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SCIENTIFIC OPINION

Scientific Opinion on the re-evaluation of ascorbic acid (E 300), sodium ascorbate (E 301) and calcium ascorbate (E 302) as food additives[1]

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

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ABSTRACT

The EFSA Panel on Food additives and Nutrient Sources added to Food (ANS Panel) provides a scientific opinion re-evaluating the safety of ascorbic acid (E 300), sodium ascorbate (E 301) and calcium ascorbate (E 302) as food additives. The use of ascorbic acid and its salts as food additives was evaluated by the Joint FAO/WHO Expert Committee on Food Additives and by the Scientific Committee on Food. Ascorbic acid is absorbed from the intestine by a sodium-dependent active transport process and, at low doses, the absorption is almost complete until a saturation point, after which increasing amounts of unabsorbed substance are excreted. Ascorbic acid and its salts have very low acute toxicities, and short-term tests in animals showed little effect, and even so only at high doses. The Panel concluded that there is no genotoxicity concern for ascorbic acid, sodium ascorbate or calcium ascorbate. Long-term carcinogenicity tests with ascorbic acid did not show any chronic toxicity, even at high doses, and also showed no signs of carcinogenicity. Prenatal developmental studies did not show adverse developmental effects. The Panel estimated the combined exposure to ascorbic acid (E 300), calcium ascorbate (E 301) and sodium ascorbate (E 302). The Panel concluded that, given the fact that adequate data on exposure and toxicity were available and no adverse effects were reported in animal studies, there is no safety concern for the use of ascorbic acid (E 300), sodium ascorbate (E 301) and calcium ascorbate (E 302) as food additives at the reported uses and use levels and there is no need for a numerical ADI for ascorbic acid and its salts.

KEY WORDS

Food additives, ascorbic acid (E 300), sodium ascorbate (E 301), calcium ascorbate (E 302), vitamin C

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SUMMARY

Following a request from the European Commission (EC), the Panel on Food Additives and Nutrient Sources added to Food (ANS) was asked to deliver a scientific opinion re-evaluating the safety of ascorbic acid (E 300), sodium ascorbate (E 301) and calcium ascorbate (E 302) as food additives.

The Panel was not provided with a newly submitted dossier and no new toxicological or biological information was submitted for the present re-evaluation. The Panel based its evaluation on previous evaluations, additional literature that had become available since the previous evaluations and the data available following a public call for data.

Ascorbic acid (E 300), sodium ascorbate (E 301) and calcium ascorbate (E 302) are authorised in the European Union (EU) as food additives in accordance with Annex II and Annex III of Regulation (EC) No 1333/2008. The use of ascorbic acid and ascorbates as food additives has been evaluated by the Joint FAO/WHO expert Committee on Food Additives (JECFA), the latest evaluation being in 1981, and by the Scientific Committee on Food (SCF), in 1987. Both committees found the use of the substances acceptable. The question of the tolerable upper intake levels of calcium and sodium has been addressed by the SCF and by the European Food Safety Authority (EFSA) (SCF, 2003; EFSA, 2005). The SCF also evaluated the use of ascorbic acid and its salts as food additives in infant formulae and in food for infants in good health and in foods for special medical purposes for infants and young children (SCF, 1994, 1998).

Ascorbic acid undergoes degradation in an aqueous environment as well as in food. The degradation rate and the decomposition pathways and products depend on various factors such as pH, temperature, light, concentration and matrix composition. Under specific conditions, degradation can proceed all the way down to very simple compounds (e.g. threonic acid, glyoxylic acid and carbon dioxide); however, in general, the presence of a variety of more complex products can be observed at intermediate degradation stages. For the majority of the degradation products, there is no indication of genotoxic and/or carcinogenic risk.

Ascorbic acid is absorbed from the intestine by a sodium-dependent active transport process and, at low doses, the absorption is almost complete until a saturation point after which increasing amounts of unabsorbed substance are excreted with the faeces. The major metabolite in the organism is dehydroascorbic acid, which can be reduced back to ascorbic acid and still has vitamin C activity. Dehydroascorbic acid can be further irreversibly oxidised to mainly L-threonic acid and oxalic acid, as well as a number of minor metabolites.

Ascorbic acid and its sodium and calcium salts have very low acute toxicities, and short-term tests on ascorbic acid in various laboratory animals show little effect, and even so only at high doses.

Chronic toxicity and carcinogenicity studies with ascorbic acid do not show any chronic toxicity, even at high doses, and also show no signs of carcinogenicity. However, sodium ascorbate administered at 5 % in the feed, but not ascorbate in equimolar concentration, has been shown to promote bladder cancer in male rats treated with an initiator of bladder cancer. This effect was, however, attributed to the sodium ion in line with the mechanism behind the carcinogenic effect of sodium saccharin, rather than to an effect of ascorbate, and was thus considered of no relevance for the use of sodium ascorbate.

The Panel noted that ascorbic acid or sodium ascorbate alone did not show any mutagenic potential. In some *in vitro* test systems including redox active substances, especially redox active metal ions, ascorbic acid and sodium ascorbate may act as pro-oxidants, thereby increasing the mutagenic potential of redox active metals or other compounds. These in vitro effects have not been confirmed in *in vivo* studies.

The Panel considered that it is unlikely that ascorbic acid and sodium ascorbate are genotoxic. In the absence of genotoxicity data on calcium ascorbate, the Panel considered that the read across approach for calcium ascorbate was possible. Overall, the Panel concluded that there is no genotoxicity concern for ascorbic acid, sodium ascorbate or calcium ascorbate.

The Panel also noted that potential reaction products which may result from the interaction of sorbic acid with ascorbic acid in the presence of iron salts were demonstrated to be mutagenic *in vitro* and that there are certain food categories for which the use of these food additives is permitted in parallel. However, these reaction products have only been shown to be formed under optimal experimental conditions in an aqueous environment and are thus unlikely to be formed to any major extent in food matrices. Consequently these interactions appear to be of limited significance and concern.

Prenatal developmental studies in mice, rats, hamsters and guinea pigs did not show adverse developmental effects. Studies on reproductive toxicity were not available.

In studies in humans, vitamin C has been investigated for the treatment of vitamin C deficiency and various diseases. Typically, the studies focused on potential positive effects, and any description of possible side-effects were mostly anecdotal, lacked control groups and were difficult to interpret.

The Panel also noted that a common concern is the possible formation of oxalate stones following the intake of large doses of ascorbic acid. The epidemiology studies give a strong indication that a daily intake of vitamin C below 1 500 mg is not a risk factor for the formation of kidney stones. However, it cannot be excluded that extremely high doses of vitamin C could be a risk factor for the development of kidney stones for a small subpopulation of particularly sensitive persons, as suggested by the study of Massey et al. (2005). The Panel, however, considered it unlikely that the use of vitamin C as a food additive would result in such high levels of intake.

Overall, the Panel noted that the available data did not report any adverse effects in animal studies, even at the highest doses tested.

The Panel estimated the combined exposure to ascorbic acid (E 300), calcium ascorbate (E 301) and sodium ascorbate (E 302) using the highest concentration reported from any of them for each food category. It was not possible to carry out an exposure assessment scenario based on maximum permitted levels (MPLs), as, for most of the food categories, these food additives are authorised according to *quantum satis*. Therefore, maximum levels of the available use data provided by industry were used to provide a conservative exposure estimate scenario (*maximum level exposure assessment* scenario).

Based on the available dataset, the Panel also calculated combined exposure estimates following two refined exposure scenarios based on different assumptions: a "brand-loyal consumer scenario" and a "non-brand-loyal scenario". The Panel considered that the refined exposure assessment approach is a more realistic scenario and that the refined exposure estimates will not cover future changes in the level of use of food additives.

Reported use levels from industry give information on the amount of the food additive added to food. By using these data, exposure to ascorbic acid and its salts (E 300–302) at the moment that the food was produced can be calculated. As ascorbic acid is degraded during processing and storage, the Panel calculated exposure estimates including loss factors. These estimates should reflect exposure to ascorbic acid and its salts in food as consumed. The analytical levels provided by the Member States reflect the levels of ascorbic acid in foods, whatever the origin (from natural and other sources). However, given the limitations of the analytical data provided by the Member States (limited number of Member States, only 28 food categories and a lack of data on foods in which ascorbic acid occurs naturally, such as raw food commodities, for example citrus fruits), the Panel noted that the exposure estimates using the analytical data will probably not reflect the exposure to ascorbic acid and its salts

via the whole diet. The real exposure will probably be higher. Overall, the Panel considered that the exposure estimates using the analytical data should be interpreted with caution.

As the analytical data did not allow for the estimation of the overall exposure to ascorbic acid and its salts via the whole diet (from natural and other sources), the refined exposure estimates—with and without considering loss via processing—were added to the exposure of vitamin C via the diet as estimated by the Panel on Dietetic Products, Nutrition and Allergies (EFSA NDA Panel, 2013) (section 2.9.4). The total exposure assessment of ascorbic acid and its salts (from their use as food additives and natural sources) would reach 1 g/person per day at the highest level for all populations, except for infants and toddlers. The exposure to ascorbic acid and its salts from their use as food additives would represent around 50–65 % (depending on whether or not the losses of ascorbic acid are taken into account).

Given the fact that adequate data on exposure and toxicity were available and no adverse effects were reported in animal studies, the Panel concluded that there is no safety concern for the use of ascorbic acid (E 300), sodium ascorbate (E 301) and calcium ascorbate (E 302) as food additives at the reported uses and use levels, and there is no need for a numerical acceptable daily intake (ADI) for ascorbic acid (E 300), sodium ascorbate (E 301) and calcium ascorbate (E 302).

The Panel concluded that the maximum limits for the impurities of toxic elements (lead, mercury and arsenic) in the EC specification for ascorbic acid and its salts (E 300–302) should be revised in order to ascertain that ascorbic acid and its salts (E 300–302) as food additives will not be a significant source of exposure to those toxic elements in food.

The Panel also concluded that the EC specifications for ascorbic acid (E 300) should be amended to include a maximum limit for iron; specifications for sodium ascorbate (E 301) should be amended to include a maximum limit for sulphates, iron, copper and nickel; and specifications for calcium ascorbate (E 302) should be amended to include a maximum limit for 4-hydroxy-5-methyl-3(2*H*)-furanone, iron, copper and aluminium.

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BACKGROUND AS PROVIDED BY THE EUROPEAN COMMISSION

Regulation (EC) No 1333/2008[4] 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.[5] 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[6] of 2001. The report "Food additives in Europe 2000[7]" submitted by the Nordic Council of Ministers to the Commission, provides additional information for the prioritisation of additives for re-evaluation. As colours were among the first additives to be evaluated, these food additives should be re-evaluated with a highest priority.

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

TERMS OF REFERENCE AS PROVIDED BY THE EUROPEAN COMMISSION

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

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

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

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

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

ASSESSMENT

1. Introduction

The present opinion deals with the re-evaluation of the safety of ascorbic acid (E 300), sodium ascorbate (E 301) and calcium ascorbate (E 302) when used as food additives.

According to Annex II of Regulation (EC) No 1333/2008[8], ascorbic acid (E 300) and its sodium salt (E 301) and calcium salt (E 302) are authorised food additives in the European Union (EU). The use of ascorbic acid and ascorbates as food additives has been evaluated by the Joint FAO/WHO expert Committee on Food Additives (JECFA), the latest in 1981 (JECFA, 1981a, b), and by the Scientific Committee on Food (SCF), in 1987 (SCF, 1989b). Both committees found the use of the substances acceptable.

The SCF also evaluated the use of the substances as food additives in infant formulae and in food for infants in good health, and in foods for special medical purposes for infants and young children (SCF, 1994, 1998).

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 had become available since the previous evaluations and the data available following an EFSA public call for data.[9,10] The Panel noted that not all original studies on which previous evaluations were based were available to the Panel.

2. Technical data

2.1. Identity of the substances

2.1.1. Ascorbic acid

Ascorbic acid (E 300, INS300) is identical to naturally occurring L-ascorbic acid (vitamin C). The molecular formula is $C_6H_8O_6$ and the molecular weight is 176.12 g/mol. The Chemical Abstracts Service (CAS) Registry Number is 50-81-7 and the European Inventory of Existing Commercial chemical Substances (EINECS) Registry Number is 200-066-2. The systematic name is (5*R*)-[(1*S*)-1,2-dihydroxyethyl]-3,4-dihydroxyfuran-2(5*H*)-one.

The structural formula of L-ascorbic acid is presented in Figure 1.

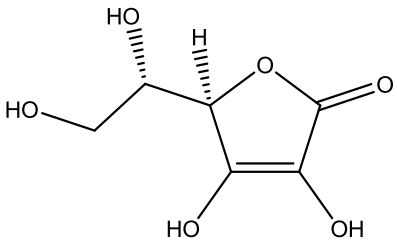

Figure 1: Structural formula of L-ascorbic acid

[8] .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.

[9] 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 online: http://www.efsa.europa.eu/en/dataclosed/call/ans091123a.htm

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

The most commonly used synonyms are vitamin C, L-ascorbic acid, 3-keto-L-gulofuranolactone, 3-oxo-L-gulofuranolactone and L-threo-hex-2-enoic acid γ lactone (ChemIDplusAdvance, online).

Ascorbic acid (E 300) is a white to pale-yellow odourless crystalline powder with an acidic taste. It discolours on exposure to air and moisture, it is freely soluble in water, it is sparingly soluble in ethanol and it is insoluble in ether (JECFA, 2006; Commission Regulation No 231/2012[11]).The p*K* values of ascorbic acid are $pK_1 = 4.17$ and $pK_2 = 11.57$ (Russell, 2013).

2.1.2. Sodium ascorbate

Sodium L-ascorbate (E 301, INS301) is the sodium salt of L-ascorbic acid. The molecular formula is $C_6H_7NaO_6$ and the molecular weight is 198.1 g/mol. The CAS Registry Number is 134-03-2 and the EINECS Registry Number is 205-126-1. Its systematic name is sodium (2*R*)-2-[(1*S*)-1,2-dihydroxyethyl]-4-hydroxy-5-oxo-2*H*-furan-3-olate.

The structural formula of sodium L-ascorbate is presented in Figure 2.

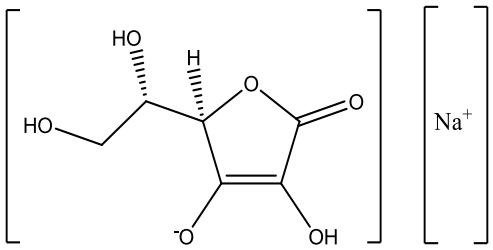

Figure 2: Structural formula of sodium L-ascorbate

The most commonly used synonyms are L-ascorbic acid, monosodium salt, 3-oxo-L-gulofuranolactone sodium, vitamin C and vitamin C sodium (ChemIDplusAdvanced, online).

Sodium ascorbate (E 301) is a white or almost white odourless crystalline powder. It gradually darkens on exposure to light. It is freely soluble in water and very slightly soluble in ethanol. A 10 % solution in water has a pH of 6.5–8 (JECFA, 2006; Commission Regulation 231/2012). It contains 11 % sodium and 89 % ascorbic acid.

2.1.3. Calcium ascorbate

Calcium L-ascorbate (E 302, INS302) is the calcium salt of L-ascorbic acid. Calcium L-ascorbate (anhydrous) has the molecular formula $C_{12}H_{14}CaO_{12}$, the molecular weight is 390.31 g/mol and the CAS Registry Number is 5743-27-1.The EINECS Registry Number is 227-261-5.

Calcium L-ascorbate (di-hydrate) has the molecular formula $C_{12}H_{14}CaO_{12}\cdot 2H_2O$, the molecular weight is 426.34 g/mol and the CAS Registry Number is 5743-28-2. No EINECS Registry Number has been identified for the di-hydrated form.The systematic name is calcium (2*R*)-2-[(1*S*)-1,2-dihydroxyethyl]-4-hydroxy-5-oxo-2*H*-furan-3-olate.

The structural formula for calcium L-ascorbate (anhydrous) is presented in Figure 3.

[11] 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 1331/2008 of the European Parliament and of the Council. OJ L 83, 22.3.2012.

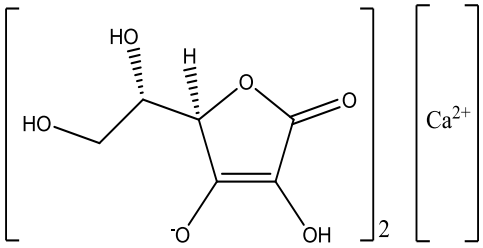

Figure 3: Structural formula of calcium L-ascorbate (anhydrous)

Common synonyms are calcium di-ascorbate, calcium L-ascorbate and hemicalcium ascorbate (ChemIDplusAdvanced, online).

Calcium ascorbate is a white to slightly greyish-yellow odourless crystalline powder. It is freely soluble in water, slightly soluble in ethanol and insoluble in ether (JECFA 2006; Commission Regulation (EU) No 231/2012).

2.2. Specifications

Specifications for ascorbic acid (E 300) (Table 1), sodium ascorbate (E 301) (Table 2) and calcium ascorbate (E 302) (Table 3) have been defined in Commission Regulation (EU) No 231/2012 and by JECFA (JECFA, 2006).

Table 1: Specifications for ascorbic acid (E 300) according to Commission Regulation (EU) No 231/2012 and JECFA (2006)

	Commission Regulation (EU) No 231/2012	**JECFA (2006)**
Assay	Contains not less than 99 % of $C_6H_8O_6$ after drying in a vacuum desiccator over sulphuric acid for 24 hours	Not less than 99 % on the dried basis
Description	White to pale yellow odourless crystalline powder	White to slightly yellow odourless crystalline powder
Melting range	Between 189 °C and 193 °C with decomposition	
Identification		
Test for ascorbic acid	Passes test	–
pH	2.4–2.8 (2 % aqueous solution)	2.4–2.8 (1 in 50 solution)
Specific rotation	$[\alpha]_D^{20}$ between +20.5 ° and +21.5 °(10 % w/v aqueous solution)	$[\alpha]_D^{25}$between +20.5 ° and +21.5 °
Colour reaction	–	To 2 mL of a 2.0 % solution in water, add 2 mL of water, 0.1 g of sodium hydrogen carbonate and about 0.02 g of ferrous sulphate. Shake and allow to stand. A deep violet colour is produced which disappears on the addition of 5 mL of dilute sulphuric acid TS
Reducing reaction	–	A solution of the sample in water immediately reduces potassium permanganate TS without heating, producing a brown precipitate. A solution of the sample in ethanol will decolourise a solution of 2,6-dichlorophenol-indophenol TS

	Commission Regulation (EU) No 231/2012	JECFA (2006)
Purity		
Loss on drying	Not more than 0.4 % (in vacuum over sulphuric acid for 24 hours)	Not more than 0.4 % (over sulphuric acid in a vacuum, 24 hours)
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 noted that the European Pharmacopoeia (2014) specifications for ascorbic acid contain limits for iron (maximum 2 mg/kg) and copper (maximum 5 mg/kg).

Table 2: Specifications for sodium ascorbate (E 301) according to Commission Regulation (EU) No 231/2012 and JECFA (2006)

	Commission Regulation (EU) No 231/2012	JECFA (2006)
Assay	Sodium ascorbate, after drying in a vacuum desiccator over sulphuric acid for 24 hours, contains not less than 99 % of $C_6H_7O_6$ Na	Not less than 99 % after drying
Description	White or almost white odourless crystalline solid which darkens on exposure to light	White or almost white odourless crystalline powder which darkens on exposure to light
Identification		
Test for ascorbate Test for sodium	Passes test Passes test	Passes test Passes test
pH	6.5–8.0(10 % aqueous solution)	6.0–7.5 (1 in 10 solution)
Specific rotation	$[\alpha]_D^{20}$ between +103 ° and +106 ° (10 % w/v aqueous solution)	$[\alpha]_D^{25}$between +95 ° and +97 ° (5 % (w/w) solution)
Purity		
Loss on drying	Not more than 0.25 % after drying in a vacuum desiccator over sulphuric acid for 24 hours	Not more than 0.25 % (vacuum desiccator over sulphuric acid, 24 hours)
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 also noted that the European Pharmacopoeia (2014) specifications for sodium ascorbate contain limits for sulphates (maximum 150 mg/kg), iron (maximum 2 mg/kg), copper (maximum 5 mg/kg) and nickel (maximum 1 mg/kg).

Table 3: Specifications for calcium ascorbate (E 302) according to Commission Regulation (EU) No 231/2012 and JECFA (2006)

	Commission Regulation (EU) No 231/2012	JECFA (2006)
Assay	Content not less than 98 % on a volatile matter-free basis	Not less than 98 % of $C_{12}H_{14}O_{12}Ca{\cdot}2H_2O$
Description	White to slightly pale greyish-yellow odourless crystalline powder	White to slightly yellow odourless crystalline powder
Identification		

	Commission Regulation (EU) No 231/2012	JECFA (2006)
Test for ascorbate	Passes test	
Test for calcium	Passes test	Passes test
pH	6.0–7.5 (10 % aqueous solution)	6.0–7.5 (1 in 10 solution)
Specific rotation	$[\alpha]_D^{20}$ between +95 ° and +97 ° (10 % w/v aqueous solution)	$[\alpha]_D^{25}$between +95 ° and +97 ° (5 % (w/w) solution)
Purity		
Fluoride	Not more than 10 mg/kg (expressed as fluorine)	Not more than 10 mg/kg
Volatile matter	Not more than 0.3 % determined by drying at room temperature for 24 hours in a desiccator containing sulphuric acid or phosphorus pentoxide	–
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 noted that the European Pharmacopoeia (2014) specifications for calcium ascorbate contain limits for iron (maximum 2 mg/kg) and copper (maximum 5 mg/kg) and that Commission Regulation (EC) No 1170/2009[12] limits threonate to 2 %.

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

2.3. Manufacturing process

Oster and Fechtel (2012) described how commercial production is based on various modifications of the classical method described by Reichstein and Grüssner (1934). In this method, D-glucose is hydrogenated using a nickel catalyst to D-sorbitol, which in turn is oxidised to L-sorbose by microbiological oxidation with *Acetobacter xylinum*. Through various oxidation steps, 2-keto-L-gulonic acid is formed, which again is converted to L-ascorbic acid or to sodium ascorbate, which can then be transformed to ascorbic acid.

Following a call for data, industry (DSM, 2010) provided information showing that ascorbic acid and its sodium and calcium salts are manufactured as follows. First, sodium ascorbate is produced. The resulting sodium ascorbate is then precipitated, centrifuged and washed (with methanol). The washed cake is then dissolved in water and further purified (removal of residual solvent) and decolourised. The purified sodium ascorbate solution is concentrated under vacuum and crystallised. The pure crystals are then milled and dried to obtain the commercial product.

Ascorbic acid is produced by passing a solution of sodium ascorbate (manufactured as described above) over cation exchange resins (DSM, 2010). To purify the ascorbic acid (solution) that is obtained, the solution is passed over anion exchange resins and the resulting product is decolourised and treated further, in the same way as is used for the production of sodium ascorbate.

[12] Commission Regulation (EC) No 1170/2009 of 30 November 2009 amending Directive 2002/46/EC of the European Parliament and of Council and Regulation (EC) No 1925/2006 of the European Parliament and of the Council as regards the lists of vitamin and minerals and their forms that can be added to foods, including food supplements. OJ L314, 1.12.2009, p. 36–42.

Calcium ascorbate is produced by reacting an aqueous solution of ascorbic acid with calcium carbonate (DSM, 2010). After the reaction is completed, the reaction product is washed (with ethanol), filtered, crystallised and dried to obtain the commercial product.

The Panel noted that, if limestone is the source of calcium carbonate, calcium ascorbate could be contaminated with aluminium. In its opinion on the re-evaluation of calcium carbonate (E 170) as a food additive (EFSA ANS Panel, 2011a), the ANS Panel noted that limestone may contain aluminium at concentrations up to 190 mg/kg. Therefore, specifications for the maximum level of aluminium in calcium ascorbate may be required.

A new manufacturing process for calcium L-ascorbate with a content of threonate and the by-product 4-hydroxy-5-methyl-3(2*H*)-furanone (4-HMF) as an impurity has been assessed by EFSA (see section 2.7) (EFSA, 2011a).

2.4. Methods of analysis in food

Pachla et al. (1985) reviewed commonly applied methods for the determination of ascorbic acid in biological samples, food products and pharmaceuticals. Most applied methods are based on high-pressure liquid chromatography (HPLC).

Kall and Andersen (1999) described a method for the determination of total vitamin C in different food and plasma samples using a dual detection system, after HPLC separation, with direct detection of ascorbic acid and indirect fluorometric detection of dehydroascorbic acid after a post-column *O*-phenylenediamine derivatisation.

Bognár and Daood (2000) described a new analytical procedure for the simultaneous determination of L-ascorbic acid, isoascorbic acid, L-dehydroascorbic acid and isodehydroascorbic acid (in selected fruits and vegetables) by HPLC.

Fontannaz et al. (2006) described a HPLC method for the quantification of total ascorbic acid and isoascorbic acid in 25 fortified food products, premixes and duomixes.

Oster and Fechtel (2012) pointed out that an important drawback with many of the chemical methods is the possible interference from non-vitamin C isomers of ascorbic acid and other antioxidants resulting in a lack of specificity.

2.5. Reaction and fate in food

The scientific literature dealing with the degradation of ascorbic acid and its salts in food and, in more general terms, in aqueous media is abundant. A few relevant examples selected from published papers are summarised below.

2.5.1. Degradation of ascorbic acid in aqueous model systems

Ascorbic acid readily undergoes degradation in an aqueous environment. Decomposition depends on pH, temperature, light, concentration and the presence of transition/heavy metal catalysts. When oxygen was present, threonic acid, oxalic acid, glyceric acid and glyoxylic acid were identified, among other chemicals, as degradation products (Shin and Feather, 1990). Furthermore, using ^{14}C-labelled ascorbic acid, it was established that the substance can be readily oxidised to dehydroascorbic acid (DHA), which will decay irreversibly to 2,3-diketogulonic acid (2,3-DKG) (Bode et al., 1990). The decay rate of dehydro-L-ascorbic acid was much higher at high pH values (7–8) than at low pH values (3–5) and increased with temperature in the range between 0 and 45 °C.

Ascorbic acid and its degradation products participate in chemical modifications of amino acids/proteins through non-enzymatic glycation typical of sugars (Maillard reaction), with formation of different products called "advanced glycation end products" (Nemet and Monnier, 2011). Degradation products such as DHA, 2,3-DKG, 3-deoxythreosone, xylosone and threosone were

detected in the human eye lens. According to the authors, "*The identification of 3-deoxythreosone as the major degradation product bound to human lens proteins provides* in vivo *evidence for the non-oxidative pathway of dehydroascorbate degradation into erythrulose as a major pathway for vitamin C degradation* in vivo".

Simpson and Ortwerth (2000) studied the degradation of ascorbic acid, DHA and 2,3-DKG under physiological conditions. Erythrulose (ERU) and oxalate were found to be the primary degradation products of ascorbic acid, regardless of which compound was used as a starting material. The molar yield of ERU from 2,3-DKG at pH 7.0 (37 °C) and with limiting oxygen was higher than 97 %. The authors observed that ERU is extremely reactive and rapidly glycates and crosslinks proteins, and therefore ERU may mediate the ascorbate-dependent modification of proteins (ascorbylation) seen *in vitro*. The authors also proposed that ascorbylation may occur *in vivo* in the human eye lens during diabetic and age-onset cataract formation.

Ascorbic acid (and its conjugated base, the ascorbate anion) is well known for its antioxidant activity (Stadtman, 1991). However, under certain conditions, ascorbate can paradoxically promote the generation of the same active oxygen species (·OH, O_2^- and H_2O_2) that otherwise would be destroyed. According to the literature, the pro-oxidant activity of ascorbate arises from its ability to reduce transition metals (e.g. Fe^{3+} or Cu^{2+}) and O_2 by, respectively, a one-electron transfer mechanism and a two-electron transfer mechanism, as per the following schematic sequence (Uchida and Kawakishi, 1988; Uchida et al., 1989):

1. $M^{[n+1]+}$ + ascorbate → $M^{[n]+}$ + dehydroascorbate
2. $M^{[n]+} + O_2 \rightarrow M^{[n+1]+} + O_2^-$
3. $2O_2^- + 2H^+ \rightarrow H_2O_2 + O_2$
4. $M^{[n]+} + H_2O_2 \rightarrow M^{[n+1]+} + OH^- + {}^{\cdot}OH$

Ascorbate is relatively stable in pure water. However, in the presence of catalytic amounts of metal ion $M^{[n+1]+}$, it is rapidly oxidised to dehydroascorbate (1): the rate of reaction depends on canonical parameters such as pH, catalyst, oxygen pressure, temperature, etc. The reduction of $M^{[n+1]+}$ to $M^{[n]+}$ is the first step in a sequence of reactions yielding the superoxide species O_2^- (2); and hydrogen peroxide H_2O_2 (3). The reduced metal ion $M^{[n]+}$ generates the very reactive oxidant hydroxyl radical ·OH (4) via Fenton's reaction (Fenton, 1894). In principle, the aforesaid reactions may be of interest for the safety of food when treated with additives, at least in specific situations. For instance, potassium sorbate, ascorbic acid and iron salts are used widely in combination: the sorbate reactivity and the oxidative potential of ascorbic acid in the presence of iron salts might result in the generation of newly formed compounds in food during storage and distribution. Indeed, Kitano et al. (2002) detected a mutagenic response *in vitro*—attributed to (unidentified) oxidative compounds formed from the sorbate moiety oxidation.

Ascorbic acid is also degraded under anaerobic conditions. However, the mechanism of degradation of ascorbic acid under anaerobic conditions has not been fully established. Direct cleavage of the 1,4-lactone bridge without prior oxidation to DHA appears to be involved. Anaerobic degradation proceeds to furfural and CO_2 (Gregory, 1996; Oster and Fechtel, 2012). Unlike in aqueous media, in the absence of moisture and in darkness, solid ascorbic acid is stable for a long time.

2.5.2. Reaction products in processed foods

Using ^{14}C-labelling radioactive techniques, Thewlis (1971) showed that, when ascorbic acid was used as a food additive for baking, about 24 % of the carbon present in it was lost, probably entirely, as carbon dioxide. The rest of the carbon remained in the bread as a mixture of water-soluble acidic substances, the major component of which appeared to be threonic acid; this accounted for about 52 % of the carbon in the added ascorbic acid. Lesser amounts of other products present included 2,3-DKG.

None of the ascorbic acid originally added to the dough, or of its likely decomposition products, DHA and oxalic acid, could be detected in the bread.

Burdurlu et al. (2006) studied the kinetics of ascorbic acid degradation in citrus juice concentrates (orange, lemon, grapefruit and tangerine) during eight-week storage at 28, 37 and 45 °C. The loss of ascorbic acid at each temperature followed first-order kinetics. Ascorbic acid retention after storage at 28, 37 and 45 °C was about 54.5–83.7, 22.5–27.0 and 15.1–20.0 %, respectively. 5-(Hydroxymethyl)furfural (5-HMF) formation during storage was investigated, as the substance is one of the decomposition products of ascorbic acid (however, other pathways of 5-HMF accumulation are known, among which is its natural generation in sugar-containing food). After eight-week storage, the 5-HMF content in citrus juice concentrates at 28 °C was found to range from 3 to 28 mg/kg. The variation of 5-HMF values at 37 °C was between 522 and 1 140 mg/kg, while values at 45 °C ranged from 1 400 to 3 250 mg/kg. The increase of 5-HMF at 45 °C was approximately 2.7 times greater than that at 37 °C. A significant correlation was obtained between 5-HMF accumulation and ascorbic acid loss at all storage temperatures in all citrus juice concentrates.

Louarme and Billaud (2012) studied the effects of conventional and ohmic heating (an electrical heating that uses a liquid's own electrical resistance to generate the heat) on the degradation of ascorbic acid in chunky fruit desserts prepared with apple puree (Golden Delicious var.) and chunky peach (Panavi var.) pieces. Concentrations of 5-HMF, furfural, 3-hydroxy-2-pyrone and furoic acid were determined so that the importance of oxidative and/or thermal reactions during processing could be assessed. Depending on thermal processing, 5-HMF and furfural levels in samples ranged from non-detected (ND) to 3 260 µg/100 g fresh weight (fw) and from ND to 570 µg/100 gfw, respectively. Production of 3-hydroxy-2-pyrone and furoic acid ranged from 480 to 2 670 µg/100 gfw and from 84 to 420 µg/100 gfw, respectively. Results showed that accumulation of 5-HMF and furfural was in relation with the severity of heating (conventional vs. ohmic) applied to the aforesaid fruit products during processing. Conversely, the production of 3-hydroxy-2-pyrone and furoic acid mainly depended on ascorbic acid oxidative degradation reactions, rather than on thermal degradations, as they were similarly formed in both heating treatments.

Conclusions

As described above, ascorbic acid undergoes degradation in an aqueous environment as well in food. The degradation rate and the decomposition pathways and products depend on various factors such as pH, temperature, light, concentration and matrix composition. Under specific conditions, degradation can proceed all the way down to very simple compounds (e.g. threonic acid, glyoxylic acid and carbon dioxide); however, in general, the presence of a variety of more complex products can be observed at intermediate degradation stages. Substantially, for the majority of these degradation products, there is no indication of genotoxic and/or carcinogenic risk from the scientific literature or by the *in silico* evaluation using the OECD QSAR Toolbox, version 3.2.0 (2013)..

In conclusion, the Panel noted that the ascorbic acid (and its conjugated base, the ascorbate anion) employed as a food additive and the ascorbic acid naturally present in food may both be expected to behave in similar chemical ways under similar environmental conditions, that is, in principle, they would give rise to degradation products along equivalent pathways.

2.5.3. Loss of ascorbic acid in foods

The loss of ascorbic acid (vitamin C) in several food categories, either during processing or during storage, has been described in the literature.

2.5.3.1. Effect of heating

Vitamin C is a heat-labile compound and vitamin C losses depend upon the heating methods. The losses of ascorbic acid in potatoes were reported to be 8–17 % using dry-heating methods and 20–40 % using wet heating (steaming or boiling) (Golaszewska and Zalewski, 2001).

Boiling can also cause losses in ascorbic acid of around 20 % in tomatoes (Alvi et al., 2003) and in carrot slices (Frias et al., 2010). The vitamin C losses in orange juice after pasteurisation (1 min/90 °C) were reported to be 20 % (Elez-Martinez and Belloso, 2007).

Slupski (2011) reported vitamin C losses in flageolet bean seeds after cooking, blanching and sterilisation. The results are given in Table 4.

Table 4: Vitamin C and L-ascorbic acid losses in processed flageolets (Slupski, 2011)

Type of processing	Processing conditions	Loss (%) of vitamin C (total of L-ascorbic acid/L-dehydroascorbic acid	Loss (%) of L-ascorbic acid
Blanching	96–98 °C/3 min	18–29	16–37
Cooking	100 °C/29–37 min	37–44	31–48
Sterilisation	120 ± 2°C/13–16 min	56–71	13–30

Pasteurisation of milk causes a 15–25 % loss in ascorbic acid, and a loss of between 15 and 32 % during ultra-high temperature (UHT)[13] treatment, which can increase further to up to 80 % during storage (Barraquio, 2014). During in-bottle sterilisation of milk, ascorbic acid losses can amount to up to 90 % (Visakh et al., 2014).

2.5.3.2. Effect of storage

The temperature, the form of vitamin and the matrix are the most important factors affecting the stability of vitamin C in foods. At comparable storage temperatures, higher degradation rate constants were found in milk than in fruit juices and drinks. In solid matrices, the rate constants were two to three times higher in bread than in bran flakes, cereals, dried apple chips and potato flakes (Steskova et al., 2006).

Bosch et al. (2013) reported that, in fruit-based infant foods with added vitamin C, more than 70 % and 50 % of ascorbic acid was preserved during 16 and 32 weeks at 25 °C, respectively.

Ancos et al. (2000) reported losses of ascorbic acid of 33–55 % in red raspberry after 12 months' frozen storage. However, for watercress, decreases of 95, 93 and 96 %, were found after 400 days of frozen storage at –7, –15 and –30 °C, respectively (Gonçalves et al., 2009).

2.5.4. Formation of benzene from benzoic acid in the presence of ascorbic acid

Under certain conditions, small amounts of benzene can be formed from benzoic acid in the presence of ascorbic acid and transition metal ions such as copper(II) and iron(III) (Chang and Ku, 1993; Gardner and Lawrence, 1993; McNeal et al., 1993). The chemical reaction is catalysed by metal ions which occur at low concentrations in drinking water. The studies performed by Chang and Ku (1993), Gardner and Lawrence (1993) and McNeal et al. (1993) were summarised by the German Federal Institute for Risk Assessment (BfR, 2005).

The international beverage industry has taken steps to minimise benzene that may be found in its products. The International Council of Beverages Associations (ICBA) has created a "Guidance Document to Mitigate the Potential for Benzene Formation in Beverages" (ICBA, 2006).

In 2006, the European Commission and Member States had become aware of the potential formation of benzene under certain conditions in soft drinks from the reaction of benzoic acid and other ingredients. The issue was considered in the meetings of the Standing Committee of the Food Chain and Animal Health in July and December 2007 (EC, 2007a, b). "The Committee noted that the

[13] UHT/high temperature–short time (HTST): short time (seconds) treatment at high temperature (135–140 °C).

reformulation work by the industry appeared to be working given the limited number of samples in which levels of benzene were above 10 ppb. However it was considered that further monitoring would be useful although no further formal action was considered necessary by the Commission at this time".

The concentrations of benzene in non-alcoholic beverages measured in Germany in 2010 were below the EU drinking water limit of 1 µg/L, while higher concentrations were found in previous years (Steinbrenner et al., 2010).

The Panel noted that benzene is a genotoxic carcinogen classified by the International Agency for Research on Cancer as "carcinogenic to humans" (Group 1) (IARC, 2012); that the World Health Organization (WHO) has derived a guideline value for benzene in drinking water of 10 µg/L (WHO, 2011); that, according to Council Directive No 98/83/EC,[14] the maximum level of benzene in drinking water is 1 µg/L in the EU; and that the German Federal Institute for Risk Assessment considered that the concentration of benzene in beverages should be as low as reasonably achievable (BfR 2013).

2.6. Case of need and proposed uses

Maximum permitted levels (MPLs) of ascorbic acid and its salts (E 300–302) have been defined in Annex II of Regulation (EC) No 1333/2008 on food additives.

Currently, ascorbic acid and its salts (E 300–302) are authorised food additives in the EU, mostly according to *quantum satis* (*QS*), except for processed cereal-based foods and baby foods for infants and young children (FCS 13.1.3). Ascorbic acid and its salts are included in Group I of food additives.

Table 5 summarises foods that are permitted to contain ascorbic acid and its salts (E 300–302) and the corresponding MPLs as set by Annex II of Regulation (EC) No 1333/2008.

Table 5: Maximum permitted levels (MPLs) of ascorbic acid and its salts (E 300–302) in foods according to Annex II of Regulation (EC) No 1333/2008

FCS[(a)] category number	FCS food category	E-number	Name	MPL (mg/L or mg/kg as appropriate)	Restrictions / exception
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 No 2001/114/EC	E 300/E 301	Ascorbic acid/sodium ascorbate	*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, and unflavoured live fermented unripened cheese
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*	

[14] Council Directive 98/83/EC of 3 November 1998 on the quality of water intended for human consumption. OJ L 330, 5.12.98.

FCS[(a)] category number	FCS food category	E-number	Name	MPL (mg/L or mg/kg as appropriate)	Restrictions / exception
02.1	Fats and oils essentially free from water (excluding anhydrous milk fat)	E 300	Ascorbic acid	*Quantum satis*	
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*	
04.1.2	Peeled, cut and shredded fruit and vegetables	E 300/E 301/E 302	Ascorbic acid/sodium ascorbate/ calcium ascorbate	*Quantum satis*	Only refrigerated unprocessed fruit and vegetables ready for consumption and prepacked unprocessed and peeled potatoes
04.1.3	Frozen fruit and vegetables	E 300/E 301/E 302	Ascorbic acid/sodium ascorbate/ calcium ascorbate	*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*	
04.2.3	Canned or bottled fruit and vegetables	E 300/E 301/E 302	Ascorbic acid/sodium ascorbate/ calcium ascorbate	*Quantum satis*	
04.2.4.1	Fruit and vegetable preparations excluding compote	Group I	Additives	*Quantum satis*	
04.2.4.2	Compote, excluding products covered by category 16	E 300/E 301/E 302	Ascorbic acid/sodium ascorbate/ calcium ascorbate	*Quantum satis*	
04.2.5.1	Extra jam and extra jelly as defined by Directive 2001/113/EEC	E 300	Ascorbic acid	*Quantum satis*	
04.2.5.2	Jam, jellies and marmalades and sweetened chestnut puree as defined by Directive 2001/113/EEC	E 300	Ascorbic acid	*Quantum satis*	
04.2.5.3	Other similar fruit or vegetable spreads	E 300	Ascorbic acid	*Quantum satis*	
04.2.5.4	Nut butters and nut spreads	Group I	Additives	*Quantum satis*	
04.2.6	Processed potato products	Group I	Additives	*Quantum satis*	

FCS[(a)] category number	FCS food category	E-number	Name	MPL (mg/L or mg/kg as appropriate)	Restrictions / exception
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*	
06.2.1	Flours	E 300/E 301/E 302	Ascorbic acid/sodium ascorbate/ calcium ascorbate	*Quantum satis*	
06.2.2	Starches	Group I	Additives	*Quantum satis*	
06.3	Breakfast cereals	Group I	Additives	*Quantum satis*	
06.4.1	Fresh pasta	E 300/E 301	Ascorbic acid/sodium ascorbate	*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
06.4.3	Fresh pre-cooked pasta	E 300/E 301	Ascorbic acid/sodium ascorbate	*Quantum satis*	
06.4.4	Potato gnocchi	Group I	Additives	*Quantum satis*	
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	Bread and rolls	Group I	Additives	*Quantum satis*	Except products in 7.1.1 and 7.1.2
07.1.1	Bread prepared solely with the following ingredients: wheat flour, water, yeast or leaven,salt	E 300/E 301/E 302	Ascorbic acid/sodium ascorbate/ calcium ascorbate	*Quantum satis*	
07.1.2	Pain courant francais, friss búzakenyér, fehér és félbarna kenyerek	E 300/E 301/E 302	Ascorbic acid/sodium ascorbate/ calcium ascorbate	*Quantum satis*	For E 301 and E 302, only friss búzakenyér, fehér és félbarna kenyerek
07.2	Fine bakery wares	Group I	Additives	*Quantum satis*	
08.2	Meat preparations as defined by Regulation (EC) No 853/2004	E 300/E 301/E 302	Ascorbic acid/sodium ascorbate/ calcium ascorbate	*Quantum satis*	Only gehakt and prepacked preparations of fresh minced meat

FCS[(a)] category number	FCS food category	E-number	Name	MPL (mg/L or mg/kg as appropriate)	Restrictions / exception
08.3.1	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, libamaj, libamáj egészben, libamáj tömbben*
08.3.2	Heat-treated processed meat	E 300/E 301	Ascorbic acid/sodium ascorbate	*Quantum satis*	Only *foie gras, foie gras entier, blocs de foie gras, libamaj, libamáj egészben, libamáj tömbben*
08.3.3	Casings and coatings and decorations for meat	Group I	Additives	*Quantum satis*	
09.1.1	Unprocessed fish	E 300/E 301/E 302	Ascorbic acid/sodium ascorbate/ calcium ascorbate	*Quantum satis*	
09.1.2	Unprocessed molluscs and crustaceans	E 300/E 301/E 302	Ascorbic acid/sodium ascorbate/ calcium ascorbate	*Quantum satis*	
09.2	Processed fish and fishery products including molluscs and crustaceans	Group I	Additives	*Quantum satis*	
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*	
13.1.3	Processed cereal-based foods and baby foods for infants and young children as defined by Directive 2006/125/EC	E 300/E 301/E 302	L-Ascorbic acid/sodium L-ascorbate/ calcium L-ascorbate	200	Only fat-containing cereal-based foods including biscuits and rusks and baby foods

FCS[(a)] category number	FCS food category	E-number	Name	MPL (mg/L or mg/kg as appropriate)	Restrictions / exception
13.1.3	Processed cereal-based foods and baby foods for infants and young children as defined by Directive 2006/125/EC	E 300/E 301/E 302	Ascorbic acid/sodium ascorbate/ calcium ascorbate	300	Only fruit- and vegetable-based drinks, juices and baby foods
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
14.1.2	Fruit juices as defined by Council Directive 2001/112/EC and vegetable juices	E 300/E 301/E 302	Ascorbic acid/sodium ascorbate/ calcium ascorbate	*Quantum satis*	For E 301 and E 302, only vegetable juices
14.1.3	Fruit nectars as defined by Council Directive 2001/112/EC and vegetable nectars and similar products	E 300/E 301/E 302	Ascorbic acid/sodium ascorbate/ calcium ascorbate	*Quantum satis*	For E 301 and E 302, only vegetable nectar
14.1.4	Flavoured drinks	Group I	Additives	*Quantum satis*	
14.1.5.2	Coffee, tea, herbal and fruit infusions, chicory; tea, herbal and fruit infusions and chicory extracts; tea, plant, fruit and cereal preparations for infusions, as well as mixes and instant mixes of these products—other	Group I	Additives	*Quantum satis*	Excluding unflavoured leaf tea; including flavoured instant coffee
14.2.1	Beer and malt beverages	E 300/E 301	Ascorbic acid/sodium ascorbate	*Quantum satis*	
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*	

FCS[(a)] category number	FCS food category	E-number	Name	MPL (mg/L or mg/kg as appropriate)	Restrictions / exception
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 categories 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 2 of Regulation (EC) No 1333/2008, ascorbic acid (E 300), sodium ascorbate (E 301) and calcium ascorbate (E 302) are authorised as food additives other than carriers in food additives in all food additive preparations at *QS*.

According to Annex III, Part 3 of Regulation (EC) No 1333/2008, ascorbic acid (E 300), sodium ascorbate (E 301) and calcium ascorbate (E 302) are also authorised as food additives including as carriers in food enzymes with a maximum level in the final food products (beverages or not) at *QS*.

According to Annex III, Part 5, Section A of Regulation (EC) No 1333/2008, ascorbic acid (E 300), sodium ascorbate (E 301) and calcium ascorbate (E 302) 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, sodium ascorbate (E 301) is authorised in the food category FCS 13.1, as this food additive can be added in foods for infants and young children in:

- vitamin D preparations at a maximum level of 100 000 mg/kg and 1 mg/L maximum carry-over in final food i.e. in that case infant formulae and follow-on formulae (FCS 13.1.1 and 13.1.2)

- coatings of nutrient preparations containing polyunsaturated fatty acids at a total carry-over of 75 mg/L in final food i.e. in that case, in foods for infant and young children (FCS 13.1).

Taking into account that at the high level, an infant consumes each day around 1 L of infant formulae (Koletzko, 2000; WHO, 2009a; EFSA Scientific Committee, 2012), this would result in an exposure

of 75 mg sodium ascorbate (E 301) per day assuming this food additive remains at the maximum carry-over level of 75 mg/L possible in this food. This corresponds to 10 mg/kg bw/day assuming an average body weight for infants of 7.5 kg. According to the Commission Directive 2006/141/EC[15] on infant formulae and follow-on formulae, the composition of infant formulae when reconstituted as instructed by the manufacturer should range from 250 kJ to 295 kJ/100 mL for the energy, and from 2.5 to 7.5 mg/100 kJ for vitamin C. Therefore, the total intake of vitamin C should range from 8.25 to 29.2 mg vitamin C/kg bw/day for infants consuming only formulae. Thus, ascorbic acid due to carry-over could represent from 33 up to 100 % of the total intake of vitamin C according to Commission Directive 2006/141/EC.

The Panel is aware that additional usages from the existing authorisation of ascorbic acid (E 300), sodium ascorbate (E 301) and calcium ascorbate (E 302) as food additives in food additive preparations, enzyme preparations or nutrients may add substantially to the overall exposure to ascorbic acid and its salts. The Panel noted that, from a methodological point of view, it was not feasible to differentiate between all contributions (i.e. uses as food additives in food, food additive preparations, enzyme preparations or nutrients) in the overall exposure to ascorbic acid and its salts. The Panel considered that the use of analytical data in the refined exposure assessment would be the most appropriate approach to capture all uses of ascorbic acid and its salts (E 300–302), but without data on all food categories (e.g. raw food commodities like citrus fruits), the estimates based on the analytical data cannot give the complete picture of the total exposure to ascorbates.

2.7. Reported use levels or data on analytical levels of ascorbic acids and its salts (E 300–302) 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[16] regarding the re-evaluation of approved food additives, EFSA issued a public call[17] for concentration data (usage and/or analytical data) on ascorbic acids and its salts (E 300–302).

In response to this public call, updated information on the actual use levels of ascorbic acids and its salts (E 300–302) in foods was made available to EFSA by industry and Member States.

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

More than 550 reported use levels have been provided by FoodDrinkEurope (FDE), the International Chewing Gum Association (ICGA), Food Chemical Risk Analysis (FCRA), Specialised Nutrition Europe (SNE) and Organisation International des Vins (OIV) on ascorbic acid (E 300), sodium ascorbate (E 301) or calcium ascorbate (E 302). According to industry, none of these food additives is used (use levels reported equal to zero) in three food categories (cheese products (FCS 01.7.6), cocoa and chocolate products (FCS 05.1) and starches (FCS 06.2.2)).

In 2010, the Union of European Soft Drinks Associations (UNESDA) submitted data to EFSA for ascorbic acid (E 300), sodium ascorbate (E 301) and calcium ascorbate (E 302) on six different kinds of non-alcoholic soft drinks or iced coffee. These data were taken into account in the present assessment.

[15] Comission Directive 2006/141/EC of 22 December 2006 on infant formulae and follow-on formulae and amending Directive 1999/21/EC. OJ L 401, 31.12.2006.

[16] 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.

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

Appendices 1, 2 and 3 provide data on the use levels of ascorbic acid (E 300), sodium ascorbate (E 301) and calcium ascorbate (E 302) in foods as reported by industry.

Industry provided EFSA with data on use levels (n = 381) of ascorbic acid (E 300) in foods for 79 food categories in which ascorbic acid is authorised.

Industry provided EFSA with data on use levels (n = 115) of sodium ascorbate (E 301) in foods for 79 food categories in which sodium ascorbate is authorised.

Industry provided EFSA with data on use levels (n = 80) of calcium ascorbate (E 302) in foods for 76 food categories in which calcium ascorbate is authorised.

2.7.2. Summarised data on concentration levels in foods from Member States

Analytical results from Member States were collected through the EFSA call for concentration data. Data referred to ascorbic acid. The Panel noted that complete information on the methods of analysis (e.g. validation) was not made available to EFSA. In total, 1 922 analytical results were reported to EFSA by four countries: Austria (n = 1256), Hungary (n = 655), Slovakia (n = 10) and the Czech Republic (n = 1). The data were mainly on fruit and vegetable juices (FCS 14.1.2), food supplements (FCS 17) and flavoured drinks (FCS 14.1.4). Foods were sampled between 2007 and 2013 and analysed during the same period of time. From this dataset, analytical results of ascorbic acid were not quantified (< limit of quantification (LOQ)) in 400 samples, not detected (< limit of detection (LOD)) in 306 samples and 1 216 were numerical values (quantified). Only one of these samples came from a non-accredited laboratory.

Some samples (n = 26) were codified as "foods for sport people" without any more information and were classified in the food category: foods intended for particular nutritional uses (FCS 13). However, foods for sport people should be classified in the corresponding food category (e.g. sport drinks in FCS 14.1 non-alcoholic beverages). As no more information was provided on those 26 samples, these could not be used in the present estimates. Other samples (n = 47) were codified as "products for special nutritional use", also in FCS 13, without any more information. They also could not be used in the present estimates.

Analytical results on honey were also provided (n = 523). These samples were analysed because they were suspected of being falsified, and resulted in having high levels of ascorbic acid (up to 2 908 mg/kg). They were excluded from the current exposure estimates. One misclassified sample was also discarded from the current exposure estimates.

Overall, 1 325 out of the 1 922 total analytical results reported for ascorbic acid and its salts in foods were considered by the Panel for the exposure estimates. Those data covered 28 food categories out of the 88 in which ascorbic acid is authorised.

Analytical results (n = 63) on foods for infants and young children were reported as FCS 13.1.

Appendix 4 shows the analytical results of ascorbic acid in foods as reported by Member States (results for all data reported (medium-bound) and for positive samples only). To consider left-censored analytical data (i.e. analytical results < LOD or < LOQ), the substitution method as recommended in the "Principles and Methods for the Risk Assessment of Chemicals in Food" (WHO, 2009b), and the EFSA scientific report "Management of left-censored data in dietary exposure assessment of chemical substances" (EFSA, 2010) is used. Analytical data below the LOD or LOQ are assigned half of the LOD or LOQ, respectively (medium-bound). Subsequently, per food category, the mean or median, as appropriate, medium-bound concentration is calculated.

2.8. Information on existing authorisations and evaluations

Ascorbic acid (E 300), sodium ascorbate (E 301) and calcium ascorbate (E 302) are authorised as food additives in the EU in accordance with Annexes II and III of Regulation (EC) No 1333/2008 on food additives. Specific purity criteria have been defined in Commission Regulation (EU) No 231/2012.

In the EU, ascorbic acid is also permitted for plastics in contact with food (Reference Number 36000) with no specific limitations (Commission Regulation No 10/2011[18]). Furthermore, ascorbic acid, sodium ascorbate and calcium ascorbate (as well as potassium ascorbate) are listed as permitted sources of vitamin C in Commission Directive No 2006/141/EC[19] and Commission Directive No 2006/125/EC.[20]

The SCF first evaluated ascorbic acid and its sodium and calcium salts in 1983 (SCF, 1983). The SCF stated at that time that the substances were acceptable as a source of vitamin C, together with the potassium salt and the esters with palmitic acid and stearic acid.

The substances (except the potassium salt) were also found acceptable as technological additives (antioxidants) in infant formulae and follow-up milks based on cow's milk proteins with a maximum level of 1 mg/100 mL as the sum of the ascorbates and tocopherols of the product ready for use when reconstituted as instructed by the manufacturer. No scientific data or explanation were presented in the report (SCF, 1983).

The SCF re-evaluated ascorbic acid and its sodium and calcium salts as food additives (antioxidants) (SCF, 1989b). In its opinion on antioxidants used as food additives, the SCF found that it would be inappropriate to allocate an acceptable daily intake (ADI) for a vitamin and argued that the intake of ascorbate from food additive use would represent only a very small fraction (not specified) of the total dietary intake, which the SCF estimated to be in the magnitude of 30–100 mg/day. In its report, the SCF listed a long list of references, but the SCF only summarised that toxicological data from short-term, reproductive and teratogenicity studies were available and that these data did not show evidence of adverse effects, even at relatively high dosages. The SCF further noted that mutagenicity data indicated that ascorbic acid did not cause gene mutations and that, although *in vitro* tests suggest that ascorbic acid caused DNA strand breaks and chromosome damage, limited *in vivo* data were negative. No further details were given (SCF, 1989b).The SCF in later opinions endorsed the use of sodium ascorbate in other types of foods for infants and young children, but still no details were given explaining the conclusions (SCF, 1989a, 1991, 1997a, 1998).

In 1992, the SCF also evaluated the requirements for vitamin C. As regards the upper levels for vitamin C, the SCF noted that gastrointestinal effects can occur after ingestion of as little as 1 g, but found that this was an effect of acidity rather than an effect from ascorbic acid per se, because the symptoms can largely be avoided by taking the vitamin under the form of a buffered salt. The SCF also noted the possibility for a higher risk of kidney stones in patients with defects in oxalate metabolism, but found that, in general, intakes of up to 10 g/day did not seem to be unsafe for healthy individuals (SCF, 1993).

The EFSA Scientific Panel on Dietetic Products, Nutrition and Allergies (NDA Panel) (EFSA, 2004), in its opinion on the tolerable upper intake level (UL) of vitamin C, concluded that "*The vitamin is of low acute toxicity as indicated by the limited data available from studies in animals and humans. Despite the extensive use of high doses of vitamin C in some vitamin supplements, there have been few controlled studies that specifically investigated adverse effects. Overall, acute gastrointestinal intolerance (e.g., abdominal distension, flatulence, diarrhoea, transient colic) is the most clearly*

[18] 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.
[19] Commission Directive No 2006/141/EC of 22 December 2006 on infant formulae and follow-on formulae and amending Directive No 1999/21/EC. OJ L401 30.1.2006, p. 1–33.
[20] Commission Directive No 2006/125/EC of 5 December 2006 on processed cereal-based foods and baby foods for infants and young children. OJ L 339, p. 16–35.

defined adverse effect at high intakes, but there are limited data on the dose–response relationship for adults or for groups such as children or the elderly. While there is uncertainty whether high intakes of vitamin C increase renal excretion of oxalate which could increase the risk of renal stones, an increased risk of kidney stones was not found in individuals with habitual intakes of 1.5 g/day". The NDA Panel was unable to establish a UL for vitamin C, but noted that, in general, intakes of vitamin C above 1 g/day would be associated with negligible increased uptake and tissue levels, but an increased risk of adverse gastrointestinal effects.

In 2007, the ANS Panel evaluated the safety of calcium ascorbate (with a content of threonate) for use as a source of vitamin C in food supplements. The Panel considered some published and unpublished data on calcium ascorbate with or without threonate and concluded that the use of calcium ascorbate containing up to 2 % threonate as a source of vitamin C in food supplements is not of safety concern (EFSA, 2007, 2008).

In calcium ascorbate, 4-HMF, which is present as an impurity, was considered by the ANS Panel. The Panel found that there were too few data on the substance as such for a full safety evaluation, but considered that a related α,β-unsaturated compound, 4-hydroxy-2,5-dimethylfuran-3(2*H*)-one (HDMF), could be considered representative for the group for read across purposes. HDMF did not show carcinogenic potential in a 2-year carcinogenicity study. From the study, a no observed adverse effect level (NOAEL) of 200 mg HDMF/kg bw/day was derived. Using the worst-case intake estimate for 4-HMF of 12.9 µg/kg bw/day, derived from the use of calcium L-ascorbate with a maximum 4-HMF residue level 0.06 % (w/w), and based on the NOAEL of 200 mg HDMF/kg bw/day, a margin of safety (MOS) of 15 000 was calculated. The Panel concluded that this MOS was large enough to cover intra- and interspecies differences, as well as uncertainties resulting from the use of the read across approach and uncertainties related to exposure to 4-HMF and related α,β-unsaturated 3(2)-furanones from other dietary sources, and considered the presence of 4-HMF to be of no safety concern (EFSA, 2011a).

In 2009, the ANS Panel issued an opinion on calcium ascorbate as a source of calcium. The Panel concluded that the bioavailability of calcium would be comparable to other fully dissociable calcium salts. In the opinion, the Panel referred to earlier evaluations of calcium ascorbate (SCF, 1989b; EFSA, 2004, 2007) and performed no further toxicological evaluation (EFSA, 2009).

In 2010, the ANS Panel expressed an opinion on the use of sodium ascorbate as a food additive in vitamin D preparations intended to be used in formulae and weaning food for infants and young children. The Panel concluded that such use would only marginally contribute to the vitamin C and sodium content of the finished products compared with the amounts already present in such products and found the use to be of no safety concern (EFSA ANS Panel, 2010).

The EFSA NDA Panel has also issued opinions on the substantiation of some health claims for the use of vitamin C (EFSA NDA Panel, 2009, 2010a, b).

In 2013, the NDA Panel did not set any UL for vitamin C and commented that: "*The limited available data from studies in animals and humans were considered to suggest a low acute toxicity of vitamin C (Johnston, 1999; EFSA, 2004). Relationships between vitamin C intakes and adverse gastrointestinal effects or renal effects in relation to urinary excretion of oxalate were assessed, and reversible acute gastrointestinal intolerance or diarrhoea was regarded as the most clearly defined adverse effect at Dietary Reference Values for vitamin C high intakes (3–4 g/day). However, data on a dose–response relationship for adults (including older adults) or for children were considered to be insufficient. Despite the extensive use of high doses of vitamin C in supplements, there were only a limited number of controlled studies that specifically investigated adverse effects. It has been suggested that vitamin C may also exert pro-oxidant effects by reducing ferric to ferrous ion, and that this might stimulate uptake of iron from the gut as iron is absorbed in the reduced state (Wollenberg and Rummel, 1987). In addition, an increase in free iron concentration through vitamin C's ability to release ferrous ions from ferritin (Halliwell and Gutteridge, 1989) may promote the generation of free radicals through*

the Fenton reaction (Prousek, 2007). Whether excess vitamin C intake leads to these mechanisms in vivo *is uncertain (Carr and Frei, 1999)*" (EFSA NDA Panel, 2013).

In that opinion, the EFSA NDA Panel derived dietary reference values for vitamin C for healthy children and adults (EFSA NDA Panel, 2013). The average requirements and population reference intake (PRI) values for different ages groups are summarised in Table 6. For pregnant and lactating women, vitamin C intakes of 10 mg/day and of 60 mg/day, in addition to the PRI of non-pregnant non-lactating women, are proposed. For infants aged 7–11 months, the NDA Panel decided to retain the PRI of 20 mg/day set by the SCF (1993), as no suitable evidence had become available since that assessment.

Table 6: Average requirements and population reference intakes of vitamin C for different population age groups (EFSA NDA Panel, 2013)

Age group	Average requirement, mg/day		Population reference intake, mg/day	
	Males	Females	Males	Females
1–3 years	15	15	20	20
4–6 years	25	25	30	30
7–10 years	40	40	45	45
11–14 years	60	60	70	70
15–17 years	85	75	100	90
Adults	90	80	110	95

The 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).

JECFA evaluated ascorbic acid and sodium ascorbate in 1961 when an unconditional[21] ADI of 0–2.5 mg/kg bw and a conditional[22] ADI of 0.5–7.5 mg/kg bw were established for the group (JECFA, 1962). In 1973, the ADI was changed to 0–15 mg/kg bw to also cover potassium salt (JECFA, 1974b). It was stressed that the ADI value was over and above the amount of ascorbic acid naturally present in foods (JECFA, 1974a). In 1981, JECFA evaluated calcium ascorbate and included in the report substantial amounts of new data on ascorbic acid and salts and allocated the group ADI "not specified" covering ascorbic acid, sodium ascorbate, calcium ascorbate and potassium ascorbate. For calcium ascorbate, the Committee noted that, as oxalate is an important metabolite of ascorbate, the use of the calcium salt in large amounts might increase the risk of crystalluria and the formation of calcium oxalate stones. However, it was concluded that the amount of calcium from the use of calcium ascorbate as a food additive would represent only a small fraction of the total dietary intake of calcium and that no special restriction on the substance would be needed (JECFA, 1981a). A toxicological monograph was prepared which also included previous monographs and covered ascorbic acid and its sodium and potassium salts beside the calcium salt, which was on the agenda (JECFA, 1981b).

Ascorbates have been evaluated and summarised by several other organisations and committees (FASEB, 1979; FNB, 2000; EVM, 2002, 2003; FAO/WHO, 2004; CIR, 2005). The two most relevant for the current evaluation are discussed below.

[21] Unconditional ADI was a term previously applied by JECFA for those substances for which the biological data available included either the results of adequate short-term and long-term toxicological investigations or information on the biochemistry and metabolic fate of the compound, or both.
[22] Conditional ADI was a term previously applied by JECFA for specific purposes arising from special dietary requirements.

The FAO/WHO (2004) mentioned three limiting factors concerning the use of high doses of vitamin C, namely the gastrointestinal effects, the potential risk of oxalate stone formation and haemolytic effects. Overall, it was concluded that 1 g of vitamin C appears to be the advisable upper limit of dietary intake.

The UK Expert Group on Vitamins and Minerals (EVM) concluded that there were insufficient data to set a safe upper level for vitamin C (EVM, 2003). However, it was noted that adverse effects on the gastrointestinal system may occur in subjects consuming high quantities of vitamin C, and this may be a serious problem for individuals with disordered gastrointestinal function. Based on a study of Cameron and Campbell (1974) (see section 3.2.6), by applying an uncertainty factor of 3 from the lowest observed adverse effect level (LOAEL) of 3 000 mg/day as the dose which was found to cause only minimal gastrointestinal disturbances, the EVM stressed that the possible adverse effects of vitamin C in vulnerable individuals appear to occur at intakes above 1 g/day (EVM, 2002, 2003).

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, 2011b)). New consumption surveys recently added in the Comprehensive database (end 2014) were taken into account to cover also estimates for infants (from 4 up to and including 11 months of age).

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.

The Panel estimated chronic exposure for the following population groups: infants, toddlers, children, adolescents, adults and the elderly. Calculations were performed using individual body weights. For the calculation of chronic exposure, intake statistics have been calculated based on individual consumption over the total survey period, excluding surveys with only one day per subject considered as not adequate to assess chronic dietary exposure. High percentile exposure was only calculated for those population groups where the sample size was sufficiently large to allow calculation of the 95th percentile of exposure (EFSA, 2011b). 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 30 different dietary surveys carried out in 17 European countries (Table 7).

Table 7: Population groups considered for the exposure estimates of ascorbic acid and its salts (E 300–302)

Population	Age range	Countries with food consumption surveys covering more than one day
Infants	From 4 up to and including 11 months of age	Bulgaria, Denmark, Finland, Germany, Italy, UK

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

(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, 2011b).

Consumption records were codified according to the FoodEx classification system (EFSA, 2011c). Nomenclature from the FoodEx classification system has been linked to the Food Classification System (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 and the exposure was calculated by multiplying values reported in Appendices 5 and 13 for each food category with their consumption amount per kg bw separately for each individual in the database. The exposure per food category was subsequently added to derive an individual total exposure per day. Finally, these exposure estimates were averaged over the number of surveys days, resulting in an individual average exposure per day for the survey period. This was done for all individuals in the survey and per population group, resulting in distributions of individual average exposure per survey and population group (Table 7). Based on these distributions, the mean and 95th percentile exposure were calculated per survey for the total population and per population group.

2.9.1.2. Food categories selected for the exposure assessment of ascorbic acids and its salts

The food categories in which the use of ascorbic acid (E 300), sodium ascorbate (E 301) and calcium ascorbate (E 302) are 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, 2011c).

Some food categories were not referenced in the EFSA Comprehensive Database and could therefore not be 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 the 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 the FCS code), the restrictions that apply to the use of ascorbic acid (E 300), sodium ascorbate (E 301) and calcium ascorbate (E 302) 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:

- 02.1. Fats and oil essentially free from water (excluding anhydrous milk fat), only cooking and/or frying purposes or the preparation of gravy
- 05.1. Cocoa and chocolate products as covered by Directive 2000/36/EC, only energy-reduced or with no added sugars.
- 07.1.2. Pain courant français, friss buzakenyer, feher es felbarna kenyerek, only friss buzakenyer, feher es felbarna kenyerek
- 08.2. Meat preparations as defined by Regulation (EC) No 853/2004, only *gehakt* and prepacked preparations of fresh minced meat
- 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
- 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. For the following two food categories, no information on processing is available in FoodEx:

- FCS 04.1.2. Peeled, cut and shredded fruit and vegetables, *only refrigerated unprocessed fruit and vegetables ready for consumption and prepacked unprocessed and peeled potatoes*
- FCS 04.1.3. Frozen vegetables.

Therefore, fruits and vegetables (usually peeled, cut, shredded or frozen) were selected at the most detailed level possible (up to FoodEx level 4). Inclusion of this selection in the exposure assessment probably resulted in an overestimation of the exposure, because these fruits and vegetables are also consumed in other forms, such as raw, cooked, etc.

Overall, 10 food categories were not taken into account in the exposure assessment because they are not referenced in the EFSA Comprehensive Database, and 11 food categories were included without considering the restrictions as set in Annex II of Regulation (EC) No 1333/2008.

For some food categories, no reported use/analytical levels were available. Instead, levels on very similar food categories were received and used. This concerns the following food categories (in ascending order of the FCS codes):

- 06.4.1. Fresh pasta: reported use levels of FCS 06.4.3. Fresh pre-cooked pasta
- 06.4.2. Dry pasta: reported use levels of FCS 06.4.3. Fresh pre-cooked pasta

- 06.4.5. Fillings of stuffed pasta: reported use levels of FCS 06.4.3. Fresh pre-cooked pasta
- 07.1. Bread and rolls: reported use levels of FCS 07.1.1. Bread prepared solely with the following ingredients: wheat flour, water, yeast or leaven, salt and 07.1.2. Pain courant français, friss buzakenyér, feher és félbarna kenverek
- 13.1.2. Follow-on formulae: reported use levels of FCS 13.1.1. Infant formulae.

2.9.2. Exposure to ascorbic acids and its salts (E 300–302) from its use as a food additive

The Panel estimated the combined exposure to ascorbic acid (E 300), calcium ascorbate (E 301) and sodium ascorbate (E 302) using the highest concentration reported from any of them for each food category. 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".

Based on the data made available to EFSA, reported use levels and analytical data from Member States (section 2.7), the Panel performed different exposure estimates scenarios.

Reported use levels from industry give information on the amount of the food additive added to food. By using these data, exposure to ascorbic acid and its salts (E 300–302) at the moment that the food was produced can be calculated (Table 8). It has been noted earlier that ascorbic acid is degraded during processing and storage (section 2.5). The loss of ascorbic acid in food is very likely to have an impact on the overall exposure estimates calculated with the reported use levels. Therefore, the Panel calculated additional exposure estimates using reported use levels from industry including potential loss factors so that these estimates reflect more closely the exposure to ascorbic acid and its salts (E 300-302) as food additives via foods as consumed (Table 8).

On the other hand, the analytical levels provided by the Member States reflect the levels of ascorbic acid in foods whatever the origin (from natural and other sources). Therefore, the exposure estimated with analytical data should reflect more closely what is ingested through the diet. However, the analytical data covered only 28 food categories out of the 88 in which the food additive is authorised. Reported use levels (including loss factors) were therefore used for the remaining food categories. In addition, it should be noted that no analytical data were made available for foods in which ascorbic acid is naturally occurring (such as raw food commodities, for example citrus fruits), and data were provided by only four Member States, making their representatives questionable. Thus, the Panel noted that the exposure estimate based on a combination of analytical data and reported use levels will not reflect the exposure to ascorbic acid and its salts in Europe via the whole diet (from natural and other sources). This exposure estimate has been calculated and is presented in Appendix 14, but was not used in the risk assessment, because of the limitations described above.

Exposure assessment to food additives under re-evaluation is carried out by the ANS Panel based on (1) MPLs set out in EU legislation (defined as the *regulatory maximum level exposure assessment* scenario) and (2) use levels or analytical data (defined as the *refined exposure assessment* scenario).

2.9.2.1. Maximum level exposure assessment scenario

The regulatory maximum level exposure assessment scenario is based on the MPLs as set out in Annex II of Regulation No 1333/2008. As ascorbic acid (E 300), sodium ascorbate (E 301) and calcium ascorbate (E 302) 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, as described in the EFSA Conceptual framework (EFSA ANS Panel, 2014).

The exposure estimates derived following this scenario should be considered as the most conservative, as this scenario assumes that the consumer will be continuously (over a lifetime) exposed to ascorbic acid (E 300), sodium ascorbate (E 301) and calcium ascorbate (E 302) present in the food at the maximum reported use levels.

2.9.2.2. Refined exposure assessment scenario

The refined exposure assessment scenario is based on information on reported use levels submitted by industry and/or analytical results submitted by Member States. This exposure scenario can only consider food categories for which data are available to the Panel. For ascorbic acid (E 300), sodium ascorbate (E 301) and calcium ascorbate (E 302), refined exposure assessments were performed using reported use levels (section 2.9.2).

Based on the available dataset, the Panel calculated two exposure estimates based on different model populations:

1. The brand-loyal consumer scenario: this scenario assumes that a consumer is exposed over a long period of time to the food additive present at the maximum reported use or analytical level for one food category and at the mean reported use or analytical level for the remaining food categories. This exposure estimate is calculated as follows:
   - Combining food consumption with the maximum reported use level or the maximum analytical level—for the main contributing food category at the individual level.
   - Using the mean of the typical reported use levels or the mean of analytical results for the remaining food categories.
2. The non-brand-loyal consumer scenario: this scenario assumes that a consumer is exposed over a long period of time to the food additive present at the mean reported use or analytical level in all food categories. This exposure estimate is calculated using the mean of the typical reported use levels or the mean of analytical results for all food categories.

Appendix 5 summarises the concentration levels used in the refined exposure assessment scenario.

In both refined exposure assessment scenarios, the concentrations considered by the Panel are extracted from the reported use levels. The mean typical reported use level per food category is calculated. Loss factors were considered to address the loss of ascorbic acid during processing and storage in one of the approaches (Table 8). For the loss factors used, see Appendix 5.

2.9.2.3. Anticipated combined exposure to ascorbic acid (E 300), calcium ascorbate (E 301) and sodium ascorbate (E 302)

Table 8 summarises the combined estimated exposure to ascorbic acid and its salts (E 300–302) in all six population groups using reported use levels from industry. Maximum level exposure assessment scenario is estimated only using reported use levels without loss factor. For the refined exposure scenarios, results are listed both with and without considering the loss of ascorbic acid during the manufacturing process and storage. See Appendix 5 for the reported use levels used in the estimates. For the exposure results per population and survey, see Appendices 6 and 7.

Table 8: Summary of anticipated combined exposure to ascorbic acid (E 300), calcium ascorbate (E 301) and sodium ascorbate (E 302) from their use as food additives in six population groups (minimum to 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[(a)]						
Mean	8.3–33.0	8.4–82.0	23.8–74.2	17.4–40.6	5.0–24.2	2.7–20.1
High level	15.3–100.1	36.1–159.2	46.4–167.3	34.1–98.9	13.6–59.7	8.1–53.9
Refined estimated exposure scenario using reported use levels without loss factor						
Brand-loyal scenario						
Mean	6.2–26.7	6.3–58.1	14.9–64.7	11.0–33.7	3.8–17.7	2.2–17.2
High level	11.1–91.7	25.0–147.1	29.2–157.8	24.1–85.1	10.8–51.4	7.0–50.5
Non-brand-loyal scenario						
Mean	3.8–7.2	2.8–18.8	7.1–15.3	4.0–8.3	1.8–5.1	1.0–4.1
High level	7.1–20.2	11.2–34.3	12.4–31.8	9.2–17.7	4.9–11.7	2.7–9.9
Refined estimated exposure scenario using reported use levels with loss factor						
Brand-loyal scenario						
Mean	5.0–13.8	4.4–21.7	5.6–15.7	3.0–8.0	1.7–6.3	1.3–3.4
High level	9.7–32.3	19.6–39.9	13.0–32.1	7.3–19.3	3.8–14.3	2.9–8.8
Non-brand-loyal scenario						
Mean	2.8–4.2	2.3–10.2	3.3–7.6	1.6–3.8	1.1–2.5	0.9–1.5
High level	5.2–9.3	9.0–16.9	6.4–14.5	3.2–8.1	2.2–5.5	1.6–3.5

(a): Using the maximum reported use levels.

The main food categories contributing to the combined exposure calculations of ascorbic acid (E 300), calcium ascorbate (E 301) and sodium ascorbate (E 302) in the different scenarios are presented in Appendices 8, 9, 10 11, 12.

Summary of the estimated exposure to ascorbic acid in all six population groups using analytical data from Member States is presented in Appendix 14. Concentration levels used in this exposure scenario are presented in Appendix 13 and the main food categories contributing to the exposure calculations in Appendices 16 and 17.

2.9.3. Exposure to ascorbic acid from natural sources

Ascorbic acid (vitamin C) is present naturally in food. In 2013, the NDA Panel issued an opinion on the dietary reference values for vitamin C (EFSA NDA Panel, 2013). This opinion reviewed vitamin C intakes among European populations for several age classes and by sex. Table 9 summarises those intakes (in mg/person per day) per population group.

Table 9: Intake range of vitamin C (mg/person/day) across various European populations excluding food supplements (EFSA NDA Panel, 2013)

	Infants (4–11 months)	Toddlers (1–3 years)	Children (4–9 years)	Adolescents (10–18 years)	Adults (19–65 years)	The elderly (> 65 years)
Lower end [(a)]	[8–37][(c)]	19–33	18–41	16–61	13–64	14–65
Mean range	[79–119][(b)]	53–91	60–172	69–222	66–138	69–132
Upper end [(a)]	[120–172][(c)]	81–205	112–261	109–502	103–275	110–347

(a): Minimum–maximum percentile (2.5–25th percentile for lower end and 75–97.5th percentile for upper end).
(b): Data from two countries (France, UK).
(c): No lower or upper ends are available. For French intakes, standard deviations (SDs) are available, thus lower or upper ends were estimated by assuming lower end (p5)/upper end (p95) = mean ± 2 SD, from French data only

2.9.4. Exposure to ascorbic acid from food additives and natural sources

Considering the exposure to ascorbic acid and its salts as food additives (Table 8) and exposure from to ascorbic acid from natural sources (Table 9), the Panel decided to present an estimation of exposure to ascorbic acid from both sources (Table 10). The results should be interpreted with caution, as intakes of vitamin C (natural sources) were reported as ranges from the literature.

Table 10: Summary of anticipated combined exposure to ascorbic acid from its use as a food additive and from natural sources in six population groups (minimum to 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)
	Refined estimated exposure scenario using reported use levels without loss factor—Non-brand-loyal scenario					
	From food additive					
Mean	3.8–7.2	2.8–18.8	7.1–15.3	4.0–8.3	1.8–5.1	1.0–4.1
High level	7.1–20.2	11.2–34.3	12.4–31.8	9.2–17.7	4.9–11.7	2.7–9.9
	From natural sources					
Mean	10.5–15.9	4.4–7.6	2.6–7.5	1.3–4.2	0.9–1.9	0.9–1.7
Upper end [(a)]	16.0–22.9	6.8–17.1	4.9–11.3	2.1–9.5	1.4–3.7	1.4–4.6
	From natural and other sources					
Mean	14.3–23.1	7.2–26.3	9.7–22.8	5.3–12.5	2.7–6.9	1.9–5.9
High level[(b)]	23.1–43.1	18.0–51.4	17.2–43.1	11.2–27.2	6.3–15.4	4.2–14.5
	Refined estimated exposure scenario using reported use levels with loss factor—Non-brand-loyal scenario					
	From food additive					
Mean	2.8–4.2	2.3–10.2	3.3–7.6	1.6–3.8	1.1–2.5	0.9–1.5
High level	5.2–9.3	9.0–16.9	6.4–14.5	3.2–8.1	2.2–5.5	1.6–3.5
	From natural sources					
Mean	10.5–15.9	4.4–7.6	2.6–7.5	1.3–4.2	0.9–1.9	0.9–1.7
Upper end [(a)]	16.0–22.9	6.8–17.1	4.9–11.3	2.1–9.5	1.4–3.7	1.4–4.6
	From natural and other sources					
Mean	13.3–20.1	6.7–17.8	5.9–15.1	2.9–7.9	2.0–4.3	1.8–3.2
High level[(b)]	21.2–32.2	15.7–34.0	11.2–25.8	5.2–17.6	3.6–9.2	3.1–8.0

(a): Minimum–maximum percentile (2.5–25th percentile for lower end and 75–97.5th percentile for upper end).
(b): High levels were estimated by summing the high level from food additives with the upper end from natural sources. This is not mathematically correct considering the populations are not the same, but the raw data for natural sources intake were not available to EFSA. It gives an approximation of the high-level exposure, with a high level of conservatism.

The Panel noted that, on average, exposure estimates from their use as food additives and considering use levels without loss factors are twice those coming from natural sources and, therefore, represent around two-thirds of the total exposure. However, for infants, exposure estimates from natural sources are twice those as food additive at the mean, and exposure estimates from both sources are equal at the high level. The Panel also noted that the exposure estimates from their use as food additives and considering use levels with loss factors are equal to those coming from natural sources (both at the mean and at the high level) and, therefore, represent around 50 % of the total exposure. For infants, natural sources provided the main amount to the total exposure estimate to ascorbic acid.

2.9.5. Uncertainty analysis

Uncertainties in the exposure assessment of ascorbic acids and its salts (E 300–302) have been discussed above. Using the guidance provided in the EFSA opinion related to uncertainties in dietary exposure assessment (EFSA, 2006), Table 11 summarises the sources of uncertainty that have been considered.

Table 11: Qualitative evaluation of influence of uncertainties on the dietary exposure estimates

	Direction[(a)]
Sources of uncertainty	
Consumption data: different methodologies/representativeness/underreporting/misreporting/no portion size standard	+/–
Use of data from food consumption survey covering a few days to estimate long-term (chronic) exposure	+
Food categories selected for the exposure assessment: exclusion of food categories due to missing FoodEx linkage	–
Food categories selected for the exposure assessment: inclusion of food categories without considering the restriction/exception	+
NDA Panel estimates of intake from natural sources might already cover partly food additives exposure	+
Reported use level and analytical data	
Correspondence of data to the food items in the EFSA Comprehensive Food Consumption Database: uncertainties on the precise types of food the data refer to	+/–
Levels considered applicable to all items within the entire food category	+
Exposure calculations based on the maximum and/or mean levels	+/–
Use of the maximum or mean use level/analytical level per food additive in the combined exposure assessment	+
Analytical data	
Not fully representative of foods on the EU market: only four Member States and limited number of food categories	–
Reported use levels	
Uncertainty in possible national differences in use levels of food categories, data not fully representative of foods on the EU market	+/–
Loss factor: mean factors related to the relevant food categories in the EFSA Comprehensive database	+/–

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

The Panel considered the impact of the uncertainties in the exposure assessment for ascorbic acid and its salts and concluded that, overall, uncertainty could lead to an overestimation of the calculated exposure estimates.

3. Biological and toxicological data

3.1. Absorption, distribution, metabolism and excretion

Ascorbic acid is absorbed from the intestine by a sodium-dependent active transport process. At low doses, the absorption efficiency is up to 98 %, i.e. only around 2 % will be excreted in the faeces (Baker et al., 1969; Hornig and Moser, 1981). Because the transporter is saturable, absorption efficiency gradually decreases at higher intakes and is thus 80–90 % up to 180 mg, 75 % at 1 g and 16 % at 12 g (Hornig and Moser, 1981; Kallner et al., 1977, 1979, 1985; Blanchard et al., 1997).

Vitamin C is readily oxidised to dehydroascorbic acid, which can be reduced back to ascorbic acid or hydrolysed (irreversibly) to diketogulonic acid, which is partly excreted with urine and partly oxidised to mainly oxalic acid and threonic acid and, to a lesser extent, to xylose, xylonic acid and lyxonic acid (EVM, 2002, 2003; EFSA, 2004) (for further information concerning the potential risk from oxalate formation, see section 3.2.6). Oxidation to carbon dioxide is not a major route, but at high doses it may occur, possibly as a result of metabolism of unabsorbed ascorbate by the intestinal microflora (Kallner et al., 1985). Ascorbic acid may also undergo limited conjugation with sulphate to form ascorbate-2-sulphate, which is excreted in the urine. Unchanged ascorbic acid and its metabolites are excreted in the urine, but the percentage that is excreted depends on the dose. Thus, only approximately 3 % of a 60 mg oral dose is eliminated in the faeces, while, at very high doses (i.e. 1 g or more), the majority of ingested ascorbic acid is excreted in the faeces. At total daily intakes above 80–100 mg/day, most of

the absorbed ascorbic acid above this dose range is excreted, unchanged, in the urine, indicating that tissue reserves are saturated at this intake level (SCF, 1993; Blanchard et al., 1997; FNB, 2000). This increasing renal elimination of ascorbic acid with increase in dose results in a decrease in the elimination half-life with increasing dosage (Kallner et al., 1979) and probably arises from saturation of re-absorption from renal tubules with consequent larger excretion (Blanchard et al., 1997).

In 2009 (EFSA, 2009), the ANS Panel—evaluating the safety of calcium ascorbate, magnesium ascorbate and zinc ascorbate added for nutritional purposes to food supplements—considered that sodium ascorbate and calcium ascorbate are fully dissociated in the stomach (acidic conditions) and that the bioavailability of calcium and ascorbic acid from calcium ascorbate would be expected to be similar to that from other dissociable forms of calcium and ascorbic acid in the gastrointestinal tract.

The pharmacokinetics of ascorbic acid was studied in 20 dogs (8 German Shepherds, 10 Labrador Retrievers and 2 Riesenschnaussers, aged 1–10 years) (Wang et al., 2001). Ascorbic acid was given orally, in single doses, to the animals at two dosage levels (15 and 50 mg/kg bw/day) and under two forms (crystalline ascorbic acid and a calcium ascorbate supplement). The pharmacokinetics of ascorbic acid in all 20 dogs was compared with the kinetics of calcium ascorbate. Groups of eight dogs were given 15 mg/kg bw/day of vitamin C, either in the form of ascorbic acid or as calcium ascorbate. Other groups of six dogs were given 50 mg/kg bw/day vitamin C as the acid or the calcium salt. After oral administration, a rapid increase was found in the plasma level of ascorbic acid, indicating a possible intestinal active transport mechanism in this species. The obtained C_{max} and area under the curve (AUC) values were found to increase in a non-linear fashion when the dose of ascorbic acid was increased. The comparison of crystalline ascorbic acid and the commercial vitamin C product did not indicate any significant differences in pharmacokinetic parameters between the two forms of the vitamin.

3.2. Toxicological data

3.2.1. Acute oral toxicity

Bächtold (1972a) and Bächtold (1973c) reported the oral lethal dose, 50 % (LD_{50}) for ascorbic acid, sodium ascorbate and calcium ascorbate for mice to be 4 380 mg/kg bw, 9 111 mg/kg bw and 8 476 mg/kg bw, respectively, and for the rat to be 6 996 mg/kg bw, 8 221 mg/kg bw and 11 289 mg/kg bw, respectively.

3.2.2. Short-term and subchronic toxicity

3.2.2.1. Mice

The National Toxicology Program (NTP) (1983) has performed studies of 14 days and 13 weeks in male and female B6C3F1 mice. In the 14-day dose-range finding study, 6-week-old mice (five animals/sex/dose; males 23 g and females 18 g) were fed diets containing 0, 6 000, 12 500, 25 000, 50 000 or 100 000 mg ascorbic acid/kg feed (equivalent[23] to 0, 1 128, 2 350, 4 700, 9 400 and 18 800 mg/kg bw/day for males and to 0, 1 344, 2 800, 5 600, 11 200 and 22 400 mg/kg bw/day for females, respectively). Mice of each sex receiving 100 000 mg/kg feed lost weight. Female mice receiving 12 500–50 000 mg/kg feed gained only 0–0.2 g in weight. Decreases in mean body weight gains were not dose related in male or female mice that received dietary concentrations between 6 000 and 50 000 mg/kg feed. No compound-related clinical signs, gross or microscopic pathological effects were observed.

In the 13-week study, 7-week-old mice (10 animals/sex/dose; males 26 g at the beginning of study and 32 g at the end of the study, and females 21 g at the beginning of study and 25 g at the end of the study) were given a diet containing 0, 25 000, 50 000 or 100 000 mg ascorbic acid/kg feed (equivalent[23] to 0, 4 225, 8 450 and 16 900 mg ascorbic acid/kg bw/day for males and to 0, 5 375,

[23] Calculated by the Panel according to EFSA Scientific Committee (2012).

10 750 and 21 500 mg ascorbic acid/kg bw/day for females, respectively). Mean body weight gain relative to controls was depressed by 37 % in male mice receiving 50 000 or 100 000 mg/kg feed. Weight gains of dosed female mice were not depressed more than 10 to 13 % compared with controls, and the depressions were not considered to be dose-related by the authors. Cystic endometrial glands were found in the uteri of four out of nine female mice receiving 100 000 mg/kg compared with none found in the controls. No other compound-related effects were observed (NTP, 1983).

3.2.2.2. Rats

Takahashi (1995) studied the effect of 5 % ascorbic acid in the diet during one week in male Jcl:SD rats (aged five weeks). The number of haemorrhages, prothrombin time and partial thromboplastic indices were not affected. Diarrhoea was observed in the treated rats throughout the experiment. At necropsy, oedema of the stomach, hypertrophy of the kidneys and enlargement of the caecum were found in 2/6, 1/6, and 6/6 rats, respectively, when compared with controls.

The NTP (1983) has performed studies of 14 days and 13 weeks in male and female F344/N rats. In the 14-day dose-range finding study, 6-week-old rats (five animals/sex/dose; males 99 g and females 87 g at the start of the study) were fed diets containing 0, 6 000, 12 500, 25 000, 50 000 or 100 000 mg ascorbic acid/kg feed (equivalent[24] to 0, 708, 1 475, 2 950, 5 900 and 11 800 mg ascorbic acid/kg bw/day for males and to 0, 702, 1 463, 2 925, 5 850 and 11 700 mg ascorbic acid/kg bw/day for females, respectively). Necropsies were performed on all animals on day 15 or 16. A decrease in mean body weight gain relative to controls was observed in all dosed groups of male rats except those fed diets containing 25 000 mg ascorbic acid/kg feed. Compared with controls, weight gains for dosed female rats were increased, except for animals in the 25 000 mg/kg group where it was decreased by 12 %. Weight gain differences were considered by the study authors to be unrelated to treatment. No compound-related clinical signs, gross or microscopic pathological effects were observed.

In the 13-week study, 6-week-old rats (10 animals/dose/sex; males 115 g and females 96 g at the start of the study) were fed diets containing 0, 25 000, 50 000 or 100 000 mg ascorbic acid/kg feed (equivalent[24] to 0, 2 045, 4 050 and 8 100 mg ascorbic acid/kg bw/day for males and to 0, 2 275, 4 550 and 9 100 mg ascorbic acid/kg bw/day for females, respectively). No effects were seen in the male rats. Myeloid depletion was observed in two of the females receiving 50 000 mg/kg feed and in four of the females receiving 100 000 mg/kg feed. Reticulum cell hyperplasia was found in the bone marrow of two of the females receiving 25 000 mg/kg feed, in one female receiving 50 000 mg/kg and in four females receiving 100 000 mg/kg feed.

To investigate the reticulum hyperplasia further, a second 13-week study in female F344/N rats was performed with doses of 0, 25 000 and 50 000 mg/kg feed (20 animals/group). Although some mean corpuscular haemoglobin values were lower in dosed groups than in controls, no consistent statistical differences were observed, and the results of haematological analyses were within the clinically normal range for all groups of animals (NTP, 1983).

3.2.2.3. Guinea pig

In a study by Hornig (1973), 19 guinea pigs (weight 205–211 g) were given a vitamin C-free diet which was enriched with 3 g ascorbic acid/kg feed. From the consumed amount of feed, a dose of approximately 30 mg ascorbic acid/day per animal was calculated for all 19 animals. Nine animals received 600 mg/day for 24 days, which was divided into two doses, each containing 1 mL of a solution of 300 mg ascorbic acid in 0.5 M disodium hydrogen phosphate. At the weekends, the 600 mg doses were given in one dose (2 mL). The remaining 10 animals were controls, drinking 1 mL of the sodium phosphate solution without ascorbic acid twice a day. Development of body weight was measured; urine was collected 16 hours before sacrifice. A series of parameters were measured and compared between the two groups, but there was no systematic description of the analysed parameters. There was a statistically significant decrease in the body weight gain in the high-dose animals

[24] Calculated by the Panel according to EFSA Scientific Committee (2012).

compared with the low-dose controls. There were no differences in urine volume and no differences in creatinine, allantoin or urea excretion between the urine samples from control and dosed animals. There was no difference in plasma vitamin C concentration. Plasma protein was decreased in high-dose animals and the concentration of the following free amino acids in plasma was increased: taurine, asparginic acid, methionine, glutamic acid, cysteine, tryptophan, tyrosine phenylalanine and phosphoserine. The concentration of arginine and glycine was decreased, while the concentrations of the other measured amino acids were unchanged. There were no changes in cholesterol or alkaline phosphatase. The activity of the erythrocyte glutamate oxaloacetate transaminase was statistically significantly lowered in the high-dose animals. There were no effects on brain or heart dopamine, but there was a significant increase in brain noradrenalin concentration in the high-dose animals. There was no change in the weight of the liver or the vitamin C content of the liver. The concentration of phospholipids and triglycerides decreased in the high-dose animals compared with the low-dose controls.

In a study by Nandi et al. (1973), male short-haired guinea pigs with an initial weight of 160 ± 10 g (strain not indicated) were given a basal nutritionally balanced fortified wheat diet and were administered, for 20 weeks, daily doses of 0.5, 1, 2, 5, 10, 20, 50 and 250 mg ascorbic acid per animal in 0.75 mL water by depositing the solution on the back of the tongue using a syringe (weight at the end of the study was 512 ± 8 g for control and 546 ± 9 g for dosed animals). Control animals were fed the basal diet only. The daily consumption of ascorbic acid from the basal diet was approximately 1.03 to 1.20 mg per animal (control as well as treated). Supplementation had no effect on food consumption, growth rate, physical appearance or behavioural pattern of the guinea pigs. The urinary excretion of ascorbic acid of the treated animals was increased compared with the control animals. The amount of ascorbic acid excreted in the urine of treated animals was 2.5 % of the administered dose. The average 24-hour urinary excretion of oxalic acid by guinea pigs fed 250 mg ascorbic acid daily was 3.5 ± 0.8 mg, similar to that of the control animals. Haemoglobin, blood glucose, serum iron, liver iron and liver glycogen of guinea pigs fed 250 mg ascorbic acid was also similar to control values. The authors concluded that large doses of ascorbic acid were neither beneficial nor toxic to guinea pigs fed a balanced diet.

In a parallel study by the same authors (Nandi et al., 1973), the guinea pigs were given doses of ascorbic acid up to 100 mg/animal/day for 25 days, but the diet consisted of whole grain flour not fortified. In this study, the mortality increased drastically at doses of 50 and 100 mg/animal. This effect was counteracted by adding casein to the diet, but not by adding vitamin mixture or salt mixture. The authors concluded that, in a population where the diet mainly consisted of cereals, the intake of large doses of ascorbic acid, well tolerated by people on a balanced diet, may be harmful. However, the Panel noted that the study is not well described and it therefore has doubts about the conclusion drawn from the study by the authors.

In a study by Singh et al. (1993), ascorbic acid was given at doses of 0, 100, 400 or 600 mg/kg bw/day by gavage for 105 days to male guinea pigs (seven animals/dose; 340–380 g, age not given). The two highest doses significantly increased oxalic acid excretion; however, upon examination, there was no crystal deposition, stone formation or calcification in the kidneys, ureter or bladder. In a parallel experiment, guinea pigs (seven males/group) made hypercalciuric with 2 % calcium oxalate in the feed or hyperoxaluric with 2 % sodium oxalate in the feed; ascorbic acid supplementation 100 mg/kg bw/day by gavage did not alter urine chemistry but histological examination revealed that ascorbic acid intensified the renal and bladder tissue calcification in both groups. The authors concluded that ascorbic acid in the doses used by clinicians did not cause urolith formation under normal conditions, but that the data suggested that high intakes of vitamin C increases the risk of renal calcification and stone formation in pre-existing hypercalciuric and hyperoxaluric conditions.

3.2.2.4. Conclusions

Overall, the Panel noted that, in some of the short-term studies, changes in weight gain were observed at high doses of ascorbic acid but none of these changes had a dose–response relationship and none

was considered treatment related. In the 13-week NTP study in rats, reticulum cell hyperplasia was found in a few (one to two per dose group) of the dosed females. This was confirmed in another 13-week study performed to investigate this. A similar effect was not found in the long-term study, but the author of the study had no explanation for this effect and disregarded it in the overall conclusion. No other adverse effects of ascorbic acid or sodium ascorbate were observed in the short-term studies and, therefore, the Panel is of the opinion that the maximum doses in the mice and rat studies of 16 900 or 21 500 mg ascorbic acid mg/kg bw/day for male and female mice, respectively, and of 8 100 or 9 100 mg ascorbic acid/kg bw/day for male and female rats, respectively, were considered as NOAELs.

3.2.3. Genotoxicity

Ascorbic acid and sodium ascorbate have been widely tested in both bacterial and mammalian genotoxicity assays.

3.2.3.1. *In vitro* studies

Gene mutation assay in bacteria

CIR (2005), in a review, reported 11 studies performed in *Salmonella typhimurium* strains (Litton Bionetics, 1975, as referred to by CIR (2005); Litton Bionetics, 1976, as referred to by CIR (2005); Stich et al., 1976; Omura et al., 1978; Bruce and Heddle, 1979; Weitzman and Stossel, 1982; Ishidate et al., 1984, 1988; Zeiger et al., 1988; Anderson et al., 1995) or *Staphylococcus aureus* strains (Amabile-Cuevas, 1988).

The Panel considered that, based on the data available, there is no evidence for a mutagenic effect of ascorbic acid in bacteria.

Gene mutation assay in yeast

CIR (2005) reported, in a review, an unpublished report from Litton Bionetics (1975, as referred to by CIR (2005)) in which ascorbic acid was tested in *Saccharomyces cerevisiae* strain D4 without metabolic activation and with metabolic activation using the liver, lung and testes of mice, rats and primates (*Macaca mulatta*) S9. No mutagenic activity was demonstrated. In another unpublished report from Litton Bionetics (1976, as referred to by CIR (2005)), sodium ascorbate was tested in the same strain using with the same metabolic activation systems at 0.075, 0.150 and 0.1 %; no mutagenic activity was observed.

Gene mutation assay in mammalian cells

Rosin et al. (1980) exposed Chinese hamster ovary (CHO) cells to ascorbate (unknown salt) (2 to 1×10^{-3} M) for three hours without metabolic activation only.This treatment resulted in the induction of mutations at the HPRT locus. The authors noted that the concentration at which ascorbate was positive in inducing the mutants was very narrow: the peak of mutation induction occurred with 5×10^{-4} M ascorbate (two assays) or 2×10^{-4} M (two assays) and a concentration of 1×10^{-4} M ascorbate resulted in a weak decrease in cell survival but induced no increase in mutation frequency. They also demonstrated that the addition of catalase prevented both mutagenesis and toxicity, suggesting that mutagenic metabolites of ascorbate may involve oxygen radicals. The Panel noted the absence of any consistent dose–response relationship (only one concentration in each of the four trials was reported as mutagenic) and the variability between assays without a clear indication of cell toxicity level in each assay. The absence of this information makes results difficult to interpret. The consideration of the positive data reported was impaired by the absence of a dose–response relationship and information on cytotoxicity.

Amacher and Paillet (1981) performed a mouse lymphoma assay (L5178Y cells) at the TK locus. Cells were treated for two hours without metabolic activation only. No mutagenic activity was observed up to the maximum toxicity level that appears for concentrations above 1.5 mM with

ascorbic acid and 0.5 mM with sodium ascorbate. The concentrations of 10 % survival were about 3.5 mM with ascorbic acid and 1 mM with sodium ascorbate.

In an additional mouse lymphoma assay at the TK locus in L5178Y cells, Myhr and Caspary (1991) evaluated ascorbic acid as a mutagenic compound, in both the absence and the presence of rat S9 metabolism in the range 750–1 500 µg/mL when acidic conditions caused by treatments were not controlled. However, when stock solutions of ascorbic acid were neutralised with NaOH to keep pH at values close to 7, no mutagenicity was observed, although toxicity was markedly enhanced (25 % RTG at 200 µg/mL and lethal effects at 300 µg/mL).

Gene mutation assay in Drosophila melanogaster

Tripathy et al. (1990) in a wing spot test in *Drosophila melanogaster* (three days of age) at concentrations of 0, 10, and 300 mM ascorbic acid in food for 48 hours, found that no gene mutation was induced.

Khan and Sinha (2008) performed a Muller-5 test (X-chromosome-linked recessive lethal mutations assay) in *Drosophila melanogaster*. First-instar larvae (age: 24 ± 2 hours) collected from culture stock were transferred to food vials containing supplementation with vitamin C (10 mg/L of food). Virgin females of Muller-5 stock were mated to treated males in vials containing normal food to obtain M1 flies. Brother–sister crosses were arranged for these M1 flies by keeping one female with one male in each vial to increase the M2 generation. A statistically significant increase (about three times) in mutation frequency was observed with respect to controls when the food was mixed with vitamin C.

Chromosomal aberration assay

Stich et al. (1980) observed clastogenic activity of neutralised culture medium extract of three different ascorbic acid pills (one pill containing 100 mg in 20 mL culture medium) in CHO cells at concentrations given for 3 hours followed by a 16-hour recovery period with extracts diluted from 1/100 to 1/1 000 (theoretically from 1 to 0.1 mg/mL ascorbic acid). Authors observed that 24–42 % of cells treated with the extract dilutions were binding chromosomal aberrations. However, CIR (2005), in a review, pointed out that the authors of this study noted that the study demonstrated chromosome damaging capacity of vitamin C in one *in vitro* test system and that they did not provide information on the possible mutagenic or clastogenic action of ascorbic acid *in vitro* in mammals, including in humans. The Panel noted that this assay did not study ascorbic acid itself but three extracts of three different pills, and that the clastogenic and cytotoxic effects are very different between extracts; that no control of the ascorbic acid extracted was performed and that excipients of the pills could interfere in the assay; that no information on the use of metabolic activation was given; and that no result of negative control was reported. The Panel considered that this study had some shortcomings, e.g. poor reporting of the methodology used for the preparation of the test substance.

Ishidate et al. (1984), in an *in vitro* chromosomal aberration test using a Chinese hamster fibroblast cell line, found no clastogenic activity of ascorbic acid when tested at up to 0.3 mg/mL in saline solution. The maximum dose was selected by a preliminary test which identified the dose needed for 50 % cell-growth inhibition. The cells were exposed to three different concentrations for 24 and 48 hours. No information about the use of metabolic activation was provided.

CHO cells were treated with L-ascorbic acid (purity 99.3 %) for 24 hours without S9 and 2 hours followed by a 24-hour recovery period (Gulati et al., 1989). L-Ascorbic acid was negative for the induction of chromosomal aberrations in either the presence or the absence of S9, although in the first trial without S9 a positive response was observed at the highest dose tested (300 µg/mL); the highest non-lethal dose achievable in three subsequent trials without S9 was 1 600 µg/mL and no increase in aberrations occurred at this level. The authors noted that a noticeable decrease in pH of the culture medium occurred at doses of 500 µg/mL and above.

Greggi et al. (1999) investigated the clastogenic effect of ascorbic acid (at concentrations of 100, 200, 500 and 1 000 mg/mL) without metabolic activation for 48 hours on human peripheral blood lymphocytes *in vitro*, in which 100 metaphases/concentrations were observed. Ascorbic acid did not show any clastogenic effect, except at 1 000 mg/mL that demonstrated an excessive cytotoxic level (60 % decrease of mitotic index). The Panel noted that no neutralisation of the acidification of the culture medium was performed.

Robichová et al. (2004), found no induction of chromosomal aberrations in human Hep G2 cells *in vitro* with ascorbic acid at 0.5 mM for 1 hour without metabolic activation.

Micronucleus assay

Miller et al. (1995) tested ascorbic acid in CHO cells without S9 with a 48-hour continuous treatment and with S9 (from livers of phenobarbital/β naphtoflavone induced-rats) with a 3-hour treatment followed by a 45-hour recovery period in only one culture/dose. Only 1 000 cells/culture were observed. There was a dose-related increase in two independent assays without metabolic activation, statistically significant at 400 µg/mL in the first assay and at 500 and 600 µg/mL in the second assay. No induction of micronuclei was observed with metabolic activation. A shorter treatment (25 to 46 hours) at concentrations of 1300 and 1730 µg/mL (10mM) in the absence of metabolic activation did not induce a significant increase in micronuclei. The authors explained this effect by the production of oxidative radicals produced at high doses only. The Panel noted that no adjustment of pH was performed and that an acidification of the medium could be at the origin of the clastogenic activity.

Comet assay

Frenzilli et al. (2000) investigated the genotoxic potential of ascorbic acid in the alkaline single-cell gel assay (Comet assay) in human leucocytes *in vitro* at concentrations up to 1 500 µM without metabolic activation for four hours and no DNA strand breaks were noted.

The genotoxic potential of vitamin C was assessed on human lymphocytes, isolated by centrifugation in a density gradient, using single-cell gel electrophoresis (Comet assay) (Blasiak et al., 2000). Fifty cells were randomly selected from each sample and the comet tail moment (a product of DNA fraction in tail and tail length) was measured. Vitamin C at 20 and 100 µmol/L, for one hour at 37 °C, significantly increased the tail moment of lymphocytes. The Panel noted that no adjustment of pH was performed and that an acidification of the medium could be the origin of the clastogenic activity.

Robichová et al. (2004) found no induction of DNA strand breaks using the Comet assay in human Hep G2 cells *in vitro* with ascorbic acid at 0.5 mM for one hour.

Duarte et al. (2007), studying the clastogenic potential of ascorbic acid, demonstrated that high concentrations of ascorbic acid (100 to 300 µM) induced DNA strand breakage in a dose-dependent manner in skin human diploid fibroblasts. The genotoxic effect of ascorbic acid was transient, required the formation of extracellular H_2O_2 and the presence of intracellular iron, but not of extracellular transition metal ions. The Panel noted that no adjustment of pH was performed and that an acidification of the medium could be the origin of the clastogenic activity.

In a study by Sharma et al. (2011), blood samples were treated with various concentrations (90, 180 and 360 µM) of antioxidants for one hour at 37 °C and analysed with the Comet assay. The results showed that there was a significant decrease in DNA damage in the samples treated with ascorbic acid at the lower concentration (90 µM), whereas there was a significant increase in DNA damage at higher concentrations > 180 µM. Glutathione treatment resulted in decreasing DNA damage at only the highest dose (360 µM). The Panel noted that this study was briefly presented.

Other genotoxicity assays

Lo and Stich (1978) demonstrated that sodium ascorbate at concentration below 1×10^{-2} M had no detectable inhibitory effect on the ultraviolet-elicited DNA repair synthesis of primary human skin fibroblasts in culture.

Galloway and Painter (1979) found that sodium ascorbate caused, at concentrations from 1×10^{-4} to 1×10^{-2} M for 27–29 hours, a dose-dependent increase in sister chromatid exchanges (SCEs) in CHO cells and from 5.4×10^{-4} to 5.4×10^{-3} M for 73 hours in human lymphocytes. In the DNA synthesis inhibition test with HeLa cells, ascorbate gave results typical of DNA-damaging chemicals at concentrations of 2 to 20 mM. No effects were seen below 1 mM. Catalase-reduced SCE induction by ascorbate prevented its cytotoxicity in CHO cells and DNA synthesis inhibition in HeLa cells, a result which is in favour of the role of radical oxygen species from H_2O_2 produced in the oxidation of ascorbate in the culture medium.

Macrae and Stich (1979) demonstrated genotoxic activity with sodium ascorbate in a SCE assay in Chinese hamster cells treated with 1×10^{-4} to 1×10^{-2} M sodium ascorbate for two to three hours. They also showed an increase of this effect when using a 24-hour continuous treatment and by the addition of copper(II) ions in the culture medium.

Speit et al. (1980) found that sodium ascorbate in concentrations from 1×10^{-6} to 1×10^{-3} M induced SCEs in V79 Chinese hamster cells *in vitro*. As it was not possible to confirm this effect *in vivo* with doses up to 10 000 mg/kg bw/day, the authors concluded that the actual mutagenic potential in humans did not appear to be as great as expected from the *in vitro* study findings. In addition, in this study, it was suggested that the positive effects *in vitro* were caused by the production of hydrogen peroxide. This mechanism has been confirmed in experiments where the genotoxic effect of ascorbic acid or ascorbates was inhibited by the addition of cysteine or reduced glutathione but not by oxidised glutathione.

Novicki et al. (1985), in an inhibition of DNA synthesis assay in rat hepatocytes, demonstrated no primary DNA damage with 1×10^{-4} to 1×10^{-6} mM ascorbic acid with a 48-hour incubation period.

In a study by Weitberg (1987), CHO cells, when exposed to sodium ascorbate at 1×10^{-3} and 1×10^{-4} M for 10 minutes without metabolic activation, developed increased numbers of SCEs without a dose–response relationship. Superoxide dismutase and catalase caused a significant reduction in the number of SCEs induced by vitamin C, which suggests that free radicals may play a role in the genotoxic effect of high doses ($\geq$ 0.1 M).

Gulati et al. (1989) performed an SCE test in CHO cells at concentrations of 0–1 600 µg L-ascorbic acid/mL with and without metabolic activation ((S9) rat liver fractions). The authors noted that there was a noticeable decrease in pH at doses $\geq$ 500 µg/mL. A dose-related increase in SCE frequencies was observed following exposure of the cells to 500–1 000 µg/mL. No increase in SCEs was observed with metabolic activation for all tested doses.

Littlefield and Hass (1995) performed a DNA damage assay determining the *in vitro* formation of DNA double-strand breaks in a cultured human B lymphoblastoid cell line (AHH-1) using a fluorescent dye that interacts with only double-strand DNA in alkaline conditions, the rate of unwinding being directly related to the presence or amount of alkali labile breaks in the DNA. Ascorbic acid at 500 µM did not produce primary DNA damage.

3.2.3.2. *In vivo* studies

Micronucleus assay

In the study by Bruce and Heddle (1979), ascorbic acid was investigated for its capability to induce micronuclei in the bone-marrow reticulocytes of C57BL/6xC3H/He female mice. Three animals per group were treated daily by intraperitoneal injection at concentrations close to 0.125, 0.25, 0.5 and 1

of the LD_{50} (actual doses not mentioned in the report) for five consecutive days and were sacrificed four hours after the last injection. A vehicle control animal group (tap water) was included and negative results were reported. However, the Panel noted that the study bears major shortcomings related to the limited number of animals employed and the number of cells scored (approximately 330 reticulocytes/animal). Furthermore, no positive control was employed. On this basis, the Panel considered the study of limited validity.

A study in mice (six animals/group) examined bone marrow micronuclei after oral administration of ascorbic acid at doses up to 622 mg/kg bw/day for two days (Pienkowska et al., 1985). The animals were sacrificed four hours after the last administration and 2 000 reticulocytes were scored per animal. No statistically significant increase in the number of micronuclei was reported. The Panel considered this study mainly consistent with the current OECD Guideline 474 (OECD, 2014), except that the choice for the maximum dose was not justified by the authors.

In the study by Shelby et al. (1993), which aimed to evaluate 49 chemicals (25 carcinogens and 24 non-carcinogens) in a mouse bone marrow micronucleus test, ascorbic acid was assessed for its capability to induce micronuclei in the bone marrow erythrocytes of male B6C3F1 mice. Groups of five mice were administered with the test compound by intraperitoneal injection on three consecutive days and bone marrow smear slides were prepared 24 hours after the last administration. Dose levels of 500, 1 000 and 1 500 mg/kg bw/day selected in a preliminary dose-range finding experiment were used. Groups of solvent and positive control-treated animals were also included. For induction of micronuclei, a minimum number of 2 000 polychromatic erythrocytes (PCEs) per animal were scored in bone marrow smears stained with acridine orange. The results obtained indicate that ascorbic acid induced dose-related increases in the incidence of micronucleated PCEs, which achieved statistical significance at the highest dose-level (1 500 mg/kg bw/day). However, the Panel noted that acceptability of results based on positive and negative control values and biological relevance of the results obtained, according to historical control range values, were not evaluated by the authors. In addition, it should be noted that the intraperitoneal route of administration employed is not recommended, as it is not a typical relevant route of human exposure, and should be used with specific justification only (OECD Guideline 474; OECD, 2014). On this basis, the Panel concluded that the positive outcome of this study should be critically considered.

Sister chromatid exchanges assay

Speit et al. (1980) tested SCEs in the bone marrow of Chinese hamsters. Ascorbic acid was administered either orally or by intraperitoneal injection at doses ranging from 200 to 10 000 mg/kg bw/day. Animals were sacrificed 16 hours after the treatment. The SCEs were counted in 50 metaphasesfrom two animals. No induction of SCEs was noted.

Krishna et al. (1986) reported that no SCEs were induced in bone marrow and spleen cells of mice seven hours after a single intraperitoneal administration of ascorbic acid at doses up to 6 680 mg/kg bw/day.

3.2.3.3. Human data

In a study by Duthie et al. (1996), smokers and non-smokers were supplemented with 100 mg vitamin C/day for 20 weeks, which resulted in a significant decrease in oxidative base damage to lymphocyte DNA as measured by a modified Comet assay. In addition, the lymphocytes showed an increased resistance to H_2O_2-induced oxidative damage *in vitro.*

In a study by Prieme et al. (1997), 21 individuals were given 250 mg ascorbic acid twice a day for two months and another 21 individuals were given 250 mg slow-release ascorbic acid twice a day for two months. The study found no significant changes in the 24-hour urinary 8-oxodG excretion compared with placebo (placebo not specified).

In a study by Podmore et al. (1998), the diets of 30 healthy volunteers (16 females and 14 males aged between 17 and 49 years) were supplemented with 500 mg ascorbic acid/day for six weeks. Supplementation of diets with 500 mg ascorbic acid/day resulted in a significant decrease in 8-oxoguanine levels in lymphocyte DNA. In contrast, a significant increase in 8-oxoadenine levels in lymphocyte DNA was observed compared with both baseline and placebo. The authors concluded that ascorbic acid administered to healthy humans exhibits pro-oxidant, as well as antioxidant, effects.

The Panel noted that the findings described in the Podmore et al. (1998) study were criticised by several authors (Levine et al., 1998; Poulsen et al., 1998; Gonzalez et al., 2002). The Panel considered that the Podmore et al. (1998) study has major shortcomings (e.g. study design and analytical methodology) and, therefore, it could not be taken into account for the risk assessment of ascorbic acid as a food additive.

3.2.3.4. Conclusion on genotoxicity

The Panel noted that ascorbic acid or sodium ascorbate alone did not show any mutagenic potential. In some *in vitro* test systems including redox active substances, especially redox active metal ions, ascorbic acid and sodium ascorbate may act as pro-oxidants, thereby increasing the mutagenic potential of redox active metals or other compounds. These *in vitro* effects have not been confirmed in *in vivo* studies.

The Panel considered that it is unlikely that ascorbic acid or sodium ascorbate are genotoxic. In the absence of genotoxicity data on calcium ascorbate, the Panel considered that the read across approach for calcium ascorbate was possible. Overall, the Panel considered that there is nogenotoxicity concern for ascorbic acid, sodium ascorbate or calcium ascorbate.

The Panel also noted that potential reaction products which may result from the interaction of sorbic acid with ascorbic acid in the presence of iron salts were demonstrated to be mutagenic *in vitro* (Kitano et al., 2002) and that there are certain food categories for which the use of these food additives is permitted in parallel. However, these reaction products have only been shown to be formed under optimal experimental conditions in aqueous environment and are thus unlikely to be formed to any major extent in food matrices. Consequently these interactions appear to be of limited significance and concern.

3.2.4. Chronic toxicity and carcinogenicity

3.2.4.1. Mouse

In a 2-year carcinogenicity mouse study (NTP, 1983), eight-week-old B6C3F1 mice (50 animals/sex/dose; 22 g (males) and 18 g (females) at the start of the study) were given 0, 25 000 or 50 000 mg ascorbic acid/kg feed corresponding, according to the authors, to a mean intake of ascorbic acid of 6 500 mg/kg bw/day (males) and 7 200 mg/kg bw/day (females) and 12 800 mg/kg bw/day (males) and 14 800 mg/kg bw/day (females), respectively, as calculated from the actual feed intake. Survival of the high-dose group of male mice was significantly greater than that of controls, whereas all control and treated groups of female mice survived equally. The incidence of haemangiosarcomas in the low-dose male mice only was significantly increased compared with the controls and occurred in the liver, bone marrow and spleen, whereas no increase was observed at the highest dose. A statistically significant negative trend occurred in the incidence of lymphocytic leukaemia in female mice. Significant negative trends were observed in the incidences of malignant lymphocytic lymphomas, all malignant lymphomas and combined lymphoma or leukaemia in male mice. A statistically significant negative trend occurred in the incidence of hepatocellular carcinomas in male mice. The authors concluded that ascorbic acid was not carcinogenic for male and female B6C3F1 mice under the conditions of this bioassay (NTP, 1983).

The Panel noted that the measured feed consumption by mice in the NTP study appeared to be two-fold higher than that used as the basis for the conversion factors for the EFSA default values(EFSA Scientific Committee, 2012).

3.2.4.2. Rat

In a study by Surber and Cerioli (1971), albino rats (26 animals/sex/dose; 165 g (males) and 130 g (female) at the start of the study) were given ascorbic acid in the diet in doses of 0, 1 000, 1 500 or 2 000 mg/kg bw/day for two years. An additional group of 10 rats of each sex was given 2 000 mg/kg bw/day and was used for checking reversibility of possible toxic phenomena. The following parameters were investigated in all animals and were observed daily: general physical condition, substance effect and possible toxic symptoms. Body weight increase and food consumption were determined weekly. In five males and five females, the following were measured before the beginning of exposures and repeated 3, 6, 9, 12, 18 and 24 months later: haematology (haemoglobin, haematocrit, erythrocyte count, leucocyte count, differential leucocyte count, reticulocytes and platelets), urine analysis (volume of urine, pH, specific weight, protein, glucose, acetone, bilirubin, haemoglobin and spun deposit), blood chemistry (serum glutamic pyruvic transaminase, serum alkaline phosphatase, leucine-aminopeptidase, bilirubin, blood urea, blood sugar and prothrombin time) and organ function tests in the kidney (determination of urine level of phenol red as percentage of the amount injected by intravenous route 30 minutes earlier) and liver (bile excretion of bromsulphalein, measurement of its disappearance from the blood stream after intravenous injection 30 minutes earlier). Intermediate autopsies were carried out 3, 6 and 12 months after the treatment started (two males and two females of each group were sacrificed). Terminal autopsy was performed on all animals surviving after the two-year test duration. The heart, liver, spleen, kidney, adrenals and gonads were removed for weighing and their external aspect was described. Histopathological investigation was performed on the following organs (at least 10 animals/sex/dose): heart, lung, liver, spleen, kidney, adrenals, thyroid, intestine, gonads and brain. At no time during the experiment could any observed adverse effect on the physical condition of the rats be attributable to the continuous intake of large doses of ascorbic acid. There was no effect on survival, food consumption, body weight or organ weights. All data on haematology, urine analysis or blood chemistry were within the normal range in all animals. At the intermediate autopsy, the observed pathology was neither dose dependent nor more strongly developed in treated animals than in controls. Histopathological changes were observed in several organs, but none of them could be attributable to the ascorbic acid treatment. It was concluded by the authors of this study that the dosage of 2 000 mg ascorbic acid/kg bw/day was well tolerated. The Panel noted that highest dose tested, 2 000 mg ascorbic acid/kg bw/day, was the NOAEL of this study.

In a 2-year carcinogenicity rat study (NTP, 1983), F344 rats (50 animals/sex/dose; 99 g (males) and 88 g (females) at the start of the study) were given 0, 25 000 or 50 000 mg ascorbic acid/kg feed corresponding, according to the authors, to a mean intake of ascorbic acid of 1 300 mg/kg bw/day (males) and 1 500 mg/kg bw/day (females) and 2 600 mg/kg bw/day (males) and 3 100 mg/kg bw/day (females), respectively, as calculated from the actual feed intake. Dosed female rats had lower mean body weights than those of controls during the second year (significance not indicated), whereas no change was observed for male rats. Compared with controls, there was no change observed in the average daily feed consumption per male or female rat for low and high doses. The survival of high-dose male rats was slightly higher than that of the controls, whereas no change in survival rate was observed in females. Pairwise comparisons of low-dose females and controls showed a statistically significant increase of undifferentiated leukaemia (equivalent to mononuclear cell leukaemia) in the low-dose group (control, 6 out of 50; low-dose, 17 out of 50). These leukaemias also occurred in increased proportions in high-dose female rats and in slightly decreased proportions in low- and high-dose males, but none of these differences was statistically significant. Statistically significant negative trends were observed in the incidences of males with adenocarcinomas of the preputial gland and of females with adenocarcinomas of the clitoral gland. Interstitial-cell tumours occurred with a negative trend, but none of the pairwise comparisons was statistically significant. Pituitary adenomas showed a decreased trend in dosed female rats when compared with controls. The NTP concluded that ascorbic

acid was not carcinogenic for male and female F344/N rats under the conditions of this bioassay. The Panel agreed with this conclusion.

The Panel noted that, in the opinion of the EFSA NDA Panel on the UL of vitamin C (EFSA, 2004), there are a number of studies in which rats have been given high dietary concentrations of the sodium ascorbate as well as of the free acid to study the possible role of sodium ions in the generation of bladder hyperplasia and cancer in male rats. Using a two-stage model of bladder carcinogenesis, in which male rats were treated with possible promoters of bladder carcinogenesis for six weeks, Cohen et al. (1991) showed that sodium ascorbate at 5 % in the diet (equivalent to about 2 500 mg/kg bw/day) increased the incidence of bladder cancers, but that an equimolar dietary concentration of ascorbic acid (4.44 %) was inactive. In a subsequent study in which sodium ascorbate was given in the diet to rats without pre-treatment with a carcinogen, significant increases in simple, papillary and nodular hyperplasia in the urinary bladder were detected in rats fed diets containing 5 or 7 % sodium ascorbate, but these effects were abolished by co-treatment with ammonium chloride which acidified the urine (Cohen et al., 1998); there was a small and non-significant increase in the numbers of papillomas and carcinomas in the urinary bladder at dietary levels of 5 % (n = 1) and 7 % (n = 2) compared with controls (n = 0) or 1 % dietary level (n = 0).

In 1993, based on studies by Tisdel et al. (1974, as referred to by JECFA, 1993), Taylor and Friedman (1974, as referred to by JECFA, 1993) and Arnold et al. (1977, 1980, as referred to by JECFA, 1993), ECFA concluded that similar effects on the urinary bladder produced by the sodium salt of saccharin were related to sodium-induced changes in urine volume, osmolarity and pH, and were not relevant to human health (JECFA, 1993). Similarly, the SCF in 1995, referring to the studies evaluated by JECFA (1993) and based on an unpublished report submitted to the SCF, concluded that the apparent carcinogenic effect of sodium saccharin was likely to be an effect of sodium and not relevant for human health and they allocated a full ADI for saccharin and its salts to replace the previously allocated temporary ADI (SCF, 1997b; Lina and Woutersen, 1989).

The Panel noted that the authors of the NTP study (NTP, 1983) considered that the increase in the incidence of haemangiosarcomas in mice given 25 000 mg ascorbic acid/kg feed was not related to administration of ascorbic acid because it was observed in females only and there was no dose–response relationship. The increase in the incidence of bladder tumours in rats given high doses of sodium ascorbate can be considered caused by sodium, osmolarity and pH and not by the ascorbate moiety as also observed with other salts of sodium (Lina and Woutersen, 1989). The Panel considered that ascorbic acid is not carcinogenic to experimental animals.

3.2.4.3. Breast cancer

The meta-analysis performed by Gandini et al. (2000) identified nine epidemiological studies in which the relationship between vitamin C and breast cancer was examined. Of these studies, three indicated a statistically significant protective effect of vitamin C with a daily dietary intake of 400 mg or more compared with an intake of 50 mg or below; four indicated a protective effect but did not reach statistical significance; one indicated no effect; and one indicated that vitamin C is a risk factor of breast cancer, but this study did not reach statistical significance. With a relative risk of 0.80 (95 % confidence interval 0.68–0.95), the meta-analysis of these nine studies indicated a small but statistically significant protective effect of vitamin C against breast cancer.

In contrast, a Danish study found an increased risk of breast cancer among a cohort of postmenopausal women in a nested case–control study (62 cases and 41 controls). A significantly increased risk was observed at intakes above 300 mg/day in comparison with intakes of 60–150 mg/day (Nissen et al., 2003).

The Panel noted that the Nissen et al. (2003) study is only a case–control study with less reliability than the meta-analysis conducted by Gandini et al. (2000).

The Panel noted that the NDA Panel (EFSA NDA Panel, 2013) reviewed a World Cancer Research Fund (WCRF) report (WCRF/AICR, 2007) and two cohort studies showing no association between dietary and/or total vitamin C intake and breast cancer risk in premenopausal and postmenopausal women (Nagel et al., 2010; Hutchinson et al., 2012).

3.2.5. Reproductive and developmental toxicity

3.2.5.1. Reproductive toxicity

No reproductive toxicity studies of ascorbic acid and its salts were available.

3.2.5.2. Developmental toxicity

Mouse

In a study by Frohberg et al. (1973), L-ascorbic acid was administered orally to pregnant NMRI mice (weight and age not given) at doses of 150, 250, 500 or 1 000 mg/kg bw/day, from gestation day (GD) 6 to 15 (21–23 animals/dose). No effects were observed on maternal toxicity, number of fetuses, fetal weight, number of resorptions, abortion rate and number of dead fetuses or malformed fetuses of the treatment groups compared with the controls.

Rat

In a study by Frohberg et al. (1973), daily oral doses of 150, 250, 500 or 1 000 mg ascorbic acid/kg bw/day were given by gavage to pregnant Wistar rats in a first trial from day 6 to day 15 of gestation and in a second trial from GD 0 to day 21 postpartum. In the first trial, no effects were observed on maternal toxicity, number of fetuses, fetal weight, number of resorptions, abortion rate and number of dead or malformed fetuses of the treatment groups compared with the controls. In the second trial, there was no effect on the embryonic and postpartum development of the young or on breeding behaviour, pregnancy, parturition or lactation capacity of the dams.

In a study by Alleva et al. (1976), three-month-old female Holtzman rats (230–304 g; 10–14 animals/dose) received ascorbic acid dissolved in deionised water in a daily oral dose of 0, 50, 150 or 450 mg/kg bw/day from GD 1 to 19. Compared with controls, in treated animals there was no increase observed in abortion, mortality of offspring or litter weight.

In a study by Simán and Eriksson (1997), Sprague–Dawley rats (4–15 animals/dose; animal weight, 247–260 g at the start of pregnancy) were fed either a standard diet or a diet with 1.8 or 4 % sodium ascorbate (equivalent[25] to 900, 1 800 or 4 000 mg sodium ascorbate/kg bw/day) from GD 0 to 20. A Caesarean section was performed on GD 20; the number of early and late resorptions and the number of malformations were comparable between the control group and the groups treated with ascorbic acid.

Hamster

In a study by Alleva et al. (1976), two-month-old female Lakeview hamsters (76–99 g; 10–14 animals/dose group) received ascorbic acid dissolved in deionised water in a daily oral dose of 0, 50, 150 or 450 mg/kg bw/day from GD 1 to 15. No increase was observed in abortion or mortality. A slight increase in pup weight was observed in the 450 mg/kg bw/day group.

Guinea pig

In a study by Alleva et al. (1976), four-month-old female guinea pigs (11 treatment animals and 13 controls; 626–958 g, strain not given) received subcutaneous injections twice daily of sodium L-ascorbate dissolved in saline (225 mg/mL) at a dose of 200 mg free acid/kg (stated by the authors to be equivalent to 400 mg/kg bw/day) beginning six days after potential pregnancy. The control group

[25] Calculated by the Panel according to EFSA Scientific Committee (2012).

received saline. After five days, the dose was given orally instead, owing to infections on the injection site. Dosing was discontinued before birth to allow for normal delivery. Another group of 29 animals (13 treatment and 16 control; strain not given) were given the same doses by oral treatment from the day pregnancy was established until before birth. No increases were observed in abortion or mortality in any of the studies.

Overall, from the available developmental toxicity studies, the Panel noted that no prenatal developmental effects of ascorbic acid were observed in mice up to doses of 1 000 mg/kg bw/day, in rats up to 4 000 mg/kg bw/day, in hamsters up to 450 mg/kg bw/day and in guinea pigs up to 400 mg/kg bw/day, the highest doses tested. Maternal toxicity was not noted at these dose levels.

3.2.6. Other studies

3.2.6.1. Human studies

A series of potential adverse effects in humans following administration of large doses of ascorbic acid have been discussed in the scientific literature. They include metabolic acidosis, oxaluria, renal stones, renal tubular disease, gastrointestinal disturbances, sensitivity reactions, conditioned scurvy, coagulation and cholesterol disturbances, vitamin B_{12} destruction, fatigue and sterility (Barness, 1975; EVM, 2003). However, the Panel noted that the NDA Panel considered several health outcomes that may be associated with vitamin C intake (EFSA NDA Panel, 2013). The NDA Panel decided that the available data on the effects of vitamin C intake and/or status on scurvy, blood lipids and blood pressure, common cold and chronic disease-related outcomes (cardiovascular disease-related, cancer, vision-related, mortality) could not be used as criteria to derive the requirement for vitamin C (see also section 2.7).

In the present opinion, the most pertinent adverse effects as described by Barnes (1975) and EVM (2003) are summarised below.

3.2.6.2. Gastrointestinal effects

The most common adverse reactions to high vitamin C intakes mentioned in the literature are gastrointestinal disturbances such as diarrhoea, nausea and abdominal cramps; however, most reports are anecdotal and/or not very well described.

In a study by Cameron and Campbell (1974), large doses of ascorbic acid were given to cancer patients to study the potential beneficial effect and any adverse effect. The ascorbic acid was administered as a mixture where the ascorbic acid had been neutralised with sodium hydrogen carbonate and dissolved in sorbitol syrup and water. The patients, during the whole cancer treatment period (i.e. until death), received four times 15 mL of the mixture, corresponding to 2.5 g ascorbic acid (and 1.2 g sodium hydrogen carbonate and 3.5 g sorbitol) per dose (i.e. in total 10 g ascorbic acid per day). In concurrent studies with normal healthy volunteers (increasing oral ascorbic acid intake by increments of 1 g per day in successive weeks), symptoms of flatulent distension, transient colic and diarrhoea were a "fairly frequent" occurrence when the 3–4 g per day level was reached.

This was the basis for the guidance value of 1 g ascorbic acid/day suggested by the EVM (2003) using an uncertainty factor of 3 to this "minimal observed effect level" (see section 2.7).

3.2.6.3. Oxalate stone formation

The observations in humans concerning the risk of development of kidney stones as a result of high intake of vitamin C are contradictory and most of the information is based on case reports with limited information.

Briggs (1976) did suggest that some individuals are more sensitive to ascorbic acid in relation to formation of kidney stones, as he found, among 68 persons, 3 individuals (2 were father and son) who

had a very large increase in the urinary oxalate excretion when they were given 4 g of ascorbic acid daily for seven days.

Stein et al. (1976) reported increased excretion of uric acid in 14 subjects after ingestion of a single dose of 4 g or 8 g of ascorbic acid, and Levine et al. (1996) reported the sample result in 7 volunteers taking daily supplements of 1 g vitamin C.

Curhan et al. (1996) examined the relationship between the intake of vitamins C and B_6, and kidney stone formation.The study was carried out on a cohort of 45 251 men, 40 to 75 years old, with no history of kidney calculi. Vitamin intake from foods and supplements was assessed using a semi-quantitative food frequency questionnaire completed in 1986. During a six-year follow-up, 751 incident cases of kidney stones were documented, but neither vitamin C nor vitamin B_6 intake was significantly associated with the risk of stone formation. For vitamin C, the age-adjusted relative risk of men consuming 1 500 mg daily or more compared with those consuming less than 250 mg daily was 0.78 (95 % confidence interval 0.54 to 1.11). After adjusting for other potential stone risk factors, the relative risks did not change significantly. The authors concluded that there was no relationship between a high daily intake of vitamin C in doses between 200 mg and 1 500 mg and the risk of stone formation, even when consumed in large doses.

Auer et al. (1998) studied the effect of ascorbic acid ingestion in 10 healthy males ingesting 4 g ascorbic acid for five days. Urine samples (24 hours) were analysed for ascorbic and for acid oxalate in the presence and absence of ethylenediaminetetraacetic acid (EDTA). No statistically significant increase in oxalate excretion was observed. Ascorbate excretion increased when vitamin C ingestion commenced but levelled out after 24 hours. There were no changes in either the calcium oxalate relative super-saturation or the Tiselius risk index. The authors concluded that ingestion of large doses of ascorbic acid did not affect the principal risk factors associated with calcium oxalate kidney stone formation.

Curhan et al. (1999) observed that, in a study in women (the Nurses' Health Study) with 64 190 participants and a 14-year follow-up period, the relative risk for kidney stones was 0.98 (95 % confidence interval 0.65 to 1.47) in individuals with a daily intake of vitamin C higher than 1 500 mg compared with individuals with a daily intake below 250 mg. These results were confirmed by Simon and Hudes (1999) in the "Second National Health and Nutrition Examination Survey" including 5 785 women and 5 214 men.

Taylor et al. (2004), in a follow-up study of the study by Curhan et al. (1996), observed that, after adjusting for age, there was no association between dietary calcium and stone formation in men aged 60 years or older. The multivariate relative risk for men who consumed 1 000 mg or greater of vitamin C per day compared with those who consumed less than the recommended dietary allowance of 90 mg/day was 1.41 (95 % confidence interval 1.11 to 1.80; P = 0.01 for trend).

In a study by Massey et al. (2005), 29 persons with a tendency for kidney stone formation and 19 persons with no tendency for kidney stone formation (age and gender matched) were given a diet with controlled oxalate content and a supplement of 1 000 mg ascorbic acid twice a day, together with a meal or no supplement for six days. It was shown that 2 g ascorbic acid a day increased urinary oxalate excretion and the risk of calcium oxalate precipitability in 40 % of the participants, both the stone-formers and the non-stone-formers. These results contradict the results of a more limited study by Auer et al. (1998). The positive results of the study by Massey et al. (2005) also contradict the results of a prospective cohort study by Curhan et al. (1996).

Lamarche et al. (2011) reported on one individual with acute renal failure who was admitted with biopsy-proven oxalate nephropathy and was reported to have ingested 480 mg to 960 mg of vitamin C daily over three to four months. The authors also compiled eight cases of renal failure with oxalate nephropathy after repeated doses ranging from 4.0 g daily by the oral route to a single dose of 60 g intravenously as an alternative therapy in cancer treatment. However, the reports do not give the

medical details necessary to rule out other potential causes of oxalate nephropathy. Furthermore, they are not sufficient to identify a level of no concern, although levels of 1 000 mg ascorbic acid daily were administered.

4. Discussion

Ascorbic acid (E 300), sodium ascorbate (E 301) and calcium ascorbate (E 302) are authorised in the EU as food additives in accordance with Annex II and Annex III of Regulation (EC) No 1333/2008. The use of ascorbic acid and ascorbates as food additives has been evaluated by JECFA, the latest evaluation being in 1981 (JECFA, 1981a, b), and by the SCF, in 1987 (SCF, 1989b). Both committees found the use of the substances acceptable. The question of the UL of calcium and sodium has been addressed by the SCF and by EFSA (SCF, 2003; EFSA, 2005).

Ascorbic acid (E 300), sodium ascorbate (E 301) and calcium ascorbate (E 302) are well described. However, the Panel noted that, in its opinions on calcium ascorbate (EFSA, 2007, 2011a), the possible content of the by-products calcium threonate and 4-HMF was taken into consideration and it was concluded that the maximum residual level of 4-HMF (0.06 %) in calcium L-ascorbate with a content of threonate was unlikely to be of safety concern (EFSA, 2011a).

The Panel also noted that the European Pharmacopoeia (2014) specifications for ascorbic acid (E 300) and for calcium ascorbate (E 302) contain limits for iron (maximum 2 mg/kg) and copper (maximum 5 mg/kg), and that the specifications for sodium ascorbate (E 301) contain limits for sulphates (maximum 150 mg/kg), iron (maximum 2 mg/kg), copper (maximum 5 mg/kg) and nickel (maximum 1 mg/kg). In addition, the Panel noted that, if calcium carbonate from limestone is used in the manufacturing process of calcium ascorbate, it could be contaminated with aluminium and, therefore, specifications for the maximum level of aluminium in calcium ascorbate may be required.

The Panel considered that the maximum limits for the impurities of toxic elements (lead, mercury and arsenic) in the EC specification for ascorbic acid and its salts (E 300–302) should be revised in order to ascertain that ascorbic acid and its salts (E 300–302) as food additives will not be a significant source of exposure to those toxic elements in food.

Overall, the Panel noted that the current EC specifications on ascorbic acid (E 300), sodium ascorbate (E 301) and calcium ascorbate (E 302) should be updated regarding the above-mentioned limits.

As previously described, ascorbic acid undergoes degradation in an aqueous environment as well in food. The degradation rate and the decomposition pathways and products depend on various factors such as pH, temperature, light, concentration and matrix composition. Under specific conditions, degradation can proceed all the way down to very simple compounds (e.g. threonic acid, glyoxylic acid and carbon dioxide); however, in general, the presence of a variety of more complex products can be observed at intermediate degradation stages. For the majority of the degradation products, there is no indication of genotoxic and/or carcinogenic risk.

For furfural, also used as food flavouring, the relevance of a genotoxic/carcinogenic risk was ruled out in its evaluation as a food flavouring, where the EFSA Panel on Food Contact Materials, Enzymes, Flavouring and Processing Aids (CEF) noted that the *in vitro* positive genotoxicity results with furfural mainly observed in cultured mammalian cells at the gene and chromosome level in the absence of metabolic activation were overruled by negative results obtained *in vivo* in the unscheduled DNA synthesis (UDS) assay in B6C3F1 mouse hepatocytes (Edwards, 1999), in Fischer 344 rat hepatocytes (Phillips et al., 1997), in a test for induction of gene mutation in liver cells of λlacZ transgenic mice (CIVO-TNO, 2003). Consequently, the absence of genotoxicity *in vivo*, particularly in male mice, the species and sex which displayed an increased tumour incidence in long-term studies, allowed to conclude that tumours arose by a secondary mechanism consequent on hepatotoxicity, which is dose dependent, displays a threshold and is seen in both rats and mice (EFSA CEF Panel, 2011). The ANS Panel agreed with this conclusion.

Another chemical that may be of toxicological concern is 5-HMF, which is present in caramel colours and expected to possibly have weak carcinogenic activity while exhibiting ("sufficient evidence") genotoxic potential *in vitro* (EFSA CEF Panel, 2010). Caramel colours were extensively tested for genotoxic potential in a variety of *in vitro* and *in vivo* assays: based on the results of these tests, the EFSA ANS Panel "*concluded that there were no concerns regarding the genotoxic potential of caramel colours*" (EFSA ANS Panel, 2011b). However, it was also noted that the composition of caramel colours exhibited a wide variability in the nature and levels of the various constituents, including those of concern, such as 5-HMF. Given this likely variability and although "*no genotoxicity or carcinogenicity is expected in humans*" from exposure to 5-HMF in caramel colours, the ANS Panel considered that it would be prudent to reduce the level of 5-HMF and other minor constituents of toxicological interest as much as technologically feasible (EFSA ANS Panel, 2011b).

Ascorbic acid (and its conjugated base, the ascorbate anion) is well known for its antioxidant activity. However, under certain conditions, ascorbate can paradoxically promote the generation of the same active oxygen species ($\cdot OH$, O_2^- and H_2O_2) that otherwise would be destroyed. The Panel also recalled that ascorbic acid and its decomposition products participate in common chemical modifications of amino acids/proteins through non-enzymatic glycation typical of sugars.

In conclusion, the Panel noted that the ascorbic acid (and its conjugated base, the ascorbate anion) employed as a food additive and the ascorbic acid naturally present in food may both be expected to behave in similar chemical ways under similar environmental conditions, that is, in principle, they would give rise to degradation products along equivalent pathways. The Panel noted that adequate studies on products from degradation of ascorbic acid or reaction with relevant food matrices are not available.

Regarding ingestion, the Panel considered that sodium ascorbate and calcium ascorbate are fully dissociated in the acidic conditions of the stomach. The calcium and sodium ions are expected to enter normal homeostatic processes and are not expected to impact on the toxicity of the salts. Thus, the properties of the cations are not discussed further in this opinion.

Ascorbic acid is absorbed from the intestine by a sodium-dependent active transport process and, at low doses, the absorption is almost complete until a saturation point after which increasing amounts of unabsorbed substance are excreted with the faeces. The major metabolite in the organism is dehydroascorbic acid, which can be reduced back to ascorbic acid and still has vitamin C activity. Dehydroascorbic acid can be further irreversibly oxidised to mainly L-threonic acid and oxalic acid, as well as a number of minor metabolites.

Ascorbic acid and its sodium and calcium salts have very low acute toxicities, and short-term tests on ascorbic acid in various laboratory animals show little effect, and even so only at high doses (up to 7 000 or 11 000 mg/kg bw/day).

The Panel noted that ascorbic acid or sodium ascorbate alone did not show any mutagenic potential. In some *in vitro* test systems including redox active substances, especially redox active metal ions, ascorbic acid and sodium ascorbate may act as pro-oxidants, thereby increasing the mutagenic potential of redox active metals or other compounds. These *in vitro* effects have not been confirmed in *in vivo* studies.

The Panel considered that it is unlikely that ascorbic acid and sodium ascorbate are genotoxic. In the absence of genotoxicity data on calcium ascorbate, the Panel considered that the read across approach for calcium ascorbate was possible. Overall, the Panel concluded that there is no genotoxicity concern for ascorbic acid, sodium ascorbate or calcium ascorbate.

The Panel also noted that potential reaction products, which may result from the interaction of sorbic acid with ascorbic acid in the presence of iron salts, were demonstrated to be mutagenic *in vitro* and that there are certain food categories for which the use of these food additives is permitted in parallel.

However, these reaction products have only been shown to be formed under optimal experimental conditions in aqueous environment and are thus unlikely to be formed to any major extent in food matrices. Consequently these interactions appear to be of limited significance and concern.

Chronic toxicity and carcinogenicity studies with ascorbic acid did not show any chronic toxicity, even at high doses (up to 3 100 mg/kg bw/day), and also showed no signs of carcinogenicity. However, sodium ascorbate administered at 5 % in the feed, but not ascorbic acid in equimolar concentration, has been shown to promote bladder cancer in male rats treated with an initiator of bladder cancer. This effect was, however, attributed to the sodium ion in line with the mechanism behind the carcinogenic effect of sodium saccharin, rather than to an effect of ascorbate, and was thus considered of no relevance for the use of sodium ascorbate (Cohen et al., 1991, 1998).

Prenatal developmental studies in mice, rats, hamsters and guinea pigs did not show adverse developmental effects at the highest dose levels tested. Studies on reproductive toxicity were not available.

In studies in humans, vitamin C has been investigated for the treatment of vitamin C deficiency and various diseases. Typically, the studies focused on potential positive effects, and any description of possible side-effects were mostly anecdotal, lacked control groups and were difficult to interpret.

The Panel also noted that a common concern is the possible formation of oxalate stones following the intake of large doses of ascorbic acid. The epidemiology studies (Curhan et al., 1996; Simon and Hudes, 1999; Taylor et al., 2004) give a strong indication that a daily intake of vitamin C below 1 500 mg is not a risk factor for the formation of kidney stones. However, it cannot be excluded that extremely high doses of vitamin C could be a risk factor for the development of kidney stones for a small subpopulation of particularly sensitive persons, as suggested by the study of Massey et al. (2005). The Panel, however, considered it unlikely that the use of vitamin C as a food additive would result in such high levels of intake.

Overall, the Panel noted that the available data did not report any adverse effects in animal studies, even at the highest doses tested.

The Panel estimated the combined exposure to ascorbic acid (E 300), calcium ascorbate (E 301) and sodium ascorbate (E 302) using the highest concentration reported from any of them for each food category.

Exposure assessment to food additives under re-evaluation is carried out by the ANS Panel based on MPLs as set out in EU legislation and reported usage levels or analytical data. For ascorbic acid (E 300), sodium ascorbate (E 301) or calcium ascorbate (E 302), it was not possible to carry out an exposure assessment scenario based on MPLs, 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 exposure estimate scenario (noted as *maximum level exposure assessment* scenario).

Based on the available dataset and added to the "*maximum level exposure assessment* scenario", the Panel calculated combined exposure estimates for ascorbic acid (E 300), sodium ascorbate (E 301) and calcium ascorbate (E 302) 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/analytical 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/analytical levels in all food.

Because of the above-mentioned assumptions, and the use of the range of data submitted to EFSA, the Panel considered the refined exposure scenario a more realistic approach than the *maximum level*

exposure assessment scenario. Exposure estimates derived following this last scenario should be considered most conservative as this scenario assumes that a consumer will be continuously (over a lifetime) exposed to a food additive present in food at the maximum reported use level. The Panel noted that the refined exposure estimates will not cover future changes in the level of use of food additives.

Reported use levels from industry give information on the amount of the food additive added to food. By using these data, exposure to ascorbic acid and its salts (E 300–302) at the moment that the food was produced can be calculated. As ascorbic acid is degraded during processing and storage, the Panel calculated exposure estimates including loss factors. These estimates should reflect exposure to ascorbic acid and its salts in food as consumed. The analytical levels provided by the Member States reflect the levels of ascorbic acid in foods, whatever the origin (from natural and other sources). However, given the limitations of the analytical data provided by the Member States (limited number of Member States, only 28 food categories and a lack of data on foods in which ascorbic acid occurs naturally, such as raw food commodities, for example citrus fruits), the Panel noted that the exposure estimates using the analytical data will probably not reflect the exposure to ascorbic acid and its salts via the whole diet. The real exposure will probably be higher. Overall, the Panel considered that the exposure estimates using the analytical data should be interpreted with caution.

As the analytical data did not allow for the estimation of the overall exposure to ascorbic acid and its salts via the whole diet (from natural and other sources), the refined exposure estimates based on reported use levels,—with and without considering loss via processing and storage—were added to the exposure of vitamin C via the diet as estimated by the NDA panel (EFSA NDA Panel, 2013) (section 2.9.4). The total exposure assessment of ascorbic acid and its salts (from their use as food additives and natural sources) would reach 1 g/person per day at the high level for all populations, except for infants and toddlers. The exposure to ascorbic acid and its salts (E 300–302) from their use as food additives only would represent around 50–65 % (depending on whether or not the losses of ascorbic acid are taken into account). For infants, natural sources would represent the main contributor to the total exposure.

Given the fact that adequate data on exposure and toxicity were available and no adverse effects were reported in animal studies, the Panel concluded that there is no safety concern for the use of ascorbic acid (E 300), sodium ascorbate (E 301) and calcium ascorbate (E 302) as food additives at the reported uses and use levels, and there is no need for a numerical ADI for ascorbic acid (E 300), sodium ascorbate (E 301) and calcium ascorbate (E 302) (EFSA ANS Panel, 2014).

CONCLUSIONS

Given the fact that adequate data on exposure and toxicity were available and no adverse effects were reported in animal studies, the Panel concluded that there is no safety concern for the use of ascorbic acid (E 300), sodium ascorbate (E 301) and calcium ascorbate (E 302) as food additives at the reported uses and use levels, and there is no need for a numerical ADI for ascorbic acid (E 300), sodium ascorbate (E 301) and calcium ascorbate (E 302).

The Panel concluded that the maximum limits for the impurities of toxic elements (lead, mercury and arsenic) in the EC specification for ascorbic acid and its salts (E 300–302) should be revised in order to ascertain that ascorbic acid and its salts (E 300–302) as food additives will not be a significant source of exposure to those toxic elements in food.

The Panel also concluded that the EC specifications for ascorbic acid (E 300) should be amended to include a maximum limit for iron; specifications for sodium ascorbate (E 301) should be amended to include a maximum limit for sulphates, iron, copper and nickel; and specifications for calcium ascorbate (E 302) should be amended to include a maximum limit for 4-HMF, iron, copper and aluminium.

DOCUMENTATION PROVIDED TO EFSA

1. Analytical data provided by Members States in response to the EFSA call for food additives usage level and/or concentration data in food and beverages intended for human consumption (November, 2013).

2. Bächtold, 1971. Prüfung im 5-tage-toxizitätsversuch an mäusen und ratten. Interne mitteilung No 3996. Unpublished study report submitted by DSM, July 2010.

3. Bächtold, 1972a. Akute Toxizitätsversuche von vitamin C, dessen Vorstufen und einigen möglichen Zersetzungsprodukten. Interne mitteilung No 4155. Unpublished study report submitted by DSM, July 2010.

4. Bächtold, 1972b. Orale 5-tage-toxizitätsversuche an mäusen und ratten. Interne mitteilung No 4028. Unpublished study report submitted by DSM, July 2010.

5. Bächtold, 1973a. Akute Toxizitätsversuche von vitamin C, dessen Vorstufen und einigen möglichen Zersetzungsprodukten und metaboliten. Interne mitteilung No 4881. Unpublished study report submitted by DSM, July 2010.

6. Bächtold, 1973b. Prüfung der toxizität von vitamin C an mäusen und ratten bei 12-maliger Verabreichung. Interne mitteilung No 4529. Unpublished study report submitted by DSM, July 2010.

7. Bächtold, 1973c. Prüfung im 5-tage-toxizitätsversuch an mäusen und ratten. Calcium ascorbat, ascorbinsäure, Natrium ascorbat. Interne mitteilung No 4670. Unpublished study report submitted by DSM, July 2010.

8. Bächtold, 1976a. Akute Toxizitätsversuche mit vitamin C, dessen Vorstufen, einigen möglichen Zersetzungsprodukten und metaboliten. Interne mitteilung No 6455. Unpublished study report submitted by DSM, July 2010.

9. Bächtold, 1976b. Orale 5-tage-toxizitätsversuche an mäusen und ratten. Natrium-ascorbat. Interne mitteilung No 6872. Unpublished study report submitted by DSM, July 2010.

10. Bächtold, 1976c. Vergleichende orale und intraperitonäale 5-tage-toxizitätsversuch an mäusen und ratten. Ascorbinsäure pulv. Interne mitteilung No 6529. Unpublished study report submitted by DSM, July 2010.

11. Bächtold, 1976d. Vergleichende orale und intraperitonäale 5-tage-toxizitätsversuche an mäusen und ratten. Natrium ascorbat. Interne mitteilung No 6843. Unpublished study report submitted by DSM, July 2010.

12. Bächtold, 1976e. Vergleichende prüfung im 5-tage-toxizitätsversuch an männlichen und weiblichen ratten. Natrium ascorbat. Interne mitteilung No 6898. Unpublished study report submitted by DSM, July 2010.

13. Bächtold, 1976f. Vergleichende prüfung im 5-tage-toxizitätsversuch an männlichen und weiblichen ratten. Calciumascorbat. Interne mitteilung No 6879. Unpublished study report submitted by DSM, July 2010.

14. Bächtold, 1976g. Vergleichende orale und intraperitonäale 5-tage-toxizitätsversuche an mäusen und ratten. Calciumascorbat. Interne mitteilung No 6829. Unpublished study report submitted by DSM, July 2010.

15. Bächtold, 1977a. Orale 5-tage-toxizitätsversuche an mäusen und ratten. Interne mitteilung No 7281. Unpublished study report submitted by DSM, July 20100.

16. Bächtold, 1977b. Vergleichende orale und intraperitonäale 5-tage-toxizitätsversuche an mäusen und ratten. Ascorbinsäure pulv. Interne mitteilung No 7095. Unpublished study report submitted by DSM, July 2010.

17. Bächtold, 1980. Acute toxicity of ascorbic acid, some intermediates of the synthesis, degradation products and metabolites. Interne mitteilung No 9020. Unpublished study report submitted by DSM, July 2010.

18. FoodDrinkEurope (FDE). Data on use levels of ascorbic acids and its salts (E 300–302) in foods in response to the EFSA call for food additives usage level and/or concentration data in food and beverages intended for human consumption (2013). Submitted on 29 November 2013.

19. Food Chemical Risk Analysis (FCRA). Data on use levels of ascorbic acids and its salts (E 300–302) in foods in response to the EFSA call for food additives usage level and/or concentration data in food and beverages intended for human consumption (2013). Submitted on 10 January 2014.

20. Hanck AB, 1971. Akute and chronische Toxizität der L(+)-Ascorbinsäure und ihrer möglichen Zersetzungsprodukte beim Versuchstier. Rapport No 76'729. Unpublished study report submitted by DSM, July 2010.

21. DSM, 2010. Information provided to EFSA following a call for scientific data on food additives permitted in the EU and belonging to the functional classes of preservatives and antioxidants (November 2009). Submitted to EFSA in July 2010.

22. Horning D,1973. Einfluss hoher dosen Ascorbinsäure auf ausgewählte parmeter beim meerschweinchen. Unpublished study report submitted by DSM, July 2010.

23. Horning D and Hartmann D, 1980. Kinetic behaviour of ascorbic acid in guinea pigs. Roche. Rapport No 88'891. Unpublished study report submitted by DSM, July 2010.

24. International Chewing Gum Association (ICGA). Data on use levels of ascorbic acids and its salts (E 300–302) in foods in response to the EFSA call for food additives usage level and/or concentration data in food and beverages intended for human consumption (2013). Submitted on 23 November 2013.

25. Mars Chocolate UK. Data provided after the public call for scientific data on food additives permitted in the EU and belonging to the functional classes of preservatives and antioxidants. Submitted to EFSA in April 2010.

26. McClain RM, 1985. Ro 5-0690: A lifespan combined carcinogenicity and toxicity study in the rat with sodium nitrite and ascorbic acid (conducted at Hazleton Laboratories Europe, Ltd.). Roche. Research report No 123571. Unpublished study report submitted by DSM, July 2010.

27. International Organisation of Vine and Wine (OIV). Data on use levels of ascorbic acids and its salts (E 300–302) in foods in response to the EFSA call for food additives usage level and/or concentration data in food and beverages intended for human consumption (2013). Submitted on 29 November 2013.

28. Pre-evaluation document prepared by the Technical University of Denmark (DTU). Submitted in March 2012.

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APPENDICES

Appendix 1. Summary of reported use levels (mg/kg) of ascorbic acid (E 300) provided by industry

FCS Category No	FCS Food category	E Number	MPL	Restrictions	Number of data	Reported use levels from industry		Information provided by	Comments
						Typical mean (range)	Highest maximum level		
01.3	Unflavoured fermented products, heat-treated after fermentation	Group I	QS		1	100	250	FCRA	
01.4	Flavoured fermented milk products including heat treated products	Group I	QS		1	100	250	FCRA	
01.5	Dehydrated milk as defined by Directive 2001/114/EC	E 300	QS		1	300	500	FCRA	
01.6.3	Other creams	Group I	QS		1	1.7	5.7	FDE	
					1	300	500	FCRA	
01.7.1	Unripened cheese excluding products falling in category 16	Group I	QS	except Mozzarella, and unflavoured live fermented unripened cheese	1	300	500	FCRA	
01.7.5	Processed cheese	Group I	QS		1	300	500	FCRA	
01.7.6	Cheese products (excluding products falling in category 16)	Group I	QS		1	0	0	FCRA	Reported as not used in this food category
01.8	Dairy analogues, including beverage whiteners	Group I	QS		1	100	250	FCRA	
02.1	Fats and oils essentially free from water (excluding anhydrous milkfat)	E 300	QS	only cooking and/or frying purposes or the preparation of gravy	1	300	500	FCRA	
02.3	Vegetable oil pan spray	Group I	QS		1	300	500	FCRA	

FCS Category No	FCS Food category	E Number	MPL	Restrictions	Reported use levels from industry			Information provided by	Comments
					Number of data	Typical mean (range)	Highest maximum level		
02.2.2	Other fat and oil emulsions including spreads as defined by Council Regulation (EC) No 1234/2007 and liquid emulsions	Group I	QS		1	300	500	FCRA	
03	Edible ices	Group I	QS		55	33.7 (0.04-523.9)	523.9	FDE	
					1	250	500	FCRA	
04.1.2	Peeled, cut and shredded fruit and vegetables	E 300	QS	only refrigerated unprocessed fruit and vegetables ready for consumption and prepacked unprocessed and peeled potatos	1	150	200	FDE	
					2	100 (100-100)	250	FCRA	
04.1.3	Frozen fruit and vegetables	E 300	QS		2	300 (300-300)	500	FCRA	
04.2.1	Dried fruit and vegetables	Group I	QS		1	60	63	FDE	
					2	300 (300-300)	500	FCRA	
04.2.2	Fruit and vegetables in vinegar, oil, or brine	Group I	QS		3	870.6 (486.67-1125)	1500	FDE	
					2	300 (300-300)	500	FCRA	
04.2.3	Canned or bottled fruit and vegetables	E 300	QS		1	100	300	FCRA	

FCS Category No	FCS Food category	E Number	MPL	Restrictions	Reported use levels from industry			Information provided by	Comments
					Number of data	Typical mean (range)	Highest maximum level		
04.2.4.1	Fruit and vegetable preparations excluding compote	Group I	QS		1	500	500	FDE	
04.2.4.2	Compote, excluding poducts covered by category 16	E 300	QS		1	100	300	FCRA	1 level for FCS 4.2.4
04.2.5.1	Extra jam and extra jelly as defined by Directive 2001/113/EEC	E 300	QS		1	100	300	FCRA	1 level for FCS 4.2.5
04.2.5.2	Jam, jellies and marmalades and sweetened chestnut puree as defined by Directive 2001/113/EEC	E 300	QS		1	100	300	FCRA	1 level for FCS 4.2.5
					2	278.1 (18.68-537.5)	537.5	FDE	
04.2.5.3	Other similar fruit or vegetable spreads	E 300	QS		1	100	300	FCRA	1 level for FCS 4.2.5
04.2.5.4	Nut butters and nut spreads	Group I	QS		1	300	500	FCRA	
04.2.6	Processed potato products	Group I	QS		5	58.5 (0.01-160.1)	160.1	FDE	
					1	100	300	FCRA	
05.1	Cocoa and Chocolate products as covered by Directive 2000/36/EC	Group I	QS	only energy-reduced or with no added sugars	1	0	0	FCRA	Reported as not used in this food category
05.2	Other confectionery including breath refreshening microsweets	Group I	QS		1	629	629	FDE	
05.2	Other confectionery including breath refreshening microsweets	Group I	QS		1	50	150	FCRA	

FCS Category No	FCS Food category	E Number	MPL	Restrictions	Reported use levels from industry				Comments
					Number of data	Typical mean (range)	Highest maximum level	Information provided by	
05.3	Chewing gum	Group I	QS		1	50	150	FCRA	
					1	1000	3000	ICGA	
05.4	Decorations, coatings and fillings, except fruit based fillings covered by category 4.2.4	Group I	QS		3	39.7 (2-114)	114	FDE	
					1	50	150	FCRA	
06.2.1	Flours	E 300	QS		1	30	100	FCRA	
06.2.2	Starches	Group I	QS		1	0	0	FCRA	Reported as not used in this food category
06.3	Breakfast cereals	Group I	QS		1	0	250	FCRA	
06.4.1	Fresh pasta	E 300	QS		1	30	100	FCRA	1 level for FCS 6.4 (pasta-raw)
06.4.2	Dry pasta	Group I	QS	only gluten free and/or pasta intended for hypoproteic diets in accordence with Directive 2009/39/EC					
06.4.3	Fresh pre-cooked pasta	E 300	QS		2	276.1 (52.12-500)	500	FDE	
06.4.4	Potato Gnocchi	Group I	QS						
06.4.5	Fillings of stuffed pasta (ravioli and similar)	Group I	QS						
06.5	Noodles	group I	QS		1	30	100	FCRA	
06.6	Batters	Group I	QS		1	30	100	FCRA	
06.7	Pre-cooked or processed cereals	Group I	QS		1	30	100	FCRA	

FCS Category No	FCS Food category	E Number	MPL	Restrictions	Reported use levels from industry			Information provided by	Comments
					Number of data	Typical mean (range)	Highest maximum level		
07.1	Bread and rolls	Group I	QS	except products in 7.1.1 and 7.1.2	3	100 (100-100)	300	FDE	The function of this additive in bread is as a 'flour treatment agent' not an 'antioxidant'
07.1.1	Bread prepared solely with the following ingredients: wheat flour, water, yeast or leaven,salt	E 300	QS		1	50	100	FCRA	
07.1.2	Pain courant francais; Friss búzakenyér, fehér és félbarna kenyerek	E 300	QS		1	50	100	FCRA	
07.2	Fine bakery wares	Group I	QS		6	3142.8 (0.23-16920)	16920	FDE	
					1	300	500	FCRA	
08.1.2[(a)]	Meat preparations as defined by Regulation (EC) No 853/2004	E 300	QS	only *gehakt* and prepacked preparations of fresh minced meat	1	1500	1500	FDE	
					1	500	1000	FCRA	
08.2.1[(a)]	Non heat treated processed meat	Group I	QS		1	500	1000	FCRA	
08.2.2[(a)]	Heat treated processed meat	Group I	QS	except f*oie gras, foie gras entier, blocs de foie gras, Libamáj, libamáj egészben, libamáj tömbben*	4	4.5 (0-10.2)	10.2	FDE	
	Heat treated processed meat	E 300	QS	only *foie gras, foie gras entier, blocs de foie gras / Libamáj, libamáj egészben, libamáj tömbben*	1	1500	1500	FDE	
					1	300	1000	FCRA	

FCS Category No	FCS Food category	E Number	MPL	Restrictions	Reported use levels from industry			Information provided by	Comments
					Number of data	Typical mean (range)	Highest maximum level		
08.2.3[(a)]	Casings and coatings and decorations for meat	Group I	QS		1	0	1000	FCRA	
09.1.1	Unprocessed fish	E 300	QS		1	100	300	FCRA	
09.1.2	Unprocessed molluscs and crustaceans	E 300	QS		1	100	300	FCRA	
09.2	Processed fish and fishery products including mollusks and crustaceans	Group I	QS		1	100	300	FCRA	
09.3	Fish roe	Group I	QS	only processed fish roe	1	100	300	FCRA	
10.2	Processed eggs and egg products	Group I	QS		1	300	500	FCRA	
11.2	Other sugars and syrups	Group I	QS		1	100	300	FCRA	
12.1.2	Salt substitutes	Group I	QS		1	50	100	FCRA	
12.2.2	Seasonings and condiments	Group I	QS		6	1046.1 (9.78-6130.4)	6130.4	FDE	
					1	50	100	FCRA	
12.3	Vinegars	Group I	QS		1	205	205	FDE	
					1	150	250	FCRA	
12.4	Mustard	Group I	QS		1	150	250	FCRA	
12.5	Soups and broths	Group I	QS		32	71.9 (0.03-380)	380.0	FDE	
					1	150	250	FCRA	
12.6	Sauces	Group I	QS		34	664.3 (0.39-4000)	4000	FDE	
					1	150	250	FCRA	

FCS Category No	FCS Food category	E Number	MPL	Restrictions	Reported use levels from industry: Number of data	Reported use levels from industry: Typical mean (range)	Reported use levels from industry: Highest maximum level	Information provided by	Comments
12.7	Salads and savoury based sandwich spreads	Group I	QS		1	150	250	FCRA	
12.8	Yeast and yeast products	Group I	QS		1	150	250	FCRA	
12.9	Protein products, excluding products covered in category 1.8	Group I	QS		1	150	250	FCRA	
13.1.3	Processed cereal-based foods and baby foods for infants and young children as defined by Directive 2006/125/EC	E 300	200	only fat-containing cereal-based foods including biscuits and rusks and baby foods	1	0	200	FCRA	1 level on FCS13.1.3
		E 300	300	only fruit - and vegetable based drinks, juices and baby foods					
13.2	Dietary foods for special medical purposes defined in Directive 1999/21/EC (excluding products from food category 13.1.5)	Group I	QS		1	250	1000	FCRA	
					1	400	670	SNE	
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	QS		1	250	1000	FCRA	
13.4	Foods suitable for people intolerant to gluten as defined by Regulation (EC) 41/2009	Group I	QS	including dry pasta	1	250	1000	FCRA	
14.1.2	Fruit juices as defined by Council Directive 2001/112/EC and vegetable juices	E 300	QS		40	297.5 (250-300)	900	FDE	
					1	300	500	FCRA	

FCS Category No	FCS Food category	E Number	MPL	Restrictions	Reported use levels from industry				Comments
					Number of data	Typical mean (range)	Highest maximum level	Information provided by	
14.1.3	Fruit nectars as defined by Council Directive 2001/112/EC and vegetable nectars and similar products	E 300	QS		37	280.5 (100-300)	700	FDE	
					1	300	500	FCRA	
14.1.4	Flavoured drinks	Group I	QS		43	189.5 (58.18-400)	1000	FDE	Mean=192
					1	300	500	FCRA	
14.1.5.2	Coffee, tea, herbal and fruit infusions, chicory; tea, herbal and fruit infusions and chicory extracts; tea, plant, fruit and cereal preparations for infusions, as well as mixes and instant mixes of these products - other	Group I	QS	excluding unflavoured leaf tea; including flavoured instant coffee	3	3564.5 (3.0-10664.2)	10664.2	FDE	
14.2.1	Beer and malt beverages	E 300	QS		2	50 (50-50)	150	FDE	2 NP[(b)]
					1	150	300	FCRA	
14.2.3	Cider and perry	Group I	QS		2	450 (400-500)	600	FDE	
					1	150	300	FCRA	
14.2.4	Fruit wine and made wine	Group I	QS		1	150	300	FCRA	
14.2.5	Mead	Group I	QS		1	150	300	FCRA	
14.2.6	Spirit drinks as defined in Regulation (EC) No 110/2008	Group I	QS	except whisky or whiskey	1	150	300	FCRA	
14.2.7.1	Aromatised wines	Group I	QS		1	35	142	OIV	1 level on FCS 14.2.7

FCS Category No	FCS Food category	E Number	MPL	Restrictions	Reported use levels from industry			Information provided by	Comments
					Number of data	Typical mean (range)	Highest maximum level		
14.2.7.2	Aromatised wine-based drinks	Group I	QS		1	150	300	FCRA	1 level on FCS 14.2.7
14.2.7.3	Aromatised wine-product cocktails	Group I	QS						
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	QS		1	150	300	FCRA	
15.1	Potato-, cereal-, flour- or starch-based snacks	Group I	QS		1 NP[b]	2	2	FDE	on a NP[b]
					1	100	200	FCRA	
15.2	Processed nuts	Group I	QS		1	300	500	FCRA	
16	Desserts excluding products covered in category 1, 3 and 4	Group I	QS		5	196 (0.06-453.5)	1882	FDE	
					1	300	500	FCRA	
17.1	Food supplements supplied in a solid form including capsules and tablets and similar forms excluding chewable forms	Group I	QS		1	0	1000	FCRA	
17.2	Food supplements supplied in a liquid form	Group I	QS		1	0	1000	FCRA	
17.3	Food supplements supplied in a syrup-type or chewable form	Group I	QS		1	0	1000	FCRA	
18	Processed foods not covered by categories 1 to 17, excluding foods for infants and young children	Group I	QS		1	300	500	FCRA	

(a): data from industry were submitted before regulation (EC) No 601/2014 amending Annex II to Regulation (EC) No 1333/2008 was published. The data are reported as received by EFSA.
(b): NP: Niche product

Appendix 2. Summary of reported use levels (mg/kg) of sodium ascorbate (E 301) provided by industry

FCS Category No	FCS Food category	E Number	MPL	Restrictions	Number of data	Reported use levels from industry		Information provided by	Comments
						Typical mean (range)	Highest maximum level		
01.3	Unflavoured fermented products, heat-treated after fermentation	Group I	QS		1	100	250	FCRA	
01.4	Flavoured fermented milk products including heat treated products	Group I	QS		1	100	250	FCRA	
01.5	Dehydrated milk as defined by Directive 2001/114/EC	E 301	QS		1	300	500	FCRA	
01.6.3	Other creams	Group I	QS		1	300	500	FCRA	
01.7.1	Unripened cheese excluding products falling in category 16	Group I	QS	except mozzarella, and unflavoured live fermented unripened cheese	1	300	500	FCRA	
01.7.5	Processed cheese	Group I	QS		1	300	500	FCRA	
01.7.6	Cheese products (excluding products falling in category 16)	Group I	QS		1	0	0	FCRA	E 301 reported as not used in this food category
01.8	Dairy analogues, including beverage whiteners	Group I	QS		1	100	250	FCRA	
02.2.2	Other fat and oil emulsions including spreads as defined by Council Regulation (EC) No 1234/2007 and liquid emulsions	Group I	QS		1	4.5	4.5	FDE	
					2	300 (300-300)	500	FCRA	
02.3	Vegetable oil pan spray	Group I	QS		1	300	500	FCRA	
03	Edible ices	Group I	QS		4	3.6 (0.3-5)	5.0	FDE	
					1	250	500	FCRA	

FCS Category No	FCS Food category	E Number	MPL	Restrictions	Number of data	Reported use levels from industry		Information provided by	Comments
						Typical mean (range)	Highest maximum level		
04.1.2	Peeled, cut and shredded fruit and vegetables	E 301	QS	only refrigerated unprocessed fruit and vegetables ready for consumption and prepacked unprocessed and peeled potatoes	2	100 (100-100)	250	FCRA	
04.1.3	Frozen fruit and vegetables	E 301	QS		2	300 (300-300)	500	FCRA	
04.2.1	Dried fruit and vegetables	Group I	QS		2	300 (300-300)	500	FCRA	
04.2.2	Fruit and vegetables in vinegar, oil, or brine	Group I	QS		2	300 (300-300)	500	FCRA	
04.2.3	Canned or bottled fruit and vegetables	E 301	QS		1	100	300	FCRA	
04.2.4.1	Fruit and vegetable preparations excluding compote	Group I	QS		1	100	300	FCRA	1 level for the FCS 04.2.4
04.2.4.2	Compote, excluding poducts covered by category 16	E 301	QS						
04.2.5.4	Nut butters and nut spreads	Group I	QS		1	100	300	FCRA	level reported as FCS 04.2.5
					1	300	500	FCRA	
04.2.6	Processed potato products	Group I	QS		1	100	300	FCRA	
05.1	Cocoa and Chocolate products as covered by Directive 2000/36/EC	Group I	QS	only energy-reduced or with no added sugars	1	0	0	FCRA	E 301 reported as not used in this food category
05.2	Other confectionery including breath refreshening microsweets	Group I	QS		1	50	150	FCRA	
					1	4916	4916	FDE	

FCS Category No	FCS Food category	E Number	MPL	Restrictions	Number of data	Reported use levels from industry		Information provided by	Comments
						Typical mean (range)	Highest maximum level		
					1	50	150	FCRA	
05.3	Chewing gum	Group I	QS		1	1000	3000	ICGA	Only a proportion of chewing gum contains this food additive. Interest expressed by ICGA members to use this food additive. Data provided are indicative but fairly representative when substance is used.
05.4	Decorations, coatings and fillings, except fruit based fillings covered by category 4.2.4	Group I	QS		1	50	150	FCRA	
06.2.1	Flours	E 301	QS		1	30	100	FCRA	
06.2.2	Starches	Group I	QS		1	0	0	FCRA	E 301 reported as not used in this food category
06.3	Breakfast cereals	Group I	QS		1	0	250	FCRA	
06.4.2	Dry pasta	Group I	QS	only gluten free and/or pasta intended for hypoproteic diets in accordance with Directive 2009/39/EC	1	30	100	FCRA	
06.4.3	Fresh pre-cooked pasta	E 301	QS		2	110.4 (26.2-194.5)	194.5	FDE	
06.5	Noodles	Group I	QS		1	30	100	FCRA	

FCS Category No	FCS Food category	E Number	MPL	Restrictions	Number of data	Reported use levels from industry		Information provided by	Comments
						Typical mean (range)	Highest maximum level		
06.6	Batters	Group I	QS		1	30	100	FCRA	
06.7	Pre-cooked or processed cereals	Group I	QS		1	30	100	FCRA	
07.1.1	Bread prepared solely with the following ingredients: wheat flour, water, yeast or leaven,salt	E 301	QS		1	50	100	FCRA	
07.1.2	Pain courant francais; Friss búzakenyér, fehér és félbarna kenyerek	E 301	QS	only *Friss búzakenyér, fehér és félbarna kenyerek*	1	50	100	FCRA	
07.2	Fine bakery wares	Group I	QS		1	40.0	40.0	FDE	
					1	300	500	FCRA	
08.1.2	Meat preparations as defined by Regulation (EC) No 853/2004	E 301	QS	only *gehakt* and prepacked preparations of fresh minced meat	1	1500	1500	FDE	
					1	500	1000	FCRA	
08.2.1	Non heat treated processed meat	Group I	QS		1	1500	1500	FDE	1 level reported as FCS 08.2 (Non-heat-treated processed meat and Heat-treated processed meat and foie gras, foie gras entier, etc.)
					1	500	1000	FCRA	

FCS Category No	FCS Food category	E Number	MPL	Restrictions	Number of data	Reported use levels from industry		Information provided by	Comments
						Typical mean (range)	Highest maximum level		
08.2.2	Heat treated processed meat	Group I	QS	except *foie gras, foie gras entier, blocs de foie gras, Libamáj, libamáj egészben, libamáj tömbben*	1	424.8	808.5	FDE	
		E 301		only *foie gras, foie gras entier, blocs de foie gras / Libamáj, libamáj egészben, libamáj tömbben*	1	300	1000	FCRA	1 level for FCS 08.2.2
08.2.3	Casings and coatings and decorations for meat	Group I	QS		1	0	1000	FCRA	
09.1.1	Unprocessed fish	E 301	QS		1	100	300	FCRA	
09.1.2	Unprocessed molluscs and crustaceans	E 301	QS		1	100	300	FCRA	
09.2	Processed fish and fishery products including molluscs and crustaceans	Group I	QS		1	100	300	FCRA	
09.3	Fish roe	Group I	QS	only processed fish roe	1	100	300	FCRA	
10.2	Processed eggs and egg products	Group I	QS		1	300	500	FCRA	
11.2	Other sugars and syrups	Group I	QS		1	100	300	FCRA	
12.1.2	Salt substitutes	Group I	QS		1	50	100	FCRA	
12.2.2	Seasonings and condiments	Group I	QS		1	35	35	FDE	
					1	50	100	FCRA	
12.3	Vinegars	Group I	QS		1	150	250	FCRA	
12.4	Mustard	Group I	QS		1	150	250	FCRA	

FCS Category No	FCS Food category	E Number	MPL	Restrictions	Number of data	Reported use levels from industry		Information provided by	Comments
						Typical mean (range)	Highest maximum level		
12.5	Soups and broths	Group I	QS		6	10.7 (0.1-38.2)	45.1	FDE	
					1	150	250	FCRA	
12.6	Sauces	Group I	QS		5	14.5 (0.8-28.8)	28.8	FDE	
					1	150	250	FCRA	
12.7	Salads and savoury based sandwich spreads	Group I	QS		1	150	250	FCRA	
12.8	Yeast and yeast products	Group I	QS		1	150	250	FCRA	
12.9	Protein products, excluding products covered in category 1.8	Group I	QS		1	150	250	FCRA	
13.1.1	Infant formulae as defined by Commission Directive 2006/141/EC	E 301	Total carry-over 75 mg/L[(a)]		1	17	75	SNE	[(a)] As in Annex III, Part 5, Section B to Regulation (EC) No 1333/2008
13.1.3	Processed cereal-based foods and baby foods for infants and young children as defined by Directive 2006/125/EC	E 301	200 300	only fat-containing cereal-based foods including biscuits and rusks and baby foods only fruit - and vegetable based drinks, juices and baby foods	1	0	200	FCRA	1 level for FCS 13.1.3
13.1.5	Dietary foods for infants and young children for special medical purposes as defined by Commission Directive 1999/21/EC and special formulae for infants	E 301	Total carry-over 75 mg/L[(a)]		1	37	75	SNE	[(a)] As in Annex III, Part 5, Section B to Regulation (EC) No 1333/2008

FCS Category No	FCS Food category	E Number	MPL	Restrictions	Number of data	Reported use levels from industry		Information provided by	Comments
						Typical mean (range)	Highest maximum level		
13.2	Dietary foods for special medical purposes defined in Directive 1999/21/EC (excluding products from food category 13.1.5)	Group I	QS		1	250	1000	FCRA	
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	QS		3	92.4 (1.9-271)	271.0	FDE	
					1	250	1000	FCRA	
13.4	Foods suitable for people intolerant to gluten as defined by Regulation (EC) 41/2009	Group I	QS	including dry pasta	1	250	1000	FCRA	
14.1.2	Fruit juices as defined by Council Directive 2001/112/EC and vegetable juices	Group I	QS	only vegetable juices	1	300	500	FCRA	
14.1.3	Fruit nectars as defined by Council Directive 2001/112/EC and vegetable nectars and similar products	Group I	QS	only vegetable nectars	1	300	500	FCRA	

FCS Category No	FCS Food category	E Number	MPL	Restrictions	Number of data	Reported use levels from industry		Information provided by	Comments
						Typical mean (range)	Highest maximum level		
14.1.4	Flavoured drinks	Group I	QS		4	161.1 (1.5-640)	650.0	FDE	Mean =189
					1	300	500	FCRA	
					1	(40-400)	400	UNESDA	Carbonates
					1	(50-580)	580		Still drinks
					1	(100-400)	400		Energy drinks
					1	(7-400)	400		Sports drinks
					1	(95-400)	400		Squashes / syrups (concentrates)
					1	(100-400)	400		Fruit powders
14.1.5.2	Coffee, tea, herbal and fruit infusions, chicory; tea, herbal and fruit infusions and chicory extracts; tea, plant, fruit and cereal preparations for infusions, as well as mixes and instant mixes of these products - other	Group I	QS	excluding unflavoured leaf tea; including flavoured instant coffee	1	(100-400)	400	UNESDA	Iced coffee
					1	(100-400)	400	UNESDA	Iced tea
14.2.1	Beer and malt beverages	E 301	QS		2	50 (50-50)	150	FDE	
					1	150	300	FCRA	
14.2.3	Cider and perry	Group I	QS		1	150	300	FCRA	
14.2.4	Fruit wine and made wine	Group I	QS		1	150	300	FCRA	
14.2.5	Mead	Group I	QS		1	150	300	FCRA	
14.2.6	Spirit drinks as defined in Regulation (EC) No 110/2008	Group I	QS	except whisky or whiskey	1	150	300	FCRA	

FCS Category No	FCS Food category	E Number	MPL	Restrictions	Number of data	Reported use levels from industry		Information provided by	Comments
						Typical mean (range)	Highest maximum level		
14.2.7.1	Aromatised wines	Group I	QS		1	150	300	FCRA	1 level on FCS 14.2.7
14.2.7.2	Aromatised wine-based drinks	Group I	QS						
14.2.7.3	Aromatised wine-product cocktails	Group I	QS						
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	QS		1	150	300	FCRA	
15.1	Potato-, cereal-, flour- or starch-based snacks	Group I	QS		1	100	200	FCRA	
15.2	Processed nuts	Group I	QS		1	300	500	FCRA	
16	Desserts excluding products covered in category 1, 3 and 4	Group I	QS		1	300	500	FCRA	
17.1	Food supplements supplied in a solid form including capsules and tablets and similar forms excluding chewable forms	Group I	QS		1	0	1000	FCRA	
17.2	Food supplements supplied in a liquid form	Group I	QS		1	0	1000	FCRA	
17.3	Food supplements supplied in a syrup-type or chewable form	Group I	QS		1	0	1000	FCRA	
18	Processed foods not covered by categories 1 to 17, excluding foods for infants and young children	Group I	QS		1	300	500	FCRA	

Appendix 3. Summary of reported use levels (mg/kg) of calcium ascorbate (E 302) provided by industry

FCS Category No	FCS Food category	MPL	Restrictions	Reported use levels from industry			Information provided by	Comments
				Number of data	Typical mean (range)	Highest maximum level		
01.3	Unflavoured fermented products, heat-treated after fermentation	QS		1	100	250	FCRA	
01.4	Flavoured fermented milk products including heat treated products	QS		1	100	250	FCRA	
01.6.3	Other creams	QS		1	300	500	FCRA	
01.7.1	Unripened cheese excluding products falling in category 16	QS	except Mozzarella, and unflavoured live fermented unripened cheese	1	300	500	FCRA	
01.7.5	Processed cheese	QS		1	300	500	FCRA	
01.7.6	Cheese products (excluding products falling in category 16)	QS		1	0	0	FCRA	E 302 not used in this food category
01.8	Dairy analogues, including beverage whiteners	QS		1	100	250	FCRA	
02.2.2	Other fat and oil emulsions including spreads as defined by Council Regulation (EC) No 1234/2007 and liquid emulsions	QS		2	300	500	FCRA	
02.3	Vegetable oil pan spray	QS		1	300	500	FCRA	
03	Edible ices	QS		1	250	500	FCRA	
04.1.2	Peeled, cut and shredded fruit and vegetables	QS	only refrigerated unprocessed fruit and vegetables ready for consumption and prepacked unprocessed and peeled potatoes	2	100	250	FCRA	

FCS Category No	FCS Food category	MPL	Restrictions	Reported use levels from industry			Information provided by	Comments
				Number of data	Typical mean (range)	Highest maximum level		
04.1.3	Frozen fruit and vegetables	QS		2	300	500	FCRA	
04.2.1	Dried fruit and vegetables	QS		2	300	500	FCRA	
04.2.2	Fruit and vegetables in vinegar, oil, or brine	QS		2	300	500	FCRA	
04.2.3	Canned or bottled fruit and vegetables	QS		1	100	300	FCRA	
04.2.4.1	Fruit and vegetable preparations excluding compote	QS		1	100	300	FCRA	levels on the food category 4.2.4
04.2.4.2	Compote, excluding poducts covered by category 16	QS						
04.2.5	Jams, jellies and marmalades and similar products			1	100	300	FCRA	
04.2.5.4	Nut butters and nut spreads	QS		1	300	500	FCRA	
04.2.6	Processed potato products	QS		1	100	300	FCRA	
05.1	Cocoa and Chocolate products as covered by Directive 2000/36/EC	QS	only energy-reduced or with no added sugars	1	0	0	FCRA	E 302 reported not used in this food category
05.2	Other confectionery including breath refreshening microsweets	QS		1	50	150	FCRA	
05.3	Chewing gum	QS		1	50	150	FCRA	
				1	0	0	ICGA	Reported as no sufficient data to proceed to proper consolidation.
05.4	Decorations, coatings and fillings, except fruit based fillings covered by category 4.2.4	QS		1	50	150	FCRA	
06.2.1	Flours	QS		1	30	100	FCRA	
06.2.2	Starches	QS		1	0	0	FCRA	E 302 reported not used in this food category

FCS Category No	FCS Food category	MPL	Restrictions	Reported use levels from industry			Information provided by	Comments
				Number of data	Typical mean (range)	Highest maximum level		
06.3	Breakfast cereals	QS		1	0	250	FCRA	
06.4.2	Dry pasta	QS	only gluten free and/or pasta intended for hypoproteic diets in accordence with Directive 2009/39/EC	1	30	100	FCRA	
06.4.4	Potato Gnocchi	QS						No data provided on FCS 06.4.4. Use of the levels provided for the food category 06.4.2
06.4.5	Fillings of stuffed pasta (ravioli and similar)	QS						No data provided on FCS 06.4.5. Use of the levels provided for the food category 06.4.2
06.5	Noodles	QS		1	30	100	FCRA	
06.6	Batters	QS		1	30	100	FCRA	
06.7	Pre-cooked or processed cereals	QS		1	30	100	FCRA	
07.1	Bread and rolls	QS	except products in 7.1.1 and 7.1.2					No data provided on FCS 07.1. Use of the levels provided for the food categories 07.1.1 and 07.1.2
07.1.1	Bread prepared solely with the following ingredients: wheat flour, water, yeast or leaven, salt	QS		1	50	100	FCRA	
07.1.2	Pain courant francais; Friss búzakenyér, fehér és félbarna kenyerek	QS	only *Friss búzakenyér, fehér és félbarna kenyerek*	1	50	100	FCRA	
07.2	Fine bakery wares	QS		1	300	500	FCRA	

FCS Category No	FCS Food category	MPL	Restrictions	Reported use levels from industry			Information provided by	Comments
				Number of data	Typical mean (range)	Highest maximum level		
08.1.2	Meat preparations as defined by Regulation (EC) No 853/2004	QS	only *gehakt* and prepacked preparations of fresh minced meat	1	1500	1500	FDE	
08.1.2	Meat preparations as defined by Regulation (EC) No 853/2004	QS	only *gehakt* and prepacked preparations of fresh minced meat	1	500	1000	FCRA	
08.2	Processed meat			1	1500	1500	FDE	
08.2.1	Non heat treated processed meat	QS		1	500	1000	FCRA	
08.2.2	Heat treated processed meat	QS	Except *foie gras, foie gras entier, blocs de foie gras, Libamáj, libamáj egészben, libamáj tömbben*	1	300	1000	FCRA	
08.2.3	Casings and coatings and decorations for meat	QS		1	0	1000	FCRA	
09.1.1	Unprocessed fish	QS		1	100	300	FCRA	
09.1.2	Unprocessed molluscs and crustaceans	QS		1	100	300	FCRA	
09.2	Processed fish and fishery products including mollusks and crustaceans	QS		1	100	300	FCRA	
09.3	Fish roe	QS	only processed fish roe	1	100	300	FCRA	
10.2	Processed eggs and egg products	QS		1	300	500	FCRA	
11.2	Other sugars and syrups	QS		1	100	300	FCRA	
12.1.2	Salt substitutes	QS		1	50	100	FCRA	
12.2.2	Seasonings and condiments	QS		1	50	100	FCRA	
12.3	Vinegars	QS		1	150	250	FCRA	
12.4	Mustard	QS		1	150	250	FCRA	
12.5	Soups and broths	QS		1	150	250	FCRA	

FCS Category No	FCS Food category	MPL	Restrictions	Reported use levels from industry			Information provided by	Comments
				Number of data	Typical mean (range)	Highest maximum level		
12.6	Sauces	QS		1	150	250	FCRA	
12.7	Salads and savoury based sandwich spreads	QS		1	150	250	FCRA	
12.8	Yeast and yeast products	QS		1	150	250	FCRA	
12.9	Protein products, excluding products covered in category 1.8	QS		1	150	250	FCRA	
13.1.3	Processed cereal-based foods and baby foods for infants and young children as defined by Directive 2006/125/EC	200	only fat-containing cereal-based foods including biscuits and rusks and baby foods	1	0	200	FCRA	1 level provided for the FCS 13.1.3
13.1.3	Processed cereal-based foods and baby foods for infants and young children as defined by Directive 2006/125/EC	300	only fruit - and vegetable based drinks, juices and baby foods					
13.2	Dietary foods for special medical purposes defined in Directive 1999/21/EC (excluding products from food category 13.1.5)	QS		1	250	1000	FCRA	
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		1	250	1000	FCRA	
13.4	Foods suitable for people intolerant to gluten as defined by Regulation (EC) 41/2009	QS	including dry pasta	1	250	1000	FCRA	
14.1.2	Fruit juices as defined by Council Directive 2001/112/EC and vegetable juices	QS	only vegetable juices	1	300	500	FCRA	

FCS Category No	FCS Food category	MPL	Restrictions	Reported use levels from industry			Information provided by	Comments
				Number of data	Typical mean (range)	Highest maximum level		
14.1.3	Fruit nectars as defined by Council Directive 2001/112/EC and vegetable nectars and similar products	QS	only vegetable nectars	1	300	500	FCRA	
14.1.4	Flavoured drinks	QS		1	300	500	FCRA	
				1	40-400	400	UNESDA	Carbonates
				1	50-580	580		Still drinks
				1	100-400	400		Energy drinks
				1	7-400	400		Sports drinks
				1	95-400	400		Squashes / syrups (concentrates)
				1	100-400	400		Fruit powders
14.1.5.2	Coffee, tea, herbal and fruit infusions, chicory; tea, herbal and fruit infusions and chicory extracts; tea, plant, fruit and cereal preparations for infusions, as well as mixes and instant mixes of these products - other	QS	excluding unflavoured leaf tea; including flavoured instant coffee	1	100-400	400	UNESDA	Iced coffee
14.2.3	Cider and perry	QS		1	150	300	FCRA	
14.2.4	Fruit wine and made wine	QS		1	150	300	FCRA	
14.2.5	Mead	QS		1	150	300	FCRA	
14.2.6	Spirit drinks as defined in Regulation (EC) No 110/2008	QS	except whisky or whiskey	1	150	300	FCRA	
14.2.7.1	Aromatised wines	QS		1	150	300	FCRA	1 level provided for the FCS 14.2.7
14.2.7.2	Aromatised wine-based drinks	QS						
14.2.7.3	Aromatised wine-product cocktails	QS						

FCS Category No	FCS Food category	MPL	Restrictions	Reported use levels from industry			Information provided by	Comments
				Number of data	Typical mean (range)	Highest maximum level		
14.2.8	Other alcoholic drinks including mixtures of alcoholic drinks with non-alcoholic drinks and spirits with less than 15 % of alcohol	QS		1	150	300	FCRA	
15.1	Potato-, cereal-, flour- or starch-based snacks	QS		1	100	200	FCRA	
15.2	Processed nuts	QS		1	300	500	FCRA	
16	Desserts excluding products covered in category 1, 3 and 4	QS		1	300	500	FCRA	
17.1	Food supplements supplied in a solid form including capsules and tablets and similar forms excluding chewable forms	QS		1	0	1000	FCRA	
17.2	Food supplements supplied in a liquid form	QS		1	0	1000	FCRA	
17.3	Food supplements supplied in a syrup-type or chewable form	QS		1	0	1000	FCRA	
18	Processed foods not covered by categories 1 to 17, excluding foods for infants and young children	QS		1	300	500	FCRA	

Appendix 4. Summary of analytical results (mg/kg) of ascorbic acid provided by Members States

FCS Category No	FCS Food category	Total number of data	% LC[(a)]	Range		All data – medium bound				Positive values				
				LOD	LOQ	min	median	mean	max	Number of positive values	min	median	mean	max
01.4	Flavoured fermented milk products including heat treated products	1	0			269.5	269.5	269.5	269.5	1	269.5	269.5	269.5	269.5
01.5	Dehydrated milk as defined by Directive 2001/114/EC	1	0	17	50	224	224	224.0	224	1	224.0	224.0	224.0	224.0
04.2.2	Fruit and vegetables in vinegar, oil, or brine	1	100	20	60	10	10	10.0	10					
04.2.4	Fruit and vegetable preparations excluding products covered by 5.4	1	0	8	25	2110	2110	2110.0	2110	1	2110.0	2110.0	2110.0	2110.0
04.2.4.1	Fruit and vegetable preparations excluding compote	1	100		50	25	25	25.0	25					
04.2.4.2	Compote, excluding products covered by category 16	1	0	17	50	2935	2935	2935.0	2935	1	2935.0	2935.0	2935.0	2935.0
04.2.5.2	Jam, jellies and marmalades and sweetened chestnut puree as defined by Directive 2001/113/EEC	7	14	8.3-16.7	25-50	25	590	1094.1	2180	6	392.0	1306.5	1272.3	2180.0
05.1	Cocoa and Chocolate products as covered by Directive 2000/36/EC	5	0			473	853	817.9	1104.7	5	473.0	853.0	817.9	1104.7
05.2	Other confectionery including breath refreshening microsweets	5	0	17	50	761.48	2680	4261.3	12785	5	761.5	2680.0	4261.3	12785.0
06.3	Breakfast cereals	1	0			35830	35830	35830.0	35830	1	35830.0	35830.0	35830.0	35830.0
06.2.1	Flours	3	67	1	3-50	0.5	25	79.5	213.1	1	213.1	213.1	213.1	213.1
08.2.1	Non heat treated processed meat	1	100	1	3	0.5	0.5	0.5	0.5					
08.2.2	Heat treated processed meat	3	0	17	50	23	260	269.3	524.8	3	23.0	260.0	269.3	524.8

FCS Category No	FCS Food category	Total number of data	% LC[(a)]	Range		All data – medium bound				Positive values				
				LOD	LOQ	min	median	mean	max	Number of positive values	min	median	mean	max
11.2	Other sugars and syrups	4	0			77.3	91.5	97.6	130.2	4	77.3	91.5	97.6	130.2
12.2.2	Seasonings and condiments	1	0	42	125	790	790	790.0	790	1	790.0	790.0	790.0	790.0
12.6	Sauces	1	0	2	5	142	142	142.0	142	1	142.0	142.0	142.0	142.0
13.1	Foods for infants and young children	13	0	1.7-83.3	5-250	115	278	315.2	682	13	115.0	278.0	315.2	682.0
13.1.1	Infant formulae (powder)	1	0			917	917	917.0	917	1	917.0	917.0	917.0	917.0
13.1.2	Follow-on formulae (powder)	3	0			922	1073	1033.3	1105	3	922.0	1073.0	1033.3	1105.0
13.1.3	Processed cereal-based foods and baby foods for infants and young children as defined by Directive 2006/125/EC	1	0			30	30	30.0	30	1	30.0	30.0	30.0	30.0
13.1.4	Other foods for young children	23	17	1	3	0.5	314	250.4	440	19	10.0	335.0	303.0	440.0
13.2	Dietary foods for special medical purposes defined in Directive 1999/21/EC (excluding products from food category 13.1.5)	12	0	1.7-1166.7	5-3500	89.3	611	31029.5	245227	12	89.3	611.0	31029.5	245227.0
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)	11	0	8.3-208.3	25-625	218	468	5692.6	58000	11	218.0	468.0	5692.6	58000.0
14.1.2	Fruit juices as defined by Council Directive 2001/112/EC and vegetable juices	596	38	1-25	2.5-75	0.1252	80.1	203.2	7580	369	0.1	264.0	326.3	7580.0
14.1.3	Fruit nectars as defined by Council Directive 2001/112/EC and vegetable nectars and similar products	57	16	2	5	2.5	116	164.4	1076	48	12.7	152.0	194.7	1076.0
14.1.4	Flavoured drinks	193	22	0-83.3	0-250	0.35	120	551.6	20410	150	0.4	168.1	709.0	20410.0

FCS Category No	FCS Food category	Total number of data	% LC[(a)]	Range		All data – medium bound				Positive values				
				LOD	LOQ	min	median	mean	max	Number of positive values	min	median	mean	max
14.1.5.2	Coffee, tea, herbal and fruit infusions, chicory; tea, herbal and fruit infusions and chicory extracts; tea, plant, fruit and cereal preparations for infusions, as well as mixes and instant mixes of these products - other	3	33		5	2.5	957.2	675.3	1066.13	2	957.2	1011.7	1011.7	1066.1
14.2.1	Beer and malt beverages	13	54	2	5	2.5	2.5	25.0	75	6	12.8	66.0	51.3	75.0
14.2.8	Other alcoholic drinks including mixtures of alcoholic drinks with non-alcoholic drinks and spirits with less than 15 % of alcohol	1	0	2	5	166	166	166.0	166	1	166.0	166.0	166.0	166.0
17	Food supplements	361	3	1-33333.3	2.5-100000	25	49300	88390.7	800000	350	375.3	50850.0	91159.3	800000.0

(a): % LC: percentage of left-censored data.

Appendix 5. Concentration used in the combined refined exposure scenarios (mg/kg) – for estimates using reported use levels (with or without loss factor)

FCS Category No	FCS Food category	MPL	E 300		E 301		E 302		Concentration levels used in the combined refined exposure assessment[a]		% loss[b]	Data source / Comments
			Mean	Max	Mean	Max	Mean	Max	Mean	Max[c]		
01.3	Unflavoured fermented milk products, heat-treated after fermentation	QS	100	250	100	250	100	250	100	250	0	Reported use levels
01.4	Flavoured fermented milk products including heat treated products	QS	100	250	100	250	100	250	100	250	0	Reported use levels
01.5	Dehydrated milk as defined by Directive 2001/114/EC	QS	300	500	300	500			300	500	0	Reported use levels
01.6.3	Other creams	QS	150	500	300	500	300	500	300	500	0	Reported use levels
01.7.1	Unripened cheese excluding products falling in category 16 [except mozzarella and unflavoured live fermented unripened cheese]	QS	300	500	300	500	300	500	300	500	0	Reported use levels
01.7.5	Processed cheese	QS	300	500	300	500	300	500	300	500	0	Reported use levels
01.7.6	Cheese products	QS	-	-	-	-	0	0	-	-	-	Not taken into account (no corresponding FoodEx code/reported as not used)
01.8	Dairy analogues, including beverage whiteners	QS	100	250	100	250	100	250	100	250	0	Reported use levels
02.1	Fats and oils essentially free from water [only cooking and/or frying purposes or the preparation of gravy]	QS	300	500					300	500	0	Reported use levels
02.2.2	Other fat and oil emulsions including spreads as defined by Council Regulation	QS	300	500	152	500	300	500	300	500	0	Reported use levels
02.3	Vegetable oil pan spray	QS	-	-	-	-	-	-	-	-	-	Not taken into account (no corresponding

FCS Category No	FCS Food category	MPL	E 300		E 301		E 302		Concentration levels used in the combined refined exposure assessment[a]		% loss[b]	Data source / Comments
			Mean	Max	Mean	Max	Mean	Max	Mean	Max[c]		
												FoodEx code)
03	Edible ices	QS	40	500	53	500	250	500	250	500	0	Reported use levels
04.1.2	Peeled, cut and shredded fruit and vegetables [only refrigerated unprocessed fruit and vegetables ready for consumption and prepacked unprocessed and peeled potatos]	QS	117	250	100	250	100	250	117	250	0	Reported use levels
04.1.3	Frozen fruit and vegetables	QS	300	500	300	500	300	500	300	500	45	Reported use levels
04.2.1	Dried fruit and vegetables	QS	220	500	300	500	300	500	300	500	8	Reported use levels
04.2.2	Fruit and vegetables in vinegar, oil, or brine	QS	642	1500	300	500	300	500	642	1500	0	Reported use levels
04.2.3	Canned or bottled fruit and vegetables	QS	100	300	100	300	100	300	100	300	40	Reported use levels
04.2.4.1	Fruit and vegetable preparations excluding compote	QS	300	500	100	300	100	300	300	500	0	Reported use levels
04.2.4.2	Compote, excluding products covered by category 16	QS	100	300	100	300	100	300	100	300	0	Reported use levels
04.2.5.1	Extra jam and extra jelly as defined by Directive 2001/113/EC	QS	280	537	-	-	-	-	280	537	0	Reported use levels
04.2.5.2	Jam, jellies and marmalades and sweetened chestnut puree as defined by Directive 2001/113/EC	QS			-	-	-	-				
04.2.5.3	Other similar fruit or vegetable spreads	QS			-	-	-	-				
04.2.5.4	Nut butters and nut spreads	QS	300	500	300	500	300	500	300	500	0	Reported use levels
04.2.6	Processed potato products	QS	65	300	100	300	100	300	100	300	8	Reported use levels

FCS Category No	FCS Food category	MPL	E 300		E 301		E 302		Concentration levels used in the combined refined exposure assessment[a]		% loss[b]	Data source / Comments
			Mean	Max	Mean	Max	Mean	Max	Mean	Max[c]		
05.1	Cocoa and Chocolate products as covered by Directive 2000/36/EC [only energy-reduced or with no added sugars]	QS	0	0	0	0	0	0	0	0	0	Not taken into account (reported as not used)
05.2	Other confectionery including breath refreshening microsweets	QS	340	629	2483	4916	50	150	2480	4915	0	Reported use levels
05.3	Chewing gum	QS	1000	3000	525	3000	50	150	1000	3000	0	Reported use levels
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)
06.2.1	Flours	QS	30	100	30	100	30	100	30	100	0	Reported use levels
06.2.2	Starches	QS	-	-	0	0	0	0	-	-	-	Not taken into account (reported as not used)
06.3	Breakfast cereals	QS	0	250	0	250	0	250	0	250	20	Reported use levels
06.4.1	Fresh pasta	QS	194	500								Reported use levels
06.4.2	Dry pasta [only gluten free and/or pasta intended for hypoproteic diets in accordance with Directive 2009/39/EC]	QS	194	500	83	195	30	100	194	500	0	Reported use levels
06.4.3	Fresh pre-cooked pasta	QS	194	500	-	-	-	-				Reported use levels
06.4.4	Potato gnocchi	QS	-	-	-	-	-	-	-	-	-	Not taken into account (no corresponding FoodEx code)
06.4.5	Fillings of stuffed pasta	QS	194	500			30	100	194	500	0	Reported use levels
06.5	Noodles	QS	30	100			30	100	30	100	0	Reported use levels
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

FCS Category No	FCS Food category	MPL	E 300		E 301		E 302		Concentration levels used in the combined refined exposure assessment[a]		% loss[b]	Data source / Comments
			Mean	Max	Mean	Max	Mean	Max	Mean	Max[c]		
												FoodEx code)
07.1	Bread and rolls [except products in 7.1.1 and 7.1.2]	QS	100	300	50	100	50	100	100	300	80	Reported use levels
07.1.1	Bread prepared solely with the following ingredients: wheat flour, water, yeast or leaven, salt	QS			50	100	50	100				
07.1.2	Pain courant francais; Friss búzakenyér, fehér és félbarna kenyerek	QS			50	100	50	100				
07.2	Fine bakery wares	QS	2737	16920	170	500	300	500	2737	16920	100	Reported use levels
08.2	Meat preparations as defined by Regulation (EC) No 853/2004 [only gehakt and prepacked preparations of fresh minced meat]	QS	1000	1500	1000	1500	500	1000	1000	1500	0	Reported use levels
08.3.1	Non heat treated processed meat	QS	500	1000	680	1000	500	1000	680	1000	0	Reported use levels
08.3.2	Heat treated processed meat - except foie gras	QS	5	10	680	1000	500	1000				Reported use levels
08.3.2	Heat treated processed meat - only foie gras	QS	900	1500	-	-	-	-	900	1500	0	Reported use levels
08.3.3	Casings and coatings and decorations for meat	QS	-	-	-	-	-	-	-	-	-	Not taken into account (no corresponding FoodEx code)
09.1.1	Unprocessed fish	QS	100	300	100	300	100	300	100	300	0	Reported use levels
09.1.2	Unprocessed molluscs and crustaceans	QS	100	300	100	300	100	300	100	300	0	Reported use levels
09.2	Processed fish and fishery products including molluscs and crustaceans	QS	100	300	100	300	100	300	100	300	0	Reported use levels

FCS Category No	FCS Food category	MPL	E 300		E 301		E 302		Concentration levels used in the combined refined exposure assessment[a]		% loss[b]	Data source / Comments
			Mean	Max	Mean	Max	Mean	Max	Mean	Max[c]		
09.3	Fish roe - only processed fish roe	QS	100	300	100	300	100	300	100	300	0	Reported use levels
10.2	Processed eggs and egg products	QS	300	500	300	500	300	500	300	500	0	Reported use levels
11.2	Other sugars and syrups	QS	100	300	100	300	100	300	100	300	0	Reported use levels
12.1.2	Salt substitutes	QS	-	-	-	-	-	-	-	-	-	Not taken into account (no corresponding FoodEx code)
12.2.2	Seasonings and condiments	QS	904	6130	42.5	100	50	100	904	6130	0	Reported use levels
12.3	Vinegars	QS	177.5	250	150	250	150	250	177.5	250	0	Reported use levels
12.4	Mustard	QS	150	250	150	250	150	250	150	250	0	Reported use levels
12.5	Soups and broths	QS	74	380	31	250	150	250	150	380	0	Reported use levels
12.6	Sauces	QS	551	4000	37	250	150	250	551	4000	0	Reported use levels
12.7	Salads and savoury based sandwich spreads	QS	150	250	150	250	150	250	150	250	0	Reported use levels
12.8	Yeast and yeast products	QS	150	250	150	250	150	250	150	250	0	Reported use levels
12.9	Protein products, excluding products covered in category 1.8	QS	150	250	150	250	150	250	150	250	0	Reported use levels
13.1.1	Infant formulae as defined by Commission Directive 2006/141/EC	Total carry-over 75 mg/L	-	-	17	75	-	-	17	75	0	Reported use levels
13.1.2	Follow-on formulae as defined by Commission Directive 2006/141/EC	Total carry-over 75 mg/L	-	-	17	75	-	-	17	75	0	Reported use levels of FCS 13.1.1

FCS Category No	FCS Food category	MPL	E 300		E 301		E 302		Concentration levels used in the combined refined exposure assessment[a]		% loss[b]	Data source / Comments
			Mean	Max	Mean	Max	Mean	Max	Mean	Max[c]		
13.1.3	Processed cereal-based foods and baby foods for infants and young children as defined by Directive 2006/125/EC - only fat-containing cereal-based foods including biscuits and rusks and baby foods	200	30	200	0	200	0	200	30	200	0	Reported use levels
	Processed cereal-based foods and baby foods for infants and young children as defined by Directive 2006/125/EC - only fruit - and vegetable based drinks, juices and baby foods	300	30	200	0	200			30	200	0	Reported use levels
13.1.5	Dietary foods for infants and young children for special medical purposes as defined by Commission Directive 1999/21/EC and special formulae for infants	Total carry-over 75 mg/L	-	-	37	75	-	-	37	75	0	Reported use levels
13.2	Dietary foods for special medical purposes defined in Directive 1999/21/EC	QS	325	1000	250	1000	250	1000	325	1000	0	Reported use levels
13.3	Dietary foods for weight control diets intended to replace total daily food intake or an individual meal	QS	250	1000	132	1000	250	1000	250	1000	0	Reported use levels
13.4	Foods suitable for people intolerant to gluten as defined by Regulation	QS	250	1000	250	1000	250	1000	250	1000	0	Reported use levels
14.1.2	Fruit juices as defined by Directive 2001/112/EC and vegetable juices	QS	298	900	300	500	300	500	300	900	18	Reported use levels
14.1.3	Fruit nectars as defined by Directive 2001/112/EC and vegetable nectars and similar products	QS	281	700	-	-	-	-	281	700	18	Reported use levels
14.1.4	Flavoured drinks	QS	192	1000	189	650	300[e]	500	192	1000	[0-75][d]	Reported use levels

FCS Category No	FCS Food category	MPL	E 300		E 301		E 302		Concentration levels used in the combined refined exposure assessment[a]		% loss[b]	Data source / Comments
			Mean	Max	Mean	Max	Mean	Max	Mean	Max[c]		
14.1.5.2	Other [excluding unflavoured leaf tea; including flavoured instant coffee]	QS	3560	10660	250	400	250	400	3560	10660	0	Reported use levels
14.2.1	Beer and malt beverages	QS	150	300	150	300			150	300	0	Reported use levels
14.2.3	Cider and perry	QS	450	600	150	300	150	300	450	600	0	Reported use levels
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 [except whisky or whiskey]	QS	150	300	150	300	150	300	150	300	0	Reported use levels
14.2.7.1	Aromatised wines	QS	150	300	150	300	150	300	150	300	0	Reported use levels
14.2.7.2	Aromatised wine-based drinks	QS			150	300	150	300				
14.2.7.3	Aromatised wine-product cocktails	QS			150	300	150	300				
14.2.8	Other alcoholic drinks including mixtures of alcoholic drinks with non-alcoholic drinks and spirits with less than 15 % of alcohol and	QS	150	300	150	300	150	300	150	300	0	Reported use levels
15.1	Potato-, cereal-, flour- or starch-based snacks	QS	100	200	100	200	100	200	100	200	8	Reported use levels
15.2	Processed nuts	QS	300	500	300	500	300	500	300	500	0	Reported use levels
16	Desserts excluding products covered in category 1, 3 and 4	QS	213	1882	300[e]	500	300[e]	500	213	1882	0	Reported use levels

FCS Category No	FCS Food category	MPL	E 300		E 301		E 302		Concentration levels used in the combined refined exposure assessment[(a)]		% loss[(b)]	Data source / Comments
			Mean	Max	Mean	Max	Mean	Max	Mean	Max[(c)]		
17.1	Food supplements supplied in a solid form including capsules and tablets and similar forms, excluding chewable forms	QS	0	1000	0	1000	0	1000	0	1000	0	Reported use levels
17.2	Food supplements supplied in a liquid form	QS									0	
17.3	Food supplements supplied in a syrup-type or chewable form	QS									0	
18	Processed foods not covered by categories 1 to 17, excluding foods for infants and young children	QS	300	500	300	500	300	500	300	500	[0-100][(d)]	Reported use levels

(a): The concentration level used for the combined exposure estimates corresponds to the highest level reported for one of the 3 food additives (E 300, E 301 or E 302).
(b): The percentage of loss during manufacturing processes was taken into account only in the scenario using reported use levels with loss factor (scenario which results are presented in appendices 7, 11 and 12; scenario using reported use levels without loss factor are in appendices 6, 8, 9 and 10).
(c): The max levels were used to estimate the maximum level exposure assessment scenario.
(d): Depending of the food items in the food category.
(e): Same unique value provided for the each food additive E300/E301/E302 by the same data provider. For E300, other levels were made available by other data provider and therefore, the mean of E300 was used to estimate the combined exposure as it was considered more representative.

Appendix 6. Anticipated combined exposure, per population group and survey, to ascorbic acid (E 300), calcium ascorbate (E 301) and sodium ascorbate (E 302) from their uses as a food additive using reported use levels without loss factor: mean and high level (mg/kg bw/day)

	Number of subjects	Maximum scenario		Brand-loyal scenario		Non-brand-loyal scenario	
		Mean	High level	Mean	High level	Mean	High level
Infants							
Bulgaria (NUTRICHILD)	659	31.9	100.1	26.7	91.7	7.2	20.2
Germany (VELS)	159	33.0	85.7	23.2	71.2	6.6	17.9
Denmark (IAT 2006 07)	826	19.4	45.0	13.6	33.2	6.1	12.2
Finland (DIPP 2001 2009)	500	8.3	15.3	6.2	11.1	3.8	7.1
United Kingdom (DNSIYC 2011)	1366	22.1	56.2	15.4	40.4	5.9	13.5
Italy (INRAN SCAI 2005 06)	12	13.0		10.1		4.2	
Toddlers							
Belgium (Regional Flanders)	36	82.0		52.2		18.8	
Bulgaria (NUTRICHILD)	428	65.9	159.2	58.1	147.1	13.4	29.3
Germany (DONALD 2006 2008)	261	29.8	77.5	23.6	69.6	7.4	17.3
Spain (enKid)	17	38.3		29.6		9.3	
Finland (DIPP 2003 2006)	497	8.4	36.1	6.3	25.0	2.8	11.2
Italy (INRAN SCAI 2005 06)	36	38.2		32.2		9.1	
Netherlands (VCP kids)	322	72.1	159.2	50.5	123.6	16.5	34.3
Children							
Belgium (Regional Flanders)	625	68.6	135.1	46.8	101.5	15.3	27.9
Bulgaria (NUTRICHILD)	433	74.2	167.3	64.7	157.8	14.8	31.8
Czech Republic (SISP04)	389	54.4	127.0	44.5	112.7	11.3	25.7
Germany (DONALD 2006 2008)	660	39.5	81.7	28.1	64.5	9.8	17.8
Denmark (Danish Dietary Survey)	490	24.7	46.4	14.9	29.2	7.1	12.4
Spain (enKid)	156	43.1	112.1	34.3	105.7	9.7	19.9
Spain (NUT INK05)	399	42.5	97.4	33.1	82.2	9.3	18.1
Finland (DIPP 2003 2006)	933	23.8	48.9	16.3	35.3	7.7	14.7
Finland (STRIP)	250	68.1	130.4	49.9	109.4	15.1	25.2
France (INCA2)	482	68.3	137.2	57.6	119.2	13.0	25.1
Greece (Regional Crete)	839	58.0	123.5	49.7	113.3	13.4	24.7
Italy (INRAN SCAI 2005 06)	193	41.9	100.0	36.1	89.4	9.1	19.3
Latvia (EFSA TEST)	189	45.4	112.3	37.3	99.6	9.2	21.2
Netherlands (VCP kids)	957	66.3	141.4	46.6	117.6	15.0	28.4
Sweden (NFA)	1473	59.1	125.0	42.4	102.6	12.9	25.0
Adolescents							
Belgium (Diet National 2004)	584	33.1	73.0	24.2	57.3	6.6	13.5
Cyprus (Childhealth)	303	17.9	45.5	13.7	34.6	4.0	9.2
Czech Republic (SISP04)	298	40.6	98.9	33.7	85.1	8.3	17.7

	Number of subjects	Maximum scenario		Brand-loyal scenario		Non-brand-loyal scenario	
		Mean	High level	Mean	High level	Mean	High level
Germany (National Nutrition Survey II)	1011	27.8	76.5	20.9	64.8	6.1	15.5
Denmark (Danish Dietary Survey)	479	17.4	34.1	11.0	24.1	4.7	9.5
Spain (AESAN FIAB)	86	22.6	57.8	19.5	53.4	4.7	10.9
Spain (enKid)	209	29.2	79.3	23.4	68.0	6.2	15.1
Spain (NUT INK05)	651	27.3	62.1	21.2	54.7	5.8	12.0
France (INCA2)	973	36.3	84.6	30.5	75.3	6.9	14.9
Italy (INRAN SCAI 2005 06)	247	23.4	63.4	19.5	57.6	5.2	12.5
Latvia (EFSA TEST)	470	30.3	80.3	24.7	71.8	6.4	15.1
Sweden (NFA)	1018	34.4	80.1	24.3	64.1	7.8	16.0
Adults							
Belgium (Diet National 2004)	1304	22.0	56.8	16.7	46.2	4.5	10.7
Czech Republic (SISP04)	1666	19.1	54.8	16.6	49.8	4.0	10.0
Germany (National Nutrition Survey II)	10419	22.4	59.7	17.7	51.4	4.8	11.7
Denmark (Danish Dietary Survey)	2822	8.6	20.4	5.7	14.2	2.3	5.0
Spain (AESAN)	410	15.2	42.3	12.4	36.0	3.3	8.3
Spain (AESAN FIAB)	981	16.2	43.7	13.7	39.2	3.4	8.2
Finland (FINDIET 2007)	1575	5.0	13.6	3.8	10.8	1.8	4.9
France (INCA2)	2276	19.9	47.9	16.7	42.1	3.9	8.6
United Kingdom (NDNS)	1724	16.9	38.0	12.9	32.2	3.2	6.9
Hungary (National Repr Surv)	1074	7.5	22.5	5.7	18.4	2.2	5.0
Ireland (NSIFCS)	958	13.7	30.9	10.7	27.3	2.8	5.8
Italy (INRAN SCAI 2005 06)	2313	10.9	29.7	9.2	27.5	2.6	5.9
Latvia (EFSA TEST)	1306	16.7	47.9	14.1	44.0	3.7	9.2
Netherlands (DNFCS 2003)	750	24.2	54.4	17.1	42.3	5.1	10.5
Sweden (Riksmaten 1997 98)	1210	20.7	44.1	16.1	37.0	4.4	8.6
The elderly							
Belgium (Diet National 2004)	1230	15.9	41.1	12.8	36.7	3.3	7.4
Germany (National Nutrition Survey II)	2496	20.1	53.9	17.2	50.5	4.1	9.9
Denmark (Danish Dietary Survey)	329	6.0	14.5	4.3	11.3	1.6	3.9
Finland (FINDIET 2007)	463	2.7	8.1	2.2	7.0	1.0	2.7
France (INCA2)	348	14.3	39.3	12.2	33.9	2.9	6.8
Hungary (National Repr Surv)	286	7.5	25.1	6.2	22.6	2.0	5.0
Italy (INRAN SCAI 2005 06)	518	8.4	23.8	7.2	22.1	2.0	4.6

Appendix 7. Anticipated combined exposure, per population group and survey, to ascorbic acid (E 300), calcium ascorbate (E 301) and sodium ascorbate (E 302) from their uses as food additives using reported use levels with loss factor: mean and high level (mg/kg bw/day)

	Number of subjects	Brand-loyal scenario		Non-brand-loyal scenario	
		Mean	High level	Mean	High level
Infants					
Bulgaria (NUTRICHILD)	659	8.2	17.5	3.0	7.3
Germany (VELS)	159	13.8	32.3	3.5	9.3
Denmark (IAT 2006 07)	826	9.7	25.4	4.2	8.8
Finland (DIPP 2001 2009)	500	5.0	9.7	2.8	5.2
United Kingdom (DNSIYC 2011)	1366	10.3	19.9	4.1	8.3
Italy (INRAN SCAI 2005 06)	12	8.7		3.3	
Toddlers					
Belgium (Regional Flanders)	36	21.7		10.2	
Bulgaria (NUTRICHILD)	428	7.9	20.4	3.8	9
Germany (DONALD 2006 2008)	261	7.3	20.1	3.8	10.1
Spain (enKid)	17	10.1		5.2	
Finland (DIPP 2003 2006)	497	4.4	19.6	2.3	9.8
Italy (INRAN SCAI 2005 06)	36	7.6		4.3	
Netherlands (VCP kids)	322	18.7	39.9	8.6	16.9
Children					
Belgium (Regional Flanders)	625	15.7	32.1	7.6	14.2
Bulgaria (NUTRICHILD)	433	8.1	19.1	4	8.6
Czech Republic (SISP04)	389	8.7	21.4	4.1	9.5
Germany (DONALD 2006 2008)	660	10.8	20.8	5.4	9.9
Denmark (Danish Dietary Survey)	490	8.9	16.7	4.9	8.8
Spain (enKid)	156	8.7	18.8	4.4	9.5
Spain (NUT INK05)	399	8.2	16.7	4	8
Finland (DIPP 2003 2006)	933	12.2	26	6.3	13
Finland (STRIP)	250	13.7	23.4	7.3	12.4
France (INCA2)	482	8.1	16.9	3.9	7.4
Greece (Regional Crete)	839	9	17.5	5.5	10.6
Italy (INRAN SCAI 2005 06)	193	5.6	13	3.3	6.4
Latvia (EFSA TEST)	189	7.7	16.7	3.5	7.7
Netherlands (VCP kids)	957	15.4	31	7.6	14.5
Sweden (NFA)	1473	12	23	6	11.5
Adolescents					
Belgium (Diet National 2004)	584	8	17.9	2.8	5.8
Cyprus (Childhealth)	303	4.1	10.3	1.7	3.7
Czech Republic (SISP04)	298	6.2	16	2.8	6.7
Germany (National Nutrition Survey II)	1011	8	19.3	3.2	7.4
Denmark (Danish Dietary Survey)	479	6.4	13.2	3.2	6.9
Spain (AESAN FIAB)	86	3	7.3	1.6	3.2

	Number of subjects	Brand-loyal scenario		Non-brand-loyal scenario	
		Mean	High level	Mean	High level
Spain (enKid)	209	5	11.3	2.5	5.4
Spain (NUT INK05)	651	5.2	10.6	2.5	4.9
France (INCA2)	973	4.3	9.6	2	4.1
Italy (INRAN SCAI 2005 06)	247	3.6	8.5	2	4.1
Latvia (EFSA TEST)	470	5.4	11.6	2.5	5
Sweden (NFA)	1018	7.7	15.3	3.8	8.1
Adults					
Belgium (Diet National 2004)	1304	5.5	14.3	2	4.5
Czech Republic (SISP04)	1666	2.6	6.7	1.3	3.1
Germany (National Nutrition Survey II)	10419	5.3	14.2	2.2	5.5
Denmark (Danish Dietary Survey)	2822	3	7.5	1.5	3.4
Spain (AESAN)	410	2.9	7.6	1.4	3.1
Spain (AESAN FIAB)	981	2.5	6	1.3	2.6
Finland (FINDIET 2007)	1575	3.2	8.9	1.6	4.3
France (INCA2)	2276	2.7	6.2	1.3	2.5
United Kingdom (NDNS)	1724	3.4	7.6	1.2	2.5
Hungary (National Repr Surv)	1074	2.4	6	1.4	2.9
Ireland (NSIFCS)	958	2.5	5.8	1.1	2.4
Italy (INRAN SCAI 2005 06)	2313	1.7	3.8	1.1	2.2
Latvia (EFSA TEST)	1306	3.1	7	1.5	3.2
Netherlands (DNFCS 2003)	750	6.3	13.3	2.5	4.8
Sweden (Riksmaten 1997 98)	1210	3.7	8.7	1.8	3.7
The elderly					
Belgium (Diet National 2004)	1230	3	7.7	1.3	2.8
Germany (National Nutrition Survey II)	2496	3.4	8.8	1.5	3.5
Denmark (Danish Dietary Survey)	329	1.8	4.7	1	2.2
Finland (FINDIET 2007)	463	1.9	5.9	0.9	2.3
France (INCA2)	348	2	4.4	1	1.8
Hungary (National Repr Surv)	286	1.6	3.1	1	1.9
Italy (INRAN SCAI 2005 06)	518	1.3	2.9	0.9	1.6

Appendix 8. Main food categories contributing to the combined exposure to ascorbic acid (E 300), calcium ascorbate (E 301) and sodium ascorbate (E 302) from their uses as a food additive using reported use levels without loss factor, "maximum level refined exposure scenario" (> 5 % to the total mean exposure) and number of surveys in which each food category is contributing

FCS Category number	Food category	Infants	Toddlers	Children	Adolescents	Adults	The elderly
		Range of % contribution to the total exposure (Number of surveys)[(a)]					
01.4	Flavoured fermented milk products including heat-treated products		7.4 (1)				
01.5	Dehydrated milk as defined by Directive 2001/114/EC			5.2 (1)			
01.7.1	Unripened cheese excluding products falling in category 16	5.6 (1)					
04.1	Unprocessed fruit and vegetables	7.7-44.1 (6)	7.4-28.3 (5)	5.1-13.2 (8)	6.7-9.5 (4)	5-20.6 (13)	7-33.1 (7)
05.2	Other confectionery including breath freshening microsweets			7.9-9.0 (2)	5.3-9.3 (2)	6.7-7 (2)	
07.1	Bread and rolls			5.7 (1)		5.8-6.5 (2)	6.1-7.2 (2)
07.2	Fine bakery wares	20.3-58.5 (4)	13.1-72.5 (7)	16-73.8 (15)	15.6-73.6 (12)	20.1-68 (14)	26.7-65 (6)
08.3	Meat products			5.7 (1)		7.1-8.3 (2)	6.4-8.9 (2)
12.5	Soups and broths	5.9 (1)					
12.6	Sauces	5.6 (1)		5.1-7.2 (4)	5.5-8.6 (6)	5.2-9.5 (8)	5.2-6.2 (2)
13.1	Foods for infants and young children	14.2-40.2 (6)	6.2-11.5 (2)				
14.1.2	Fruit juices as defined by Directive 2001/112/EC and vegetable juices	11.8-11.9 (2)	6.8-15.9 (7)	5.5-33.1 (12)	5.0-15.5 (6)	10.6-27.2 (3)	7.2-26.1 (3)
14.1.3	Fruit nectars as defined by Directive 2001/112/EC and vegetable nectars and similar products	5.5 (1)					
14.1.4	Flavoured drinks	8.2 (1)	5-18.8 (3)	5.1-25.9 (12)	5.4-34.9 (12)	6.4-22.4 (12)	5.2-11.6 (3)
14.2	Alcoholic beverages, including alcohol-free and low-alcohol counterparts					5.4-8.7 (5)	9.4-9.4 (1)

FCS Category number	Food category	Infants	Toddlers	Children	Adolescents	Adults	The elderly
		Range of % contribution to the total exposure (Number of surveys)[a]					
16	Desserts excluding products covered in category 1, 3 and 4	6.2 (1)	6.4-6.6 (2)	5.3-5.3 (1)			

Appendix 9. Main food categories contributing to the combined exposure to ascorbic acid (E 300), calcium ascorbate (E 301) and sodium ascorbate (E 302) from their uses as a food additive using reported use levels without loss factor, "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	Food category	Infants	Toddlers	Children	Adolescents	Adults	The elderly
		Range of % contribution to the total exposure (Number of surveys)[(a)]					
01.4	Flavoured fermented milk products including heat-treated products		6.4 (1)				
01.7.1	Unripened cheese excluding products falling in category 16	5.1 (1)					
04.1	Unprocessed fruit and vegetables	5.9-45.8 (6)	5.4-30.1 (5)	6.4-13.6 (4)	5.4-8.9 (4)	5.5-20.7 (8)	5.5-35.1 (7)
05.2	Other confectionery including breath freshening microsweets			7.6-9 (2)	9.0 (1)	6.3-7.4 (2)	
06.4	Pasta	5.3 (1)					
07.2	Fine bakery wares	22.4-69.3 (4)	15.0-84.7 (7)	16.6-88.8 (15)	18.9-88.5 (12)	25.5-83.1 (14)	35.9-78 (6)
08.3	Meat products			6.0 (1)		7.3-8.8 (2)	6.3-9.5 (2)
12.5	Soups and broths	7.5 (1)					
13.1	Foods for infants and young children	10.7-40.4 (6)	10.1 (1)				
14.1.2	Fruit juices as defined by Directive 2001/112/EC and vegetable juices	9.7-13.9 (2)	6.9-19.8 (6)	5-42.9 (7)	7.4-13.7 (3)	8.8-33.7 (3)	5.2-32.4 (3)
14.1.3	Fruit nectars as defined by Directive 2001/112/EC and vegetable nectars and similar products	7.1 (1)					
14.1.4	Flavoured drinks	6.8 (1)	11.2 (1)	7.8-27 (5)	6.6-38.7 (6)	5.1-24.1 (10)	6-9.7 (2)
14.2	Alcoholic beverages, including alcohol-free and low-alcohol counterparts					5.4-8.7 (4)	9.6 (1)

Appendix 10. Main food categories contributing to the combined exposure to ascorbic acid (E 300), calcium ascorbate (E 301) and sodium ascorbate (E 302) from their uses as a food additive using reported use levels without loss factor, "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	Food category	Infants	Toddlers	Children	Adolescents	Adults	The elderly
		Range of % contribution to the total exposure (Number of surveys)[(a)]					
01.4	Flavoured fermented milk products including heat-treated products		7.5 (1)				
01.5	Dehydrated milk as defined by Directive 2001/114/EC	6.1 (1)		13.0 (1)			
01.7.2	Unripened cheese excluding products falling in category 16	12.5 (1)					
02.1	Fats and oils essentially free from water (excluding anhydrous milkfat)	5.4 (1)					
04.1	Unprocessed fruit and vegetables	20.4-57.8 (6)	10.9-42.7 (7)	5.9-23.5 (15)	6.1-22.2 (12)	9.1-33.9 (15)	17.1-43.5 (7)
04.2	Processed fruit and vegetables	5.2-5.3 (2)					
05.2	Other confectionery including breath freshening microsweets		5.8 (1)	6.5-13.8 (6)	11.3-15.2 (2)	8.3-9.9 (2)	
06.4	Pasta	5.1 (1)	5.1 (1)		5.1 (1)		
07.1	Bread and rolls	5.0 (1)		5.8 (1)		5.7-6.2 (2)	6.0-6.5 (2)
07.2	Fine bakery wares	10.4-42.1 (4)	5.4-50.4 (7)	7.3-57.4 (15)	8.2-57.6 (12)	9.5-47.6 (14)	11.6-42.8 (6)
08.3	Meat products	7.0-9.1 (2)	5.5-11.0 (4)	5.5-10.9 (11)	5.3-10.2 (9)	6.1-15.9 (13)	5.8-12.9 (6)
12.5	Soups and broths	7.1 (1)		6.0 (1)	5.4 (1)	6.4 (1)	6.7 (1)
12.6	Sauces				5-5 (1)	5.5 (1)	
13.1	Foods for infants and young children	7.1-19.8 (6)	5.2 (1)				
14.1.2	Fruit juices as defined by Directive 2001/112/EC and vegetable juices	8.0-17.6 (3)	9.7-20.6 (7)	5-30.9 (15)	5.8-21.6 (11)	5.0-21.1 (9)	9.7-18.5 (3)
14.1.3	Fruit nectars as defined by Directive 2001/112/EC and vegetable nectars and similar products	6.8 (1)	5.1 (1)			6.5 (1)	
14.1.4	Flavoured drinks	7.9 (1)	6.4-14.6 (2)	5.2-15.1 (9)	5.5-21.8 (10)	5.2-17.3 (10)	6.6-6.6 (1)
14.2	Alcoholic beverages, including alcohol-free and low-alcohol counterparts					5.1-17 (9)	5.7-12.6 (2)

Appendix 11. Main food categories contributing to the combined exposure to ascorbic acid (E 300), calcium ascorbate (E 301) and sodium ascorbate (E 302) from their uses as a food additive using reported use levels with loss factor, "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	Food category	Infants	Toddlers	Children	Adolescents	Adults	The elderly
		Range of % contribution to the total exposure (Number of surveys)[(a)]					
01.4	Flavoured fermented milk products including heat-treated products		5.3-10.2 (2)	5.1 (1)			
01.5	Dehydrated milk as defined by Directive 2001/114/EC			28.5 (1)			
01.7.1	Unripened cheese excluding products falling in category 16	8.1 (1)				5.5 (1)	
01.7.5	Processed cheese		7.9 (1)				
02.1	Fats and oils essentially free from water (excluding anhydrous milkfat)			5.0 (1)		5.4 (1)	5.6 (1)
04.1	Unprocessed fruit and vegetables	6.3-29.2 (6)	5.5-22.4 (7)	5.4-22.8 (14)	7.2-19.7 (9)	6.8-32.2 (14)	13.0-46.1 (7)
04.2	Processed fruit and vegetables					5.1 (1)	6.8 (1)
05.2	Other confectionery including breath freshening microsweets		6.5 (1)	8.3-17.4 (7)	6.6-18.2 (5)	5.7-13.1 (3)	5.9 (1)
06.4	Pasta	6.2 (1)	7.9 (1)	5.3-8.7 (2)	5.6-7.4 (2)	5.8 (1)	6.6 (1)
08.3	Meat products	6.1-6.5 (2)	5.1-11.6 (6)	5.7-13.4 (14)	5.2-15.7 (9)	5.9-20.6 (13)	7.1-21.7 (7)
12.2	Herbs, spices, seasonings		7.8 (1)		9.4 (1)	13.8 (1)	11.4 (1)
12.5	Soups and broths	8.8 (1)		10.5 (1)	9.6 (1)	12.7 (1)	11.9 (1)
12.6	Sauces	8.1 (1)	5.4 (1)	5.0-22.7 (7)	11.4-23.4 (7)	10.9-29.2 (8)	18.1-20.7 (3)
13.1	Foods for infants and young children	43.7-70.4 (6)	16.1-17.7 (2)				
14.1.2	Fruit juices as defined by Directive 2001/112/EC and vegetable juices	6.1-30.6 (3)	23.8-41.7 (7)	8.0-50.4 (15)	8.5-37.8 (12)	5.5-34.2 (13)	6.5-35.2 (6)
14.1.3	Fruit nectars as defined by Directive 2001/112/EC and vegetable nectars and similar products	5.3-6.8 (2)	13.9 (1)	9.8 (1)		10.2 (1)	
14.1.4	Flavoured drinks	7.9 (1)	6.2-29 (4)	6.0-33.7 (14)	14.9-50.1 (12)	7.7-40.1 (15)	6.9-12.1 (3)
14.2	Alcoholic beverages, including alcohol-free and low-alcohol counterparts					6.5-32.1 (10)	7.9-22.3 (3)
16	Desserts excluding products covered in category 1, 3 and 4	8.9 (1)	15.1-21.6 (2)	6.6-15.7 (4)	9.3 (1)	5.1-6.2 (2)	6.5-8.6 (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.

Appendix 12. Main food categories contributing to the combined exposure to ascorbic acid (E 300), calcium ascorbate (E 301) and sodium ascorbate (E 302) from their uses as a food additive using reported use levels with loss factor, "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	Food category	Infants	Toddlers	Children	Adolescents	Adults	The elderly
		Range of % contribution to the total exposure (Number of surveys)[(a)]					
01.4	Flavoured fermented milk products including heat-treated products		5.4-10.3 (4)	5.5-7.6 (3)			
01.5	Dehydrated milk as defined by Directive 2001/114/EC	8.3 (1)		30.9 (1)			
01.7.1	Unripened cheese excluding products falling in category 16	18.3 (1)		6.3-6.5 (2)	7.1-7.1 (1)	7.6 (1)	5.6 (1)
01.7.5	Processed cheese		8.5 (1)				
02.1	Fats and oils essentially free from water (excluding anhydrous milkfat)	6.9 (1)	5.5 (1)	5.2-7.5 (2)	6.5-7.2 (2)	6-7.9 (4)	6.3-8 (2)
02.2	Fat and oil emulsions mainly of type water-in-oil						5.1 (1)
03	Edible ices		5.6 (1)	5-5.6 (2)			
04.1	Unprocessed fruit and vegetables	23.3-43.3 (6)	10.9-32.7 (7)	6.8-30.4 (15)	6.9-28.1 (12)	9.3-37.8 (15)	21.2-48.3 (7)
04.2	Processed fruit and vegetables	5.5-7.5 (3)	5.9 (1)			7.3 (1)	5.8-8.3 (2)
05.2	Other confectionery including breath freshening microsweets		10.7 (1)	5.2-20.3 (9)	6.2-22.6 (7)	5.6-14.7 (5)	5.9 (1)
06.4	Pasta	6.6 (1)	10.2 (1)	6.9-9.9 (2)	7.8-11.0 (2)	7.4 (1)	8.3 (1)
08.3	Meat products	6.8-13.4 (3)	6.4-19.8 (7)	6.7-21.7 (15)	8.6-23.5 (12)	8.5-25.0 (15)	9.8-23.1 (7)
12.5	Soups and broths	9.2 (1)	6.4 (1)	5.5-14.6 (2)	12.6 (1)	6.4-13.9 (2)	13.7 (1)
12.6	Sauces			5.2-8.5 (5)	6.1-10.6 (7)	5.2-11.3 (8)	5.9-7.0 (3)
12.7	Salads and savoury-based sandwich spreads					6.3 (1)	
13.1	Foods for infants and young children	16.5-29.2 (6)	7.2 (1)				
14.1.2	Fruit juices as defined by Directive 2001/112/EC and vegetable juices	12.4-34.2 (3)	14.9-31.3 (7)	8.4-32.2 (15)	9.4-32.8 (12)	5.3-23.4 (11)	5.6-19.6 (5)
14.1.3	Fruit nectars as defined by Directive 2001/112/EC and vegetable nectars and similar products	7.2-8.6 (2)	12.0 (1)	8.3 (1)		11.3 (1)	
14.1.4	Flavoured drinks	9.6 (1)	6.3-16.1 (2)	6.7-16.8 (10)	6.6-28.3 (12)	6.7-20.3 (12)	5.5 (1)
14.2	Alcoholic beverages, including alcohol-free and low-alcohol counterparts					5.3-31.0 (12)	9.6-19.7 (3)

FCS Category number	Food category	Infants	Toddlers	Children	Adolescents	Adults	The elderly
		Range of % contribution to the total exposure (Number of surveys)[(a)]					
16	Desserts excluding products covered in category 1, 3 and 4		5.6 (1)				

(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.

Appendix 13. Concentration levels of ascorbic acid used in the exposure scenarios estimated using analytical data or reported use levels with loss factor for food categories for which no analytical data were provided (mg/kg)

FCS Category No	FCS Food category	MPL	Concentration levels used in the exposure assessment			Data source / Comments
			Mean	Max	% loss	
01.3	Unflavoured fermented milk products, heat-treated after fermentation	QS	100	250	0	Reported use levels
01.4	Flavoured fermented milk products including heat treated products	QS	270	270	-	Analytical data
01.5	Dehydrated milk as defined by Directive 2001/114/EC	QS	224	224	-	Analytical data
01.6.3	Other creams	QS	150	500	0	Reported use levels
01.7.1	Unripened cheese excluding products falling in category 16 [except mozzarella and unflavoured live fermented unripened cheese]	QS	300	500	0	Reported use levels
01.7.5	Processed cheese	QS	300	500	0	Reported use levels
01.7.6	Cheese products	QS	-	-	-	Not taken into account (no corresponding FoodEx code)
01.8	Dairy analogues, including beverage whiteners	QS	100	250	100	Reported use levels
02.1	Fats and oils essentially free from water [only cooking and/or frying purposes or the preparation of gravy]	QS	300	500	0	Reported use levels
02.2.2	Other fat and oil emulsions including spreads as defined by Council Regulation	QS	300	500	0	Reported use levels
02.3	Vegetable oil pan spray	QS	-	-	-	Not taken into account (no corresponding FoodEx code)
03	Edible ices	QS	40	500	100	Reported use levels
04.1.2	Peeled, cut and shredded fruit and vegetables [only refrigerated unprocessed fruit and vegetables ready for consumption and prepacked unprocessed and peeled potatoes]	QS	117	250	100	Reported use levels
04.1.3	Frozen fruit and vegetables	QS	300	500	45	Reported use levels
04.2.1	Dried fruit and vegetables	QS	220	500	8	Reported use levels
04.2.2	Fruit and vegetables in vinegar, oil, or brine	QS	10	10	-	Analytical data
04.2.3	Canned or bottled fruit and vegetables	QS	100	300	40	Reported use levels
04.2.4.1	Fruit and vegetable preparations excluding compote	QS	25	25	-	Analytical data

FCS Category No	FCS Food category	MPL	Concentration levels used in the exposure assessment			Data source / Comments
			Mean	Max	% loss	
04.2.4.2	Compote, excluding products covered by category 16	QS	2935	2935	-	Analytical data
04.2.5.1	Extra jam and extra jelly as defined by Directive 2001/113/EC	QS	1100	2180	-	Analytical data
04.2.5.2	Jam, jellies and marmalades and sweetened chestnut puree as defined by Directive 2001/113/EC	QS				
04.2.5.3	Other similar fruit or vegetable spreads	QS				
04.2.5.4	Nut butters and nut spreads	QS	300	500	100	Reported use levels
04.2.6	Processed potato products	QS	65	300	8	Reported use levels
05.1	Cocoa and Chocolate products as covered by Directive 2000/36/EC [only energy-reduced or with no added sugars]	QS	820	1100	-	Analytical data
05.2	Other confectionery including breath refreshening microsweets	QS	4260	12785	-	Analytical data
05.3	Chewing gum	QS	1000	3000	0	Reported use levels
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)
06.2.1	Flours	QS	80	213	100	Analytical data
06.2.2	Starches	QS	-	-		Not taken into account (reported as not used)
06.3	Breakfast cereals	QS	35830	35830	-	Analytical data
06.4.1	Fresh pasta	QS	194	500	100	Reported use levels
06.4.2	Dry pasta [only gluten free and/or pasta intended for hypoproteic diets in accordance with Directive 2009/39/EC]	QS	194	500	100	Reported use levels
06.4.3	Fresh pre-cooked pasta	QS	194	500	100	Reported use levels
06.4.4	Potato gnocchi	QS	-	-		Not taken into account (no corresponding FoodEx code)
06.4.5	Fillings of stuffed pasta	QS	194	500	100	Reported use levels
06.5	Noodles	QS	194	500	100	Reported use levels
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)

FCS Category No	FCS Food category	MPL	Concentration levels used in the exposure assessment			Data source / Comments
			Mean	Max	% loss	
07.1	Bread and rolls [except products in 7.1.1 and 7.1.2]	QS	100	300	80	Reported use levels
07.1.1	Bread prepared solely with the following ingredients: wheat flour, water, yeast or leaven, salt	QS				
07.1.2	Pain courant francais; Friss búzakenyér, fehér és félbarna kenyerek	QS				
07.2	Fine bakery wares	QS	2737	16920	0	Reported use levels
08.2	Meat preparations as defined by Regulation (EC) No 853/2004 [only *gehakt* and prepacked preparations of fresh minced meat]	QS	200	525	-	Analytical data
08.3.1	Non heat treated processed meat	QS	200	525	-	Analytical data
08.3.2	Heat treated processed meat	QS	200	525	-	Analytical data
08.3.3	Casings and coatings and decorations for meat	QS	-	-		Not taken into account (no corresponding FoodEx code)
09.1.1	Unprocessed fish	QS	100	300	0	Reported use levels
09.1.2	Unprocessed molluscs and crustaceans	QS	100	300	0	Reported use levels
09.2	Processed fish and fishery products including molluscs and crustaceans	QS	100	300	0	Reported use levels
09.3	Fish roe - only processed fish roe	QS	100	300	0	Reported use levels
10.2	Processed eggs and egg products	QS	300	500	0	Reported use levels
11.2	Other sugars and syrups	QS	100	130	-	Analytical data
12.1.2	Salt substitutes	QS	-	-		Not taken into account (no corresponding FoodEx code)
12.2.2	Seasonings and condiments	QS	790	790	-	Analytical data
12.3	Vinegars	QS	178	250	0	Reported use levels
12.4	Mustard	QS	150	250	0	Reported use levels
12.5	Soups and broths	QS	74	380	0	Reported use levels
12.6	Sauces	QS	140	140	-	Analytical data
12.7	Salads and savoury based sandwich spreads	QS	150	250	0	Reported use levels
12.8	Yeast and yeast products	QS	150	250	0	Reported use levels
12.9	Protein products, excluding products covered in category 1.8	QS	150	250	0	Reported use levels

FCS Category No	FCS Food category	MPL	Concentration levels used in the exposure assessment			Data source / Comments
			Mean	Max	% loss	
13.1.1	Infant formulae as defined by Commission Directive 2006/141/EC	E 301: Total carry-over 75 mg/L	115[(a)]	115[(a)]	0	Analytical data[(b)]
13.1.2	Follow-on formulae as defined by Commission Directive 2006/141/EC	E 301: Total carry-over 75 mg/L	134[(a)]	138[(a)]	0	Analytical data[(b)]
13.1.3	Processed cereal-based foods and baby foods for infants and young children as defined by Directive 2006/125/EC - only fat-containing cereal-based foods including biscuits and rusks and baby foods	200	30	30	0	Analytical data
	Processed cereal-based foods and baby foods for infants and young children as defined by Directive 2006/125/EC - only fruit - and vegetable based drinks, juices and baby foods	300				
13.1.4	Other foods for young children	E 301: Total carry-over 75 mg/L	314	440	0	Analytical data[(a)]
13.2	Dietary foods for special medical purposes defined in Directive 1999/21/EC	QS	31000	245000	-	Analytical data
13.3	Dietary foods for weight control diets intended to replace total daily food intake or an individual meal	QS	5700	58000	-	Analytical data
13.4	Foods suitable for people intolerant to gluten as defined by Regulation	QS	250	1000	0	Reported use levels
14.1.2	Fruit juices as defined by Directive 2001/112/EC and vegetable juices	QS	200	7580	-	Analytical data
14.1.3	Fruit nectars as defined by Directive 2001/112/EC and vegetable nectars and similar products	QS	165	1080	-	Analytical data
14.1.4	Flavoured drinks	QS	550	20400	-	Analytical data
14.1.5.2	Other [excluding unflavoured leaf tea; including flavoured instant coffee]	QS	675	1070	-	Analytical data
14.2.1	Beer and malt beverages	QS	25	75	-	Analytical data
14.2.3	Cider and perry	QS	350	600	0	Reported use levels
14.2.4	Fruit wine and made wine	QS	-	-		Not taken into account (no corresponding FoodEx code)

FCS Category No	FCS Food category	MPL	Concentration levels used in the exposure assessment			Data source / Comments
			Mean	Max	% loss	
14.2.5	Mead	QS	-	-		Not taken into account (no corresponding FoodEx code)
14.2.6	Spirit drinks as defined in Regulation [except whisky or whiskey]	QS	150	300	0	Reported use levels
14.2.7.1	Aromatised wines	QS	150	300	0	Reported use levels
14.2.7.2	Aromatised wine-based drinks	QS				
14.2.7.3	Aromatised wine-product cocktails	QS				
14.2.8	Other alcoholic drinks including mixtures of alcoholic drinks with non-alcoholic drinks and spirits with less than 15 % of alcohol and	QS	166	166	-	Analytical data
15.1	Potato-, cereal-, flour- or starch-based snacks	QS	100	200	8	Reported use levels
15.2	Processed nuts	QS	300	500	0	Reported use levels
16	Desserts excluding products covered in category 1, 3 and 4	QS	213	1882	0	Reported use levels
17.1	Food supplements supplied in a solid form including capsules and tablets and similar forms, excluding chewable forms	QS	171600	800000	-	Analytical data
17.2	Food supplements supplied in a liquid form	QS				
17.3	Food supplements supplied in a syrup-type or chewable form	QS				
18	Processed foods not covered by categories 1 to 17, excluding foods for infants and young children	QS	300	500	[0-100] (c)	Reported use levels

(a): A dilution factor of 8 has been applied to convert the concentration levels provided for the products in powder (Appendix 4) into the product as consumed (liquid).
(b): The high presence of vitamin C in this food category can be due to the permitted use according to Commission Directive 2006/141/EC and Commission Directives 2006/125/EC.
(c): Depending of the food items in the food category.

Appendix 14. Summary of anticipated combined exposure, in six population groups, to ascorbic acid and its salts using analytical data and reported use levels with loss factor for food categories with no analytical data (minimum to 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)
Estimated exposure scenario using analytical data						
Brand-loyal scenario						
Mean	32-118	49–341	50–267	39–161	17–120	10–38
High level	134-481	195–582	133–671	127–432	66–341	36–136
Non-brand-loyal scenario						
Mean	8-64	9–33	10–88	5–21	3–26	2–12
High level	24-373	31–94	34–268	20–59	10–106	7–46

Appendix 15. Anticipated combined exposure to ascorbic acid and its salts using analytical data and reported use levels with loss factor for food categories with no analytical data per population group and survey: mean and high level (mg/kg bw/day)

	Number of subjects	Brand-loyal scenario		Non-brand-loyal scenario	
		Mean	High level	Mean	High level
Infants					
Bulgaria (NUTRICHILD)	659	43.1	142.5	8.1	23.8
Germany (VELS)	159	117.6	481.3	64.0	372.7
Denmark (IAT 2006 07)	826	68.3	172.1	63.6	152.3
Finland (DIPP 2001 2009)	500	50.4	134.0	42.8	113.7
United Kingdom (DNSIYC 2011)	1366	59.8	214.3	46.2	159.1
Italy (INRAN SCAI 2005 06)	12	31.6		8.8	
Toddlers					
Belgium (Regional Flanders)	36	340.5		33.4	
Bulgaria (NUTRICHILD)	428	85.2	256.9	10.1	31.3
Germany (DONALD 2006 2008)	261	80.0	256.8	16.5	61.3
Spain (enKid)	17	73.7		23.0	
Finland (DIPP 2003 2006)	497	48.6	195.0	22.4	86.1
Italy (INRAN SCAI 2005 06)	36	63.3		9.5	
Netherlands (VCP kids)	322	204.3	581.8	28.6	93.8
Children					
Belgium (Regional Flanders)	625	267.1	671.2	35.1	90.7
Bulgaria (NUTRICHILD)	433	118.8	356.8	12.6	34.4
Czech Republic (SISP04)	389	130.4	496.0	20.1	74.8
Germany (DONALD 2006 2008)	660	171.6	481.2	28.1	82.1
Denmark (Danish Dietary Survey)	490	158.5	347.7	26.4	63.2
Spain (enKid)	156	92.3	258.1	24.3	112.0
Spain (NUT INK05)	399	79.9	208.3	20.5	68.7
Finland (DIPP 2003 2006)	933	126.1	292.2	23.2	59.6
Finland (STRIP)	250	214.7	475.9	88.5	268.3

	Number of subjects	Brand-loyal scenario		Non-brand-loyal scenario	
		Mean	High level	Mean	High level
France (INCA2)	482	107.3	321.5	30.2	83.6
Greece (Regional Crete)	839	67.6	172.6	14.5	52.3
Italy (INRAN SCAI 2005 06)	193	49.8	132.9	9.8	36.5
Latvia (EFSA TEST)	189	103.2	291.7	29.0	107.4
Netherlands (VCP kids)	957	180.1	438.4	23.5	68.4
Sweden (NFA)	1473	241.0	536.0	45.9	156.2
Adolescents					
Belgium (Diet National 2004)	584	161.4	431.8	16.7	59.1
Cyprus (Childhealth)	303	72.3	221.4	14.7	42.1
Czech Republic (SISP04)	298	118.4	375.2	11.5	49.0
Germany (National Nutrition Survey II)	1011	108.2	335.6	12.2	39.3
Denmark (Danish Dietary Survey)	479	133.8	324.4	15.5	39.7
Spain (AESAN FIAB)	86	38.7	150.2	6.5	20.2
Spain (enKid)	209	55.7	210.2	9.6	35.4
Spain (NUT INK05)	651	64.7	186.8	11.4	42.9
France (INCA2)	973	62.5	181.3	15.0	47.7
Italy (INRAN SCAI 2005 06)	247	41.6	127.3	5.2	20.5
Latvia (EFSA TEST)	470	62.4	183.3	11.7	53.5
Sweden (NFA)	1018	149.5	346.1	21.1	55.6
Adults					
Belgium (Diet National 2004)	1304	95.6	339.4	8.8	31.6
Czech Republic (SISP04)	1666	36.2	170.7	4.5	12.5
Germany (National Nutrition Survey II)	10419	63.9	217.1	7.4	25.3
Denmark (Danish Dietary Survey)	2822	54.1	182.7	6.4	19.2
Spain (AESAN)	410	47.4	168.1	6.7	26.9
Spain (AESAN FIAB)	981	33.0	130.4	4.9	20.9
Finland (FINDIET 2007)	1575	45.4	138.2	9.3	26.6
France (INCA2)	2276	30.6	121.4	5.4	22.0
United Kingdom (NDNS)	1724	65.1	181.3	19.4	58.2
Hungary (National Repr Surv)	1074	40.2	139.1	4.2	11.0
Ireland (NSIFCS)	958	53.9	166.1	13.8	35.8
Italy (INRAN SCAI 2005 06)	2313	16.5	65.6	3.0	10.0
Latvia (EFSA TEST)	1306	22.8	86.8	5.2	22.1
Netherlands (DNFCS 2003)	750	119.9	341.1	9.8	29.5
Sweden (Riksmaten 1997 98)	1210	73.4	214.8	25.6	105.8
The elderly					
Belgium (Diet National 2004)	1230	32.1	116.5	8.3	46.0
Germany (National Nutrition Survey II)	2496	25.8	96.7	5.6	24.6
Denmark (Danish Dietary Survey)	329	22.7	79.1	4.5	15.7

	Number of subjects	Brand-loyal scenario		Non-brand-loyal scenario	
		Mean	High level	Mean	High level
Finland (FINDIET 2007)	463	37.9	136.2	12.0	30.1
France (INCA2)	348	12.0	36.3	3.8	12.8
Hungary (National Repr Surv)	286	25.6	90.3	3.1	7.6
Italy (INRAN SCAI 2005 06)	518	10.3	38.8	2.4	7.0

Appendix 16. Main food categories contributing to exposure to ascorbic acid and its salts using analytical data, "brand-loyal exposure scenario" (> 5 % to the total mean exposure) and number of surveys in which each food category is contributing

FCS Category number	Food category	Infants	Toddlers	Children	Adolescents	Adults	The elderly
		Range of % contribution to the total exposure (Number of surveys)[(a)]					
04.1	Unprocessed fruit and vegetables					5.6 (1)	6.7-11.2 (2)
04.2	Processed fruit and vegetables						9.2 (1)
06.3	Breakfast cereals	44.1-75.2 (4)	6.8-30.4 (4)	5.8-35.0 (14)	5.9-17.7 (10)	5.3-30.6 (9)	8.6-21.5 (5)
13.1	Foods for infants and young children	7.1-17.4 (6)					
13.2	Dietary foods for special medical purposes defined in Directive 1999/21/EC (excluding products from food category 13.1.5)		8.8 (1)			6.2 (1)	5.9 (1)
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)						17.0 (1)
14.1.2	Fruit juices as defined by Directive 2001/112/EC and vegetable juices	40.9-73.4 (2)	14.5-69.0 (7)	5.5-53.2 (12)	10.3-25.8 (8)	6.6-28.9 (8)	8.7-49.4 (6)
14.1.4	Flavoured drinks	8.7-41.8 (3)	18.1-79.2 (5)	27.9-86.2 (15)	65.3-92.5 (12)	30.8-89.6 (15)	8.4-86.9 (7)
17	Food supplements as defined in Directive 2002/46/EC excluding food supplements for infants and young children	5.9-30.2 (3)	18.1 (1)	9.1 (1)		5.0-26.1 (7)	36.2-45.2 (2)

Appendix 17. Main food categories contributing to exposure to ascorbic acid and its salts using analytical data, "non-brand-loyal exposure scenario" (> 5 % to the total mean exposure) and number of surveys in which each food category is contributing

FCS Category number	Food category	Infants	Toddlers	Children	Adolescents	Adults	The elderly
		Range of % contribution to the total exposure (Number of surveys)[(a)]					
01.4	Flavoured fermented milk products including heat-treated products		5.2-7.1 (5)	7.7 (1)			
01.5	Dehydrated milk as defined by Directive 2001/114/EC			9.6 (1)			
01.7.1	Unripened cheese excluding products falling in category 16					5.1 (1)	
02.1	Fats and oils essentially free from water (excluding anhydrous milkfat)					5.4 (1)	6.1 (1)
04.1	Unprocessed fruit and vegetables	10.0-11.1 (2)	5.5-21.0 (5)	5.3-15.0 (3)	5.2-16.1 (4)	5.4-25.6 (10)	5.8-37.2 (6)
04.2	Processed fruit and vegetables	22.3 (1)	27.7 (1)	7.5-23.7 (4)	9.9-10.7 (2)	7.2-22.4 (5)	8.0-33.6 (4)
05.2	Other confectionery including breath freshening microsweets		6.6 (1)	5.2-8.6 (4)	5.0-10.2 (3)	10.1 (1)	
06.3	Breakfast cereals	75.9-82.5 (4)	7.3-70.9 (7)	18.2-84.9 (15)	38.2-79.4 (12)	20.5-87.6 (15)	7.7-67.9 (7)
13.1	Foods for infants and young children	8.6-62.0 (6)	10.6-10.8 (2)				
13.2	Dietary foods for special medical purposes defined in Directive 1999/21/EC (excluding products from food category 13.1.5)		7.4 (1)				
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)						5.3 (1)
14.1.2	Fruit juices as defined by Directive 2001/112/EC and vegetable juices	10.6 (1)	5.9-11.0 (6)	5.8-9.3 (6)	6.8-8.4 (2)	8.2 (1)	5.1-6.6 (2)
14.1.4	Flavoured drinks		6.1-27.0 (4)	5.8-20.2 (13)	8.2-25.8 (12)	5.5-31.6 (14)	6.3-20.2 (3)
17	Food supplements as defined in Directive 2002/46/EC excluding food supplements for infants and young children	12.0 (1)	13.4 (1)			5.1-17.5 (5)	17.1-17.7 (2)

ABBREVIATIONS

ADI	Acceptable daily intake
ANS	Panel on Food Additives and Nutrient Sources added to Food
AUC	Area under the curve
bw	Body weight
CEF	EFSA Panel on Food Contact Materials, Enzymes, Flavouring and Processing Aids
CHO	Chinese hamster ovary
CIVO-TNO	Central Institute for Food and Nutrition Research
Cmax	Peak plasma concentration
DHA	Dehydroascorbic acid
2,3-DKG	2,3-diketogulonic acid
DNA	Deoxyribonucleic acid
EC	European Commission
EINECS	European Inventory of Existing Commercial chemical Substances
ERU	Drythrulose
EU	European Union
EVM	Expert Group on Vitamins and Minerals
FAO	Food and Agriculture Organization of the United Nations
FCRA	Food Chemical Risk Analysis
FCS	Food Categorisation System
FDA	Food and Drug Administration
FDE	FoodDrinkEurope
FEEDAP	Panel on Additives and Products or Substances used in Animal Feed
fw	Fresh weight
GD	Gestation day
HDMF	4-hydroxy-2,5-dimethylfuran-3(2H)-one
4-HMF	4-hydroxy-5-methyl-3(2H)-furanone
5-HMF	5-(hydroxymethyl)furfural
HPLC	High-performance liquid chromatography
IARC	International Agency for Research on Cancer
ICBA	International Council of Beverages Associations

ICGA	International Chewing Gum Association
JECFA	Joint FAO/WHO Expert Committee on Food Additives
LD50	Lethal dose, 50 %, i.e. dose that causes death among 50 % of treated animals
LOD	Limit of detection
LOQ	Limit of quantification
MOS	Margin of safety
MPL	Maximum permitted level
ND	Non-detected
NDA	Panel on Dietetic Products, Nutrition and Allergies
NOAEL	No observed adverse effect level
NTP	National Toxicology Program
OECD	Organisation for Economic Co-operation and Development
OIV	Organisation International des Vins
PRI	Population reference intake
PCE	Polychromatic erythrocytes
ppb	Parts per billion
QS	Quantum satis
QSAR	Quantitative structure–activity relationship
SCE	Sister chromatid exchange
SCF	EU Scientific Committee on Food
SNE	Specialised Nutrition Europe
UDS	Unscheduled DNA synthesis
UL	Tolerable upper intake level
UNESDA	Union of European Soft Drinks Associations
WCRF	World Cancer Research Fund
WHO	World Health Organization