC	Ascorbyl stearate	Whole weight	100		1	0.0	100.0

FCS category number	FCS food category	paramCode_text	exprRes	MPL	Restrictions	n	Reported use levels	
							Typical mean	Highest maximum level
13.1.4	Other foods for young children	Ascorbyl palmitate	Whole weight	100		2	5.0	100.0
13.1.4	Other foods for young children	Ascorbyl stearate	Whole weight	100		1	0.0	100.0
13.1.5.1	Dietary foods for infants for special medical purposes and special formulae for infants	Ascorbyl palmitate	Fat weight	100		1	0.0	100.0
13.1.5.1	Dietary foods for infants for special medical purposes and special formulae for infants	Ascorbyl palmitate	Whole weight	100		5	7.3	13.0
13.1.5.1	Dietary foods for infants for special medical purposes and special formulae for infants	Ascorbyl stearate	Fat weight	100		1	0.0	100.0
13.1.5.2	Dietary foods for babies and young children for special medical purposes as defined in Directive 1999/21/EC	Ascorbyl palmitate	Whole weight	100		3	8.7	10.0
13.2	Dietary foods for special medical purposes defined in Directive 1999/21/EC (excluding products from food category 13.1.5)	Ascorbyl palmitate	Fat weight	*QS*		1	0.0	100.0
13.2	Dietary foods for special medical purposes defined in Directive 1999/21/EC (excluding products from food category 13.1.5)	Ascorbyl palmitate	Whole weight	*QS*		1	7.7	14.6
13.2	Dietary foods for special medical purposes defined in Directive 1999/21/EC (excluding products from food category 13.1.5)	Ascorbyl stearate	Fat weight	*QS*		1	0.0	100.0
13.3	Dietary foods for weight control diets intended to replace total daily food intake or an individual meal (the whole or part of the total daily diet)	Ascorbyl palmitate	Fat weight	*QS*		1	0.0	100.0

FCS category number	FCS food category	paramCode_text	exprRes	MPL	Restrictions	n	Reported use levels	
							Typical mean	Highest maximum level
13.3	Dietary foods for weight control diets intended to replace total daily food intake or an individual meal (the whole or part of the total daily diet)	Ascorbyl stearate	Fat weight	*QS*		1	0.0	100.0
13.4	Foods suitable for people intolerant to gluten as defined by Regulation (EC) 41/2009	Ascorbyl palmitate	Fat weight	*QS*	Including dry pasta	1	0.0	100.0
13.4	Foods suitable for people intolerant to gluten as defined by Regulation (EC) 41/2009	Ascorbyl stearate	Fat weight	*QS*	Including dry pasta	1	0.0	100.0
14.1.2	Fruit juices as defined by Council Directive 2001/112/EC and vegetable juices	Ascorbyl palmitate	Fat weight	*QS*	Only vegetable juices	1	300.0	500.0
14.1.2	Fruit juices as defined by Council Directive 2001/112/EC and vegetable juices	Ascorbyl stearate	Fat weight	*QS*	Only vegetable juices	1	300.0	500.0
14.1.3	Fruit nectars as defined by Council Directive 2001/112/EC and vegetable nectars and similar products	Ascorbyl palmitate	Fat weight	*QS*	Only vegetable nectars	1	300.0	500.0
14.1.3	Fruit nectars as defined by Council Directive 2001/112/EC and vegetable nectars and similar products	Ascorbyl stearate	Fat weight	*QS*	Only vegetable nectars	1	300.0	500.0
14.1.4	Flavoured drinks	Ascorbyl palmitate	Fat weight	*QS*		1	300.0	500.0
14.1.4	Flavoured drinks	Ascorbyl stearate	Fat weight	*QS*		1	300.0	500.0
14.2.1	Beer and malt beverages	Ascorbyl palmitate	Fat weight	*QS*		1	300.0	500.0
14.2.1	Beer and malt beverages	Ascorbyl stearate	Fat weight	*QS*		1	300.0	500.0
14.2.3	Cider and perry	Ascorbyl palmitate	Fat weight	*QS*		1	300.0	500.0
14.2.3	Cider and perry	Ascorbyl stearate	Fat weight	*QS*		1	300.0	500.0

FCS category number	FCS food category	paramCode_text	exprRes	MPL	Restrictions	n	Reported use levels	
							Typical mean	Highest maximum level
14.2.4	Fruit wine and made wine	Ascorbyl palmitate	Fat weight	*QS*		1	300.0	500.0
14.2.4	Fruit wine and made wine	Ascorbyl stearate	Fat weight	*QS*		1	300.0	500.0
14.2.5	Mead	Ascorbyl palmitate	Fat weight	*QS*		1	300.0	500.0
14.2.5	Mead	Ascorbyl stearate	Fat weight	*QS*		1	300.0	500.0
14.2.6	Spirit drinks as defined in Regulation (EC) No 110/2008	Ascorbyl palmitate	Fat weight	*QS*	Except whisky or whiskey	1	300.0	500.0
14.2.6	Spirit drinks as defined in Regulation (EC) No 110/2008	Ascorbyl stearate	Fat weight	*QS*	Except whisky or whiskey	1	300.0	500.0
14.2.7	Aromatised wine-based products	Ascorbyl palmitate	Fat weight	*QS*		1	300.0	500.0
14.2.7	Aromatised wine-based products	Ascorbyl stearate	Fat weight	*QS*		1	300.0	500.0
14.2.8	Other alcoholic drinks, including mixtures of alcoholic drinks with non-alcoholic drinks and spirits less than 15 % alcohol	Ascorbyl palmitate	Fat weight	*QS*		1	300.0	500.0
14.2.8	Other alcoholic drinks, including mixtures of alcoholic drinks with non-alcoholic drinks and spirits less than 15 % alcohol	Ascorbyl stearate	Fat weight	*QS*		1	300.0	500.0
15.1	Potato-, cereal-, flour- or starch-based snacks	Ascorbyl palmitate	Fat weight	*QS*		1	300.0	500.0
15.1	Potato-, cereal-, flour- or starch-based snacks	Ascorbyl stearate	Fat weight	*QS*		1	300.0	500.0
15.2	Processed nuts	Ascorbyl palmitate	Fat weight	*QS*		1	300.0	500.0
15.2	Processed nuts	Ascorbyl stearate	Fat weight	*QS*		1	300.0	500.0
16	Desserts, excluding products covered in categories 1, 3 and 4	Ascorbyl palmitate	Fat weight	*QS*		1	300.0	500.0
16	Desserts excluding products covered in categories 1, 3 and 4	Ascorbyl palmitate	Whole weight	*QS*		4	37.1	100.0
16	Desserts excluding products covered in categories 1, 3 and 4	Ascorbyl stearate	Fat weight	*QS*		1	300.0	500.0

FCS category number	FCS food category	paramCode_text	exprRes	MPL	Restrictions	n	Reported use levels	
							Typical mean	Highest maximum level
17.1	Food supplements supplied in a solid form, including capsules and tablets and similar forms, excluding chewable forms	Ascorbyl palmitate	Fat weight	*QS*		1	0.0	1 000.0
17.1	Food supplements supplied in a solid form, including capsules and tablets and similar forms, excluding chewable forms	Ascorbyl stearate	Fat weight	*QS*		1	0.0	1 000.0
17.2	Food supplements supplied in a liquid form	Ascorbyl palmitate	Fat weight	*QS*		1	0.0	1 000.0
17.2	Food supplements supplied in a liquid form	Ascorbyl stearate	Fat weight	*QS*		1	0.0	1 000.0
17.3	Food supplements supplied in a syrup-type or chewable form	Ascorbyl palmitate	Fat weight	*QS*		1	0.0	1 000.0
17.3	Food supplements supplied in a syrup-type or chewable form	Ascorbyl stearate	Fat weight	*QS*		1	0.0	1 000.0
18	Processed foods not covered by categories 1 to 17, excluding foods for infants and young children	Ascorbyl palmitate	Fat weight	*QS*		1	0.0	1 000.0
18	Processed foods not covered by categories 1 to 17, excluding foods for infants and young children	Ascorbyl stearate	Fat weight	*QS*		1	0.0	1 000.0

Appendix B. Concentration levels of fatty acid esters of ascorbic acid (E 304) used in the maximum level exposure assessment scenario and in the refined exposure scenarios (mg/kg or ml/kf as appropriate)

FCS category number	FCS food category	Restrictions/exceptions	MPL (mg/L or mg/kg as appropriate)	Concentration levels used in the refined exposure assessment		Data sources/comments
				Mean	Maximum	
01.3	Unflavoured fermented products, heat-treated after fermentation		*QS*	100	250	Reported use levels provided in fat weight
01.4	Flavoured fermented milk products, including heat treated products		*QS*	100	250	Reported use levels provided in fat weight
01.5	Dehydrated milk as defined by Directive 2001/114/EC		*QS*	300	500	Reported use levels provided in fat weight
01.6.3	Other creams		*QS*	11.2	53.8	
01.7.1	Unripened cheese, excluding products falling in category 16	Except *mozzarella*	*QS*	100	250	Reported use levels provided in fat weight
01.7.5	Processed cheese		*QS*	100	250	Reported use levels provided in fat weight
01.7.6	Cheese products (excluding products falling in category 16)		*QS*			Not taken into account (no corresponding FoodEx code)
01.8	Dairy analogues, including beverage whiteners		*QS*	100	250	Reported use levels provided in fat weight
02.1	Fats and oils essentially free from water (excluding anhydrous milk fat)	Except virgin oils and olive oils	*QS*	200	300	Reported use levels provided in fat weight
02.2.2	Other fat and oil emulsions including spreads as defined by Council Regulation (EC) No 1234/2007 and liquid emulsions		*QS*	0.5	0.8	
02.3	Vegetable oil pan spray		*QS*			Not taken into account (no corresponding FoodEx code)
03	Edible ices		*QS*	15.9	100	
04.2.1	Dried fruit and vegetables		*QS*	300	500	Reported use levels provided in fat weight
04.2.2	Fruit and vegetables in vinegar, oil or brine		*QS*	300	500	Reported use levels provided in fat weight
04.2.4.1	Fruit and vegetable preparations, excluding compote		*QS*	300	500	Reported use levels provided in fat weight
04.2.5.4	Nut butters and nut spreads		*QS*	200	300	Reported use levels provided in fat weight
04.2.6	Processed potato products		*QS*	122.3	349	Reported use levels provided in fat weight

FCS category number	FCS food category	Restrictions/exceptions	MPL (mg/L or mg/kg as appropriate)	Concentration levels used in the refined exposure assessment		Data sources/comments
				Mean	Maximum	
05.1	Cocoa and Chocolate products as covered by Directive 2000/36/EC	Only energy-reduced or with no added sugars	*QS*	250	350	Reported use levels provided in fat weight
05.2	Other confectionery, including breath refreshening microsweets		*QS*	300	500	Reported use levels provided in fat weight
05.3	Chewing gum		*QS*	25 000	35 000	
05.4	Decorations, coatings and fillings, except fruit-based fillings covered by category 4.2.4		*QS*			Not taken into account (no corresponding FoodEx code)
06.2.2	Starches		*QS*			Not taken into account (no concentration data available)
06.3	Breakfast cereals		*QS*	38.5	192	
06.4.2	Dry pasta	Only gluten free and/or pasta intended for hypoproteic diets in accordance with Directive 2009/39/EC	*QS*	0	250	Reported use levels provided in fat weight
06.4.4	Potato Gnocchi	Only fresh refrigerated potato gnocchi	*QS*			Not taken into account (no corresponding FoodEx code)
06.4.5	Fillings of stuffed pasta (ravioli and similar)		*QS*	0	250	Reported use levels provided in fat weight
06.5	Noodles		*QS*	0	250	Reported use levels provided in fat weight
06.6	Batters		*QS*			Not taken into account (no corresponding FoodEx code)
06.7	Pre-cooked or processed cereals		*QS*			Not taken into account (no corresponding FoodEx code)
07.1.1	Bread prepared solely with the following ingredients: wheat flour, water, yeast or leaven, salt		*QS*	150	50	Reported use levels provided in fat weight
07.1.2	Pain courant francais; Friss búzakenyér, fehér és félbarna kenyerek	Only *Friss búzakenyér, fehér és félbarna kenyerek*	*QS*	150	50	Reported use levels provided in fat weight
07.1	Bread and rolls	Except products in categories 7.1.1 and 7.1.2	*QS*	150	50	Reported use levels provided in fat weight
07.2	Fine bakery wares		*QS*	54.5	54.5	
08.2.1	Non-heat-treated processed meat		*QS*	1 500	1 500	

FCS category number	FCS food category	Restrictions/exceptions	MPL (mg/L or mg/kg as appropriate)	Concentration levels used in the refined exposure assessment		Data sources/comments
				Mean	Maximum	
08.3.2	Heat-treated processed meat	Except Foie gras, foie gras entier, blocs de foie gras, Libamáj, libamáj egészben, libamáj tömbben	*QS*	1 500	1500	
08.3.3	Casings and coatings and decorations for meat		*QS*			Not taken into account (no corresponding FoodEx code)
09.2	Processed fish and fishery products, including molluscs and crustaceans		*QS*	100	250	Reported use levels provided in fat weight
09.3	Fish roe	Only processed fish roe	*QS*	100	250	Reported use levels provided in fat weight
10.2	Processed eggs and egg products		*QS*	100	250	Reported use levels provided in fat weight
11.2	Other sugars and syrups		*QS*			Not taken into account (levels provided in fat weight, considered not relevant for the exposure assessment)
12.1.2	Salt substitutes		*QS*			Not taken into account (no corresponding FoodEx code)
12.2.2	Seasonings and condiments		*QS*	8.9	33.8	
12.3	Vinegars		*QS*			Not taken into account (levels provided in fat weight, considered not relevant for the exposure assessment)
12.4	Mustard		*QS*	0.9	0.9	
12.5	Soups and broths		*QS*	2.3	10.2	
12.6	Sauces		*QS*	5.8	64.2	
12.7	Salads and savoury-based sandwich spreads		*QS*	5.8	64.2	
12.8	Yeast and yeast products		*QS*			Not taken into account (levels provided in fat weight, considered not relevant for the exposure assessment)
12.9	Protein products, excluding products covered in category 1.8		*QS*	100	250	Reported use levels provided in fat weight
13.1.1	Infant formulae as defined by Directive 2006/141/EC		10	5.5	10	
13.1.2	Follow-on formulae as defined by Directive 2006/141/EC		10	5.1	10	
13.1.3	Processed cereal-based foods and	Only fat-containing cereal-	100	14.3	100	

FCS category number	FCS food category	Restrictions/exceptions	MPL (mg/L or mg/kg as appropriate)	Concentration levels used in the refined exposure assessment		Data sources/comments
				Mean	Maximum	
	baby foods for infants and young children as defined by Directive 2006/125/EC	based foods, including biscuits and rusks and baby foods				
13.1.4	Other foods for young children		100	5	100	
13.1.5.1	Dietary foods for infants for special medical purposes and special formulae for infants		100	7.3	13	
13.1.5.2	Dietary foods for babies and young children for special medical purposes as defined in Directive 1999/21/EC		100	8.7	10	
13.2	Dietary foods for special medical purposes defined in Directive 1999/21/EC (excluding products from food category 13.1.5)		*QS*	7.7	14.6	
13.3	Dietary foods for weight control diets intended to replace total daily food intake or an individual meal (the whole or part of the total daily diet)		*QS*	0	100	Reported use levels provided in fat weight
13.4	Foods suitable for people intolerant to gluten as defined by Regulation (EC) 41/2009	Including dry pasta	*QS*	0	100	Reported use levels provided in fat weight
14.1.2	Fruit juices as defined by Council Directive 2001/112/EC and vegetable juices	Only vegetable juices	*QS*			Not taken into account (levels provided in fat weight, considered not relevant for the exposure assessment)
14.1.3	Fruit nectars as defined by Council Directive 2001/112/EC and vegetable nectars and similar products	Only vegetable nectars	*QS*			Not taken into account (levels provided in fat weight, considered not relevant for the exposure assessment)
14.1.4	Flavoured drinks		*QS*			Not taken into account (levels provided in fat weight, considered not relevant for the exposure assessment)
14.1.5.2	Other	Excluding unflavoured leaf tea; including flavoured instant coffee	*QS*			Not taken into account (levels provided in fat weight, considered not relevant for the exposure assessment)
14.2.3	Cider and perry		*QS*			Not taken into account (levels provided in

FCS category number	FCS food category	Restrictions/exceptions	MPL (mg/L or mg/kg as appropriate)	Concentration levels used in the refined exposure assessment		Data sources/comments
				Mean	Maximum	
						fat weight, considered not relevant for the exposure assessment)
14.2.4	Fruit wine and made wine		*QS*			Not taken into account (no corresponding FoodEx code)
14.2.5	Mead		*QS*			Not taken into account (no corresponding FoodEx code)
14.2.6	Spirit drinks as defined in Regulation (EC) No 110/2008	Except whisky or whiskey	*QS*			Not taken into account (levels provided in fat weight, considered not relevant for the exposure assessment)
14.2.7.1	Aromatised wines		*QS*			Not taken into account (levels provided in fat weight, considered not relevant for the exposure assessment)
14.2.7.2	Aromatised wine-based drinks		*QS*			Not taken into account (levels provided in fat weight, considered not relevant for the exposure assessment)
14.2.7.3	Aromatised wine-product cocktails		*QS*			Not taken into account (levels provided in fat weight, considered not relevant for the exposure assessment)
14.2.8	Other alcoholic drinks, including mixtures of alcoholic drinks with non-alcoholic drinks and spirits less than 15 % alcohol		*QS*			Not taken into account (levels provided in fat weight, considered not relevant for the exposure assessment)
15.1	Potato-, cereal-, flour- or starch-based snacks		*QS*	300	500	Reported use levels provided in fat weight
15.2	Processed nuts		*QS*	300	500	Reported use levels provided in fat weight
16	Desserts, excluding products covered in categories 1, 3 and 4		*QS*	37.1	100	Reported use levels provided in fat weight
17.1	Food supplements supplied in a solid form including capsules and tablets and similar forms excluding chewable forms		*QS*	0	1 000	Reported use levels provided in fat weight
17.2	Food supplements supplied in a liquid form		*QS*	0	1 000	Reported use levels provided in fat weight
17.3	Food supplements supplied in a syrup-		*QS*	0	1 000	Reported use levels provided in fat weight

FCS category number	FCS food category	Restrictions/exceptions	MPL (mg/L or mg/kg as appropriate)	Concentration levels used in the refined exposure assessment		Data sources/comments
				Mean	Maximum	
	type or chewable form					
18	Processed foods not covered by categories 1 to 17, excluding foods for infants and young children		*QS*	0	1 000	Reported use levels provided in fat weight

Appendix C. Summary of total estimated combined exposure of fatty acid esters of ascorbic acid (E 304) from their use as food additives for the maximum level exposure scenario and the refined exposure assessment scenarios per population group and survey: mean and high level (mg/kg bw/day)

	Number of subjects	Maximum level scenario		Brand-loyal scenario		Non-brand-loyal scenario	
		Mean	High level	Mean	High level	Mean	High level
Toddlers							
Belgium (Regional Flanders)	36	5.2		4.2		3.7	
Bulgaria (NUTRICHILD)	428	1.4	5.2	1.4	5.0	1.4	5.0
Germany (VELS)	348	4.4	10.4	3.7	9.2	3.3	8.8
Denmark (IAT 2006 07)	917	4.6	9.8	3.9	8.6	3.8	8.4
Spain (enKid)	17	4.2		3.7		3.4	
Finland (DIPP 2001 2009)	500	4.0	8.6	3.3	7.3	2.2	6.1
United Kingdom (NDNS-RollingProgrammeYears1-3)	185	2.7	5.9	2.2	4.8	1.7	4.8
United Kingdom (DNSIYC 2011)	1 314	2.4	6.0	2.0	5.2	1.4	4.3
Italy (INRAN SCAI 2005 06)	36	2.2		2.1		1.8	
Netherlands (VCP kids)	322	4.3	10.3	3.7	8.9	3.4	8.9
Children							
Austria (ASNS Children)	128	2.9	6.4	2.6	5.9	2.5	5.7
Belgium (Regional Flanders)	625	4.7	9.5	3.8	8.2	3.5	8.1
Bulgaria (NUTRICHILD)	433	2.1	7.3	2.0	7.3	2.0	7.3
Czech Republic (SISP04)	389	2.6	7.7	2.4	7.1	2.3	7.0
Germany (EsKiMo)	835	3.3	7.7	2.8	6.9	2.7	6.7
Germany (VELS)	293	5.1	12.5	4.4	12.3	3.9	9.9
Denmark (DANSDA 2005-08)	298	3.9	8.8	3.3	8.2	3.0	6.4
Spain (enKid)	156	4.5	11.5	4.1	11.0	3.8	10.0
Spain (NUT INK05)	399	3.6	8.0	3.1	7.0	3.0	7.0
Finland (DIPP 2001 2009)	750	4.6	10.4	3.9	9.1	3.5	8.5
France (INCA2)	482	3.1	6.4	2.5	5.4	2.4	5.3
United Kingdom (NDNS-RollingProgrammeYears1-3)	651	2.5	5.9	2.0	4.8	1.7	4.6
Greece (Regional Crete)	838	2.3	6.4	2.0	5.7	1.5	5.6
Italy (INRAN SCAI 2005 06)	193	2.3	5.8	2.0	5.2	1.8	5.2
Latvia (EFSA TEST)	187	3.2	8.3	2.6	6.6	2.2	6.4
Netherlands (VCP kids)	957	3.8	8.3	3.3	7.4	3.0	7.3
Netherlands (VCPBasis AVL2007 2010)	447	3.9	9.7	3.4	8.6	3.2	8.1
Sweden (NFA)	1 473	4.1	8.4	3.3	7.1	3.0	6.7
Adolescents							
Austria (ASNS Children)	237	1.7	4.1	1.5	3.9	1.5	3.9
Belgium (Diet National 2004)	576	1.6	3.9	1.3	3.4	1.1	3.1
Cyprus (Childhealth)	303	0.8	1.9	0.7	1.7	0.6	1.6
Czech Republic (SISP04)	298	2.3	6.6	2.3	6.6	2.2	6.6
Germany (National Nutrition Survey II)	1 011	1.6	4.3	1.4	3.9	1.3	3.7
Germany (EsKiMo)	393	2.5	5.9	2.2	5.3	2.0	5.3
Denmark (DANSDA 2005-08)	377	2.4	6.7	2.1	6.3	1.7	4.8
Spain (AESAN FIAB)	86	1.6	3.9	1.5	3.9	1.5	3.9
Spain (enKid)	209	3.0	8.4	2.8	7.7	2.5	7.7
Spain (NUT INK05)	651	2.3	5.4	2.1	4.8	2.0	4.8
Finland (NWSSP07 08)	306	2.5	5.0	2.1	4.4	1.8	3.9
France (INCA2)	973	1.8	4.2	1.5	3.5	1.4	3.2
United Kingdom (NDNS-RollingProgrammeYears1-3)	666	1.5	3.8	1.3	3.4	1.1	3.3

	Number of subjects	Maximum level scenario		Brand-loyal scenario		Non-brand-loyal scenario	
		Mean	High level	Mean	High level	Mean	High level
Italy (INRAN SCAI 2005 06)	247	1.6	3.9	1.4	3.4	1.3	3.3
Latvia (EFSA TEST)	453	2.5	5.7	2.1	5.0	1.7	4.6
Netherlands (VCPBasis AVL2007 2010)	1 142	2.7	7.0	2.3	6.1	2.1	5.9
Sweden (NFA)	1 018	2.6	5.6	2.2	4.6	1.9	4.4
Adults							
Austria (ASNS Adults)	308	1.3	3.9	1.2	3.9	1.1	3.9
Belgium (Diet National 2004)	1 292	1.4	3.4	1.2	2.9	1.0	2.8
Czech Republic (SISP04)	1 666	1.7	4.9	1.6	4.9	1.6	4.9
Germany (National Nutrition Survey II)	10 419	1.4	3.5	1.2	3.2	1.1	3.2
Denmark (DANSDA 2005-08)	1 739	1.7	4.7	1.5	4.3	1.2	3.5
Spain (AESAN)	410	1.1	3.4	1.1	3.4	1.1	3.4
Spain (AESAN FIAB)	981	1.2	2.8	1.2	2.8	1.2	2.8
Finland (FINDIET2012)	1 295	1.8	4.6	1.5	4.0	1.3	3.7
France (INCA2)	2 276	1.3	2.8	1.1	2.4	1.0	2.3
United Kingdom (NDNS-RollingProgrammeYears1-3)	1 266	1.0	2.5	0.8	2.2	0.7	2.2
Hungary (National Repr Surv)	1 074	1.5	3.8	1.5	3.8	1.5	3.8
Ireland (NANS 2012)	1 274	1.2	2.8	1.0	2.3	0.8	2.1
Italy (INRAN SCAI 2005 06)	2 313	1.0	2.4	0.9	2.2	0.8	2.1
Latvia (EFSA TEST)	1 271	1.7	4.1	1.4	3.4	1.2	3.3
Netherlands (VCPBasis AVL2007 2010)	2 057	1.6	4.2	1.4	3.8	1.3	3.6
Romania (Dieta Pilot Adults)	1 254	0.9	2.6	0.9	2.5	0.8	2.5
Sweden (Riksmaten 2010)	1 430	1.5	3.4	1.2	3.0	1.0	2.8
The elderly							
Austria (ASNS Adults)	92	1.2	3.5	1.1	3.3	1.0	3.3
Belgium (Diet National 2004)	1 215	1.5	3.3	1.3	2.7	1.0	2.6
Germany (National Nutrition Survey II)	2 496	1.4	3.1	1.2	2.7	1.1	2.7
Denmark (DANSDA 2005-08)	286	1.5	2.7	1.3	2.3	1.0	1.8
Finland (FINDIET2012)	413	1.5	3.9	1.2	3.3	1.0	2.9
France (INCA2)	348	1.2	2.4	1.0	2.2	0.9	2.1
United Kingdom (NDNS-RollingProgrammeYears1-3)	305	1.1	2.4	0.9	1.9	0.7	1.9
Hungary (National Repr Surv)	286	1.2	3.0	1.1	3.0	1.1	3.0
Ireland (NANS 2012)	226	1.5	3.4	1.2	2.6	0.9	2.5
Italy (INRAN SCAI 2005 06)	518	0.8	1.9	0.7	1.7	0.6	1.5
Netherlands (VCPBasis AVL2007 2010)	173	1.5	3.3	1.3	2.9	1.1	2.9
Netherlands (VCP-Elderly)	739	1.3	3.0	1.1	2.5	0.9	2.4
Romania (Dieta Pilot Adults)	128	0.8	2.1	0.7	2.0	0.7	2.0
Sweden (Riksmaten 2010)	367	1.6	3.6	1.4	3.0	1.1	2.8

ABBREVIATIONS

ADI	Acceptable Daily Intake
ANS	Scientific Panel on Food Additives and Nutrient Sources added to Food
bw	body weight

CAS	Chemical Abstracts Service
CIR	Cosmetic Ingredient Review
CONTAM	EFSA Panel on Contaminants in Food Chain
EC	European Commission
EINECS	European Inventory of Existing Commercial chemical Substances
EU	European Union
FAO	Food and Agriculture Organization of the United Nations
FASEB	Federation of American Societies for Experimental Biology
FCRA	Food Chemical Risk Analyses
FCS	Food Categorisation System
FDA	Food and Drug Administration
FDE	FoodDrinkEurope
FEEDAP	Scientific Panel on Additives and Products or Substances used in Animal Feed
FSMP	Foods for Special Medical Purposes
GMP	Good Manufacturing Practice
GRAS	Generally Recognized as Safe
HPLC	high-performance liquid chromatography
ICGA	International Chewing Gum Association
JECFA	Joint FAO/WHO Expert Committee on Food Additives
LD_{50}	median lethal dose
MPL	maximum permitted level
NDA	Panel on Dietetic Products, Nutrition and Allergies
OEDC	Organisation for Economic Co-operation and Development
QS	*quantum satis*
SCC	Scientific Committee on Cosmetology
SCF	Scientific Committee on Food
SNE	Specialised Nutrition Europe
TemaNord	Nordic Working Group on Food Toxicology and Risk Assessment
WHO	World Health Organization