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Re-evaluation of sulphuric acid and its sodium, potassium, calcium and ammonium salts (E 513, 514 (i), 514 (ii), 515 (i), 515 (ii), 516 and 517) as food additive

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Abstract

The Panel on Food Additives and Flavourings (FAF) provided a scientific opinion re-evaluating the safety of sulphuric acid (E 513) and its sodium (E 514), potassium (E 515), calcium (E 516) and ammonium (E 517) salts when used as a food additive. The Panel considered that adequate exposure and toxicity data were available. Sulphuric acid and its sodium, potassium, calcium and ammonium salts (E 513, E 514, E 515, E 516, E 517) are authorised food additives in the EU, in accordance with Annex II and Annex III to Regulation (EC) No 1333/2008. In the *refined estimated exposure non brand-loyal scenario*, mean exposure ranged from 0.4 mg sulphate/kg body weight (bw) per day in infants to 35 mg sulphate/kg bw per day in toddlers. The high percentile of exposure ranged from 3 mg sulphate/kg bw per day in adolescents to 68 mg sulphate/kg bw per day in toddlers. The Panel considered sulphates of low acute toxicity and there is no concern with respect to genotoxicity and carcinogenicity. The Panel noted that the exposure to sulphates at mean and 95th percentile in the *non brand-loyal scenario* as well as in the other scenarios, is far below the 300 mg/kg a dose that induced laxative effect in humans. Based on the toxicological database available, the Panel concluded that the exposure to sulphuric acid (E 513), sodium sulphate (E 514), potassium sulphates (E 515), calcium sulphate (E 516) and ammonium sulphate (E 517) does not raise a safety concern at the reported uses and use levels and there is no need for a numerical acceptable daily intake (ADI).

Keywords: sulphate, sulphuric acid, food additive, safety, risk assessment, dietary exposure

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Summary

The present opinion document deals with the re-evaluation of sulphuric acid (E 513), sodium sulphate (E 514 (i)), sodium hydrogen sulphate (E 514 (ii)), potassium sulphate (E 515 (i)), potassium hydrogen sulphate (E 515 (ii)), calcium sulphate (E 516) and ammonium sulphate (E 517) when used as a food additive.

Sulphuric acid (E 513) and its sodium (E 514), potassium (E 515), calcium (E 516) and ammonium (E 517) salts are authorised food additives in the EU, in accordance with Annex II and Annex III to Regulation (EC) No 1333/2008 and specific purity criteria have been defined in the Commission Regulation (EU) No 231/2012.

They were previously evaluated by JECFA several times, the latest in 2010 (JECFA, 2010b) and the Scientific Committee on Food (SCF) in 1991 (SCF, 1991). Both committees established a group acceptable daily intake (ADI) 'not specified' for sulphuric acid and its sodium, potassium, calcium and ammonium salts.

Sulphate is absorbed the gastrointestinal tract, and after absorption, sulphate is freely distributed in blood and does not accumulate in tissues. Sulphates are usually eliminated by renal excretion; however at high doses, sulphate is also excreted in faeces.

The Panel noted that sulphates are of low acute oral toxicity and there is no concern with respect to genotoxicity.

In a subchronic oral toxicity study, no effects were noticed, except for diarrhoea in males at dose of 2,025 mg sulphate/kg body weight (bw)/day, which the Panel considered treatment-related but not as an adverse effect. Based on the results, the Panel considered the 2,025 mg sulphate/kg bw/day as the no observed adverse effect level (NOAEL), the highest dose tested.

Based on the results of the chronic toxicity and carcinogenicity studies in rats, the Panel considered that ammonium sulphate is not carcinogenic and that the NOAEL is 1,090 mg sulphate/kg bw per day, the highest dose tested.

No reproductive or developmental toxicity studies according to the current OECD Guidelines were available.

Dietary exposure to sulphuric acid and its sodium, potassium, calcium and ammonium salts (E 513, E 514, E 515, E 516, E 517) from their use as food additives was calculated according to different exposure scenarios based on the provided use levels. The Panel considered the *non brand-loyal scenario* covering the general population as the most appropriate scenario for risk characterisation and estimated that in the *refined estimated exposure non brand-loyal scenario*, mean exposure ranged from 0.4 mg sulphate/kg bw per day in infants to 35 mg sulphate/kg bw per day in toddlers. The 95th percentile of exposure ranged from 3 mg sulphate/kg bw per day in adolescents to 68 mg sulphate/kg bw per day in toddlers.

Data in humans indicated that sodium sulphate at 300 mg/kg bw and higher (corresponding to 207 mg sulphate/kg bw) induced laxative effect. The Panel noted that the exposure to sulphates at mean and 95th percentile in the *non brand-loyal scenario* as well as in the other scenarios is far below this dose.

In conclusion, sulphate is a natural constituent of human, animals and plants and is present in all biological materials, including foodstuffs. Based on the toxicological database available, the Panel concluded that the exposure to sulphuric acid (E 513), sodium sulphate (E 514), potassium sulphates (E 515), calcium sulphate (E 516) and ammonium sulphate (E 517) does not raise a safety concern at the reported uses and use levels and there is no need for a numerical ADI.

The Panel recommend that the European Commission considers lowering the current limits for toxic elements (arsenic, lead and mercury) in the EU specifications for sulphuric acid (E 513), sodium sulphates (E 514), potassium sulphates (E 515), calcium sulphate (E 516) and ammonium sulphate (E 517) in order to ensure that sulphuric acid (E 513), sodium sulphates (E 514), potassium sulphates (E 515), calcium sulphate (E 516) and ammonium sulphate (E 517) as a food additive will not be a significant source of exposure to those toxic elements in food.

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1. Introduction

The present opinion document deals with the re-evaluation of sulphuric acid (E 513), sodium sulphate (E 514 (i)), sodium hydrogen sulphate (E 514 (ii)), potassium sulphate (E 515 (i)), potassium hydrogen sulphate (E 515 (ii)), calcium sulphate (E 516) and ammonium sulphate (E 517) when used as a food additive. For brevity, these food additives will be referred as sulphates in this document.

Sulphuric acid (E 513) and its sodium (E 514), potassium (E 515), calcium (E 516) and ammonium (E 517) salts are authorised food additives in the EU, in accordance with Annex II and Annex III to Regulation (EC) No 1333/2008[1].

1.1. Background and Terms of Reference as provided by the European Commission

1.1.1. Background

Regulation (EC) No 1333/2008[2] 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[3]. This Regulation also foresees that food additives are re-evaluated whenever necessary in the 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[4] of 2001. The report "Food additives in Europe 2000[5]" 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.

1.1.2. Terms of Reference

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.

1.1.3. Interpretation of Terms of Reference

The Panel considered that sodium, potassium, calcium and ammonium salts of sulphate are expected to dissociate in the gastrointestinal tract into sulphate and their corresponding cations. The safety of resulting sodium, potassium, calcium and ammonium cations is not the focus of this opinion.

[1] 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.
[2] Regulation (EC) No 1333/2008 of the European Parliament and of the Council of 16 December 2008 on food additives. OJ L 354, 31.12.2008, p. 16–33.
[3] Commission Regulation (EU) No 257/2010 of 25 March 2010 setting up a programme for the re-evaluation of approved food additives in accordance with Regulation (EC) No 1333/2008 of the European Parliament and of the Council on food additives. OJ L 80, 26.3.2010, p. 19–27.
[4] COM(2001) 542 final.
[5] Food Additives in Europe 2000, Status of safety assessments of food additives presently permitted in the EU, Nordic Council of Ministers, TemaNord 2002, 560.

1.2. Information on existing authorisations and evaluations

Sulphuric acid and sodium, potassium, calcium and ammonium sulphate, used as food additives, have previously been evaluated by the SCF in 1978 and 1991 (SCF, 1978, 1991).

In 1976, JECFA established specifications for identity and purity of sulphuric acid, but no toxicological evaluation was performed at that time and no acceptable daily intake (ADI) was established (JECFA, 1977).

In 1978, the SCF stated that calcium sulphate and ammonium sulphate were acceptable for use in fine baker wares when used as yeast improvers. No detailed evaluation was performed, but it was stated that the Committee accepted, on a provisional basis, the ADIs established by JECFA ('not specified') (SCF, 1978).

Calcium sulphate for use as a firming agent was evaluated by JECFA in 1969 (JECFA, 1969) and the Committee concluded that there was no need for any formal toxicological testing due to calcium and sulphate ions being normal constituents of the human body. The Committee did not set any restrictions for use of calcium sulphate as a firming agent except for Good Manufacturing Practice (GMP).

In 1986, JECFA evaluated potassium sulphate as well as sulphates in general, for use as food additives (JECFA, 1986). In that evaluation, JECFA established an ADI 'not specified' for potassium sulphate as well as for the sulphate moiety (JECFA, 2000b).

JECFA evaluated sodium sulphate in 2000 (JECFA, 2000a,b, 2001) and 2002 (JECFA, 2002). In the toxicological evaluation from 2000, JECFA allocated a temporary ADI 'not specified'. It was noted that sodium sulphate has a laxative action, which is the basis for its clinical use. The ADI was made temporary because no information was available on the functional effect and actual uses of sodium sulphate in foods. In 2002, JECFA (2002) allocated an ADI 'not specified' for sodium sulphate based on the absence of evidence of toxicity and the (at the time) current uses of the substance.

Sodium hydrogen sulphate was evaluated, for use as an acidifier, by JECFA in 2010 (JECFA, 2009b, 2010b). Sodium hydrogen sulphate was assessed in terms of the sulphate component because of its dissociation to the constituent ions and given that sodium and hydrogen ions are ubiquitous and natural constituents of foods. Considering that the available evidence did not provide any indication of toxicity, sodium hydrogen sulphate was allocated an ADI 'not specified', in line with the principles established for ionisable salts when used in the applications specified and in accordance with GMP (JECFA, 2009b, 2010b).

In 1991, the SCF established a group ADI 'not specified' for sulphuric acid and sodium, potassium, calcium and ammonium sulphate (SCF, 1991). The SCF report stated the following:

> '*These anions [chloride, sulphate and carbonate] are natural constituents of man, animals and plants, and therefore occur in foodstuffs. They, together with certain cations constitute the major electrolytes present in all biological materials. The Committee therefore established a group ADI not specified for these anions, although exhaustive systematic toxicological studies have not been carried out with these ions. No safety problems are likely to arise, provided the contributions from food do not disturb the homoeostatic mechanisms controlling the electrolyte balance of the body*'.

EFSA has evaluated potassium and sodium sulphate in 2010 (EFSA-ANS-Panel, 2010) and calcium sulphate for various uses on several occasions (EFSA, 2003, 2004, 2008). Sodium and potassium sulphate were evaluated for use as sources of, respectively, sodium and potassium added for nutritional purposes to food supplements (EFSA-ANS-Panel, 2010). The Panel concluded that there was no safety concern for the proposed use and use levels of potassium sulphate, sodium sulphate and sodium sulphate decahydrate in food supplements.

Calcium sulphate was evaluated by EFSA in 2003, 2004 and 2008 for use in foods for particular nutritional uses (EFSA, 2003), as a mineral substance in foods intended for the general population (EFSA, 2004) and for use as a source of calcium in food supplements (EFSA, 2008). The overall conclusion in the evaluations was that calcium sulphate as a source of calcium or as a mineral substance in foods is of no safety concern (EFSA, 2003, 2004, 2008). In addition the Panel concluded, on basis of clinical trials (Cocchetto and Levy, 1981; Morris and Levy, 1983), that sufficient reassurance is provided for the safety of a 'worst case' exposure scenario to 6 g of sulphate ion from calcium sulphate (EFSA, 2008).

In addition to the use as food additive calcium sulphate (E 516) is included in the list of vitamin formulations and mineral substances which may be added to foods reported in the Annex II of

Regulation (EC) No 1925/2006[6] and in the Union list set out in the Annex to Regulation (EU) No 609/2013[7] as permitted for use in: food for special medical purposes and total diet replacement for weight control.

2. Data and methodologies

2.1. Data

The Panel on Food Additives and Flavourings (FAF) was not provided with a newly submitted dossier. The Panel based its assessment on information submitted to EFSA following the public call for data,[8] information from previous evaluations and additional available literature up to 17 May 2017. Attempts were made at retrieving relevant original study reports on which previous evaluations or reviews were based. However, these were not always available to the Panel.

Food consumption data used to estimate the dietary exposure to sulphuric acid and its sodium, potassium, calcium and ammonium salts (E 513, 514, 515, 516 and 517) were derived from the EFSA Comprehensive European Food Consumption Database (Comprehensive Database[9]).

The Mintel's Global New Products Database (GNPD) was checked to identify the uses of sulphuric acid and its sodium, potassium, calcium and ammonium salts (E 513, 514 515, 516 and 517) in food and beverage products and food supplements. The Mintel's GNPD is an online database that contains the compulsory ingredient information present on the label of numerous products.

2.2. Methodologies

This opinion was formulated following the principles described in the EFSA Guidance on transparency with regard to scientific aspects of risk assessment (EFSA Scientific Committee, 2009) and following the relevant existing guidance documents from the EFSA Scientific Committee.

The FAF Panel assessed the safety of sulphuric acid and its sodium, potassium, calcium and ammonium salts (E 513, 514,515, 516 and 517) as food additives in line with the principles laid down in Regulation (EU) 257/2010 and in the relevant guidance documents: Guidance on submission for food additive evaluations by the Scientific Committee on Food (SCF, 2001) and taking into consideration the Guidance for submission for food additive evaluations in 2012 (EFSA ANS Panel, 2012).

When the test substance was administered in the feed or in the drinking water, but doses were not explicitly reported by the authors as mg/kg body weight (bw) per day based on actual feed or water consumption, the daily intake was calculated by the Panel using the relevant default values as indicated in the EFSA Scientific Committee Guidance document (EFSA Scientific Committee, 2012) for studies in rodents or, in the case of other animal species, by JECFA (2000a,b). In these cases, the daily intake is expressed as equivalent. When in human studies in adults (aged above 18 years), the dose of the test substance administered was reported in mg/person per day, the dose in mg/kg bw per day was calculated by the Panel using a body weight of 70 kg as default for the adult population as described in the EFSA Scientific Committee Guidance document (EFSA Scientific Committee, 2012).

Dietary exposure to sulphuric acid and its sodium, potassium, calcium and ammonium salts (E 513, 514, 515, 516 and 517) from their use as food additives was estimated combining food consumption data available within the EFSA Comprehensive European Food Consumption Database with the maximum levels according to Annex II to Regulation (EC) No 1333/2008[10] and reported use levels submitted to EFSA following a call for data. Different scenarios were used to calculate exposure (see Section 3.4). Uncertainties on the exposure assessment were identified and discussed.

[6] Regulation (EC) No 1925/2006 of the European Parliament and of the Council of 20 December 2006 on the addition of vitamins and minerals and of certain other substances to foods. OJ L 404, 30.12.2006, p. 26–38.

[7] Regulation (EU) No 609/2013 of the European Parliament and of the Council of 12 June 2013 on food intended for infants and young children, food for special medical purposes, and total diet replacement for weight control and repealing Council Directive 92/52/EEC, Commission Directives 96/8/EC, 1999/21/EC, 2006/125/EC and 2006/141/EC, Directive 2009/39/EC of the European Parliament and of the Council and Commission Regulations (EC) No 41/2009 and (EC) No 953/2009. OJ L 181, 29.6.2013, p. 35–56.

[8] Call for scientific data on food additives permitted in the EU and belonging to the functional classes of emulsifiers, stabilisers and gelling agents. Published: 22 November 2009. Available from: http://www.efsa.europa.eu/en/dataclosed/call/ans091123

[9] Available online: http://www.efsa.europa.eu/en/food-consumption/comprehensive-database

[10] Commission 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.

3. Assessment

3.1. Technical data

3.1.1. Identity of the substances

Sulphuric acid (E 513)

According to Commission Regulation (EU) No 231/2012[11]), sulphuric acid (E 513) has chemical formula H_2SO_4, European Inventory of Existing Commercial chemical Substances (EINECS) (EC) No 231-639-5, and molecular weight 98.07 g/mol. The corresponding Chemical Abstract Service (CAS) Registry number is 7664-93-9: this identifier is not present in the Regulation. Sulphuric acid is a clear, colourless or slightly brown, very corrosive oily liquid, miscible with water, with generation of much heat and with ethanol. Sulphuric acid is commercially available in varying concentrations; the concentrated form contains not less than 96.0%. Concentration limits are indicated for the following toxic metals: iron, selenium, arsenic, lead and mercury.

In JECFA (2006a), the description of food additive sulphuric acid is in general consistent with that of the aforementioned Regulation. The substance is identified with INS No 513 and CAS No 7664-93-9. As to toxic metals, concentration limits are given for iron, selenium and lead.

The Panel noted that in the JECFA monograph, the limit for iron is 10-fold higher than in the Regulation (200 and 20 mg/kg, respectively).

Sodium sulphate (E 514(i))

According to Commission Regulation (EU) No 231/2012[11]), sodium sulphate (E 514(i)) has chemical formula $Na_2SO_4 \cdot nH_2O$ (n = 0 or 10) and molecular weight 142.04 or 322.04 g/mol, respectively. No EINECS (EC) or CAS Registry identifiers are present in the Regulation. Sodium sulphate occurs as colourless crystals or a fine, white, crystalline powder, the decahydrate form being efflorescent. The anhydrous salt has a purity of not less than 99.0%; the loss on drying is not more than 1.0% (anhydrous) or not more than 57% (decahydrate) at 130°C. Concentration limits are indicated for the following toxic metals: selenium, arsenic, lead and mercury.

In JECFA (2009a), the description of food additive sodium sulphate is in general consistent with that of the aforementioned Regulation. The substance is identified with INS No 514(i) and CAS Registry numbers 7757-82-6 (anhydrous) and 7727-73-3 (decahydrate); it is described as being freely soluble in water and practically insoluble in ethanol. As to toxic metals, concentration limits are given for selenium and lead.

Sodium hydrogen sulphate (E 514(ii))

According to Commission Regulation (EU) No 231/2012[11], sodium hydrogen sulphate (E 514(ii)) has chemical formula $NaHSO_4$ and molecular weight 120.06 g/mol. No EINECS (EC) or CAS Registry identifiers are present in the Regulation. Sodium hydrogen sulphate occurs as white, odourless crystals or granules; the marketed substance is at least 95.2% pure. Solutions are strongly acidic. Concentration limits are indicated for the following toxic metals: selenium, arsenic, lead and mercury.

In JECFA (2009b), the description of food additive sodium hydrogen sulphate is in general consistent with that of the aforementioned Regulation. However, the following specifications are also reported: 'Sodium chloride and sulphuric acid are combined at elevated temperatures to produce molten sodium hydrogen sulphate. The molten sodium hydrogen sulphate is sprayed and cooled to form a solid product with uniform particle size'. The substance is identified with INS No 514(ii) and CAS Registry No 7681-38-1; it is described as being freely soluble in water. The marketed chemical is at least 85% pure. As to toxic metals, concentration limits are given for selenium and lead.

The Panel noted that different requirements are indicated in the Regulation and in the JECFA monograph as to the minimum content of the substance in the marketed product (95.2 and 85%, respectively).

[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 1333/2008 of the European Parliament and of the Council. OJ L 83, 22.3.2012, p. 1–295.

Potassium sulphate (E 515(i))

According to Commission Regulation (EU) No 231/2012[11]), potassium sulphate (E 515(i)) has chemical formula K_2SO_4 and molecular weight 174.25 g/mol. No EINECS (EC) or CAS Registry identifiers are present in the Regulation. Potassium sulphate occurs as colourless or white crystals or a crystalline powder; it is freely soluble in water and insoluble in ethanol. The marketed substance is at least 99.0% pure. Concentration limits are indicated for the following toxic metals: selenium, arsenic, lead and mercury.

In JECFA (2009c), the description of food additive potassium sulphate is in general consistent with that of the aforementioned Regulation. The chemical is identified with INS No 515(i) and CAS Registry No 7778-80-5. As to toxic metals, concentration limits are given for selenium and lead.

Potassium hydrogen sulphate (E 515(ii))

According to Commission Regulation (EU) No 231/2012[11], potassium hydrogen sulphate (E 515(ii)) has chemical formula $KHSO_4$ and molecular weight 136.17 g/mol. No EINECS (EC) or CAS Registry identifiers are present in the Regulation. Potassium hydrogen sulphate occurs as white deliquescent crystals, pieces or granules, with a melting point at 197°C; it is freely soluble in water and insoluble in ethanol. Concentration limits are indicated for the following toxic metals: selenium, arsenic, lead and mercury.

No JECFA monograph seems to be available for potassium hydrogen sulphate.

Calcium sulphate (E 516)

According to Commission Regulation (EU) No 231/2012[11]), calcium sulphate (E 516) has chemical formula $CaSO_4 \cdot nH_2O$ (n = 0 or 2), EINECS (EC) No 231-900-3 and molecular weight 136.14 or 172.18 g/mol (anhydrous and dihydrate forms, respectively). Calcium sulphate occurs as a fine, white to slightly yellow-white, odourless powder; it is slightly soluble in water and insoluble in ethanol. The anhydrous salt has a purity of not less than 99.0%; the loss on drying is not more than 1.5% (anhydrous) or not more than 23% (dihydrate) at 250°C. Concentration limits are indicated for the following toxic metals: selenium, arsenic, lead and mercury.

In JECFA (2006b), the description of food additive calcium sulphate is in general consistent with that of the aforementioned Regulation. The chemical is identified with INS No 516 and CAS Registry No 7778-18-9. As to toxic metals, concentration limits are given for selenium and lead.

Ammonium sulphate (E 517)

According to Commission Regulation (EU) No 231/2012[11], ammonium sulphate (E 517) has chemical formula $(NH_4)_2SO_4$, EINECS (EC) No 231-984-1 and molecular weight 132.14 g/mol. The corresponding CAS Registry number is 7783-20-2: this identifier is not present in the Regulation. Ammonium sulphate occurs as a white powder, shining plates or crystalline fragments, freely soluble in water and insoluble in ethanol. Concentration limits are indicated for the following toxic metals: selenium and lead.

No JECFA monograph seems to be available for ammonium sulphate.

3.1.2. Specifications

The specifications for sulphuric acid (E 513), sodium sulphate (E 514(i)), sodium hydrogen sulphate (E 514(ii)), potassium sulphate (E 515(i)), potassium hydrogen sulphate (E 515(ii)), calcium sulphate (E 516) and ammonium sulphate (E 517) as defined in the Commission Regulation (EU) No 231/2012 and by JECFA (2006a,b, 2009a) are listed in Tables 1–7 (JECFA data are missing for E 515(ii) and E 517).

Table 1: Specifications for sulphuric acid (E 513) according to Commission Regulation (EU) No 231/2012 and JECFA (2006a)

	Commission Regulation (EU) No 231/2012	JECFA (2006a)
Synonyms	Oil of vitriol; Dihydrogen sulphate	INS No 513
Definition	EINECS (EC) No: 231-639-5	CAS No: 7664-93-9
	Chemical name: sulphuric acid	Chemical name: sulphuric acid
	Chemical formula: H_2SO_4	Chemical formula: H_2SO_4
	Molecular weight (g/mol): 98.07	Formula weight (g/mol): 98.07

	Commission Regulation (EU) No 231/2012	JECFA (2006a)
	Assay: sulphuric acid is commercially available in varying concentrations. The concentrated form contains not less than 96.0%	Assay: not less than the minimum amount of H_2SO_4 specified by the vendor
Description	Clear, colourless or slightly brown, very corrosive oily liquid	Clear, colourless or slightly brown, very corrosive oily liquid
Functional uses	—	Acid
Identification	Test for acid: passes test	Test for acid: passes test[(a)]
	Test for sulphate: passes test	Test for sulphate: passes test
	Solubility: miscible with water, with generation of much heat; also with ethanol	Solubility: miscible with water, with generation of much heat and with ethanol
Purity	Ash: not more than 0.02%	Ash: not more than 0.02% (w/w)[(a)]
	Reducing matter: not more than 40 mg/kg (as SO_2)	Reducing substances: not more than 40 mg/kg as SO_2[(a)]
	Nitrate: not more than 10 mg/kg (on H_2SO_4 basis)	Nitrate: not more than 10 mg/kg on H_2SO_4 basis
	Chloride: not more than 50 mg/kg	Chlorides: not more than 50 mg/kg[(a)]
	Iron: not more than 20 mg/kg	Iron: not more than 200 mg/kg[(a)]
	Selenium: not more than 20 mg/kg	Selenium: not more than 20 mg/kg
	Arsenic: not more than 3 mg/kg	—
	Lead: not more than 2 mg/kg	Lead: not more than 2 mg/kg
	Mercury: not more than 1 mg/kg	—

(a): In JECFA (2006a), a specific test is directly available from the data sheet.

Table 2: Specifications for sodium sulphate (E 514(i)) according to Commission Regulation (EU) No 231/2012 and JECFA (2009a)

	Commission Regulation (EU) No 231/2012	JECFA (2009a)
Synonyms	—	Glauber's salt (decahydrate form); INS No 514(i)
Definition	EINECS (EC) No: —	CAS No: 7757-82-6 (anhydrous) 7727-73-3 (decahydrate)
	Chemical name: sodium sulphate	Chemical name: sodium sulphate
	Chemical formula: $Na_2SO_4 \cdot nH_2O$ (n = 0 or 10)	Chemical formula: $Na_2SO_4 \cdot nH_2O$ (n = 0 or 10)
	Molecular weight (g/mol): 142.04 (anhydrous) 322.04 (decahydrate)	Formula weight: 142.04 (anhydrous) 322.19 (decahydrate)
	Assay: content not less than 99.0% on the anhydrous basis	Assay: not less than 99.0% on the dry basis
Description	Colourless crystals or a fine, white, crystalline powder. The decahydrate is efflorescent	—
Functional uses	—	Acidity regulator
Identification	Test for sodium: passes test	Test for sodium: passes test
	Test for sulphate: passes test	Test for sulphate: passes test
	pH: neutral or slightly alkaline to litmus paper (5% solution)	—
	—	Solubility: freely soluble in water; practically insoluble in ethanol

	Commission Regulation (EU) No 231/2012	JECFA (2009a)
Purity	Loss on drying: not more than 1.0% (anhydrous) or not more than 57% (decahydrate) at 130°C	Loss on drying: anhydrous: not more than 1% (105°C, 4 h) decahydrate: between 51.0% and 57.0% (105°C, 4 h)
	Selenium: not more than 30 mg/kg	Selenium: not more than 30 mg/kg
	Arsenic: not more than 3 mg/kg	—
	Lead: not more than 2 mg/kg	Lead: not more than 2 mg/kg
	Mercury: not more than 1 mg/kg	—

Table 3: Specifications for sodium hydrogen sulphate (E 514(ii)) according to Commission Regulation (EU) No 231/2012 and JECFA (2009b)

	Commission Regulation (EU) No 231/2012	JECFA (2009b)
Synonyms	Acid sodium sulphate; Sodium bisulphate; Nitre cake	Sodium acid sulphate; Nitre cake; Sodium bisulphate; Sulphuric acid, monosodium salt; INS No 514(ii)
Definition	—	Sodium chloride and sulphuric acid are combined at elevated temperatures to produce molten sodium hydrogen sulphate. The molten sodium hydrogen sulphate is sprayed and cooled to form a solid product with uniform particle size
	EINECS (EC) No: —	CAS No: 7681-38-1
	Chemical name: sodium hydrogen sulphate	Chemical name: sodium hydrogen sulphate
	Chemical formula: $NaHSO_4$	Chemical formula: $NaHSO_4$
	Molecular weight (g/mol): 120.06	Formula weight (g/mol): 120.06
	Assay: content not less than 95.2%	Assay: not less than 85%
Description	White, odourless crystals or granules	White crystals or granules
Functional uses	—	Acidifier, acidity regulator
Identification	Test for sodium: passes test	Test for sodium: passes test
	Test for sulphate: passes test	Test for sulphate: passes test
	pH: solutions are strongly acidic	—
	—	Solubility: freely soluble in water
Purity	Loss on drying: not more than 0.8%	Loss on drying: not more than 0.8 %[(a)]
	Water insoluble matter: not more than 0.05%	Water insoluble matter: not more than 0.05%
	Selenium: not more than 30 mg/kg	Selenium: not more than 5 mg/kg
	Arsenic: not more than 3 mg/kg	—
	Lead: not more than 2 mg/kg	Lead: not more than 2 mg/kg
	Mercury: not more than 1 mg/kg	—

(a): In JECFA (2009b) a specific test is directly available from the data sheet.

Table 4: Specifications for potassium sulphate (E 515(i)) according to Commission Regulation (EU) No 231/2012 and JECFA (2009c)

	Commission Regulation (EU) No 231/2012	JECFA (2009c)
Synonyms	—	INS No 515(i)
Definition	EINECS (EC) No: —	CAS No: 7778-80-5
	Chemical name: potassium sulphate	Chemical name: potassium sulphate

	Commission Regulation (EU) No 231/2012	JECFA (2009c)
	Chemical formula: K_2SO_4	Chemical formula: K_2O_4S Structural formula: K_2SO_4
	Molecular weight (g/mol): 174.25	Formula weight (g/mol): 174.25
	Assay: content not less than 99.0%	Assay: not less than 99.0%
Description	Colourless or white crystals or crystalline powder	Colourless or white crystals or crystalline powder
Functional uses	—	Salt substitute, acidity regulator
Identification	Test for potassium: passes test	Test for potassium: passes test
	Test for sulphate: passes test	Test for sulphate: passes test
	pH: between 5.5 and 8.5 (5% solution)	pH: 5.5–8.5 (1 in 20 solution)
	Solubility: freely soluble in water; insoluble in ethanol	Solubility: freely soluble in water; insoluble in ethanol
Purity	Selenium: not more than 30 mg/kg	Selenium: not more than 30 mg/kg
	Arsenic: not more than 3 mg/kg	—
	Lead: not more than 2 mg/kg	Lead: not more than 2 mg/kg
	Mercury: not more than 1 mg/kg	—

Table 5: Specifications for potassium hydrogen sulphate (E 515(ii)) according to Commission Regulation (EU) No 231/2012a

	Commission Regulation (EU) No 231/2012
Synonyms	Potassium bisulphate; Potassium acid sulphate
Definition	EINECS (EC) No: —
	Chemical name: potassium hydrogen sulphate
	Chemical formula: $KHSO_4$
	Molecular weight (g/mol): 136.17
	Assay: content not less than 99.0%
Description	White deliquescent crystals, pieces, or granules
Functional uses	—
Identification	Melting point: 197°C
	Test for potassium: passes test
	Solubility: freely soluble in water; insoluble in ethanol
Purity	Selenium: not more than 30 mg/kg
	Arsenic: not more than 3 mg/kg
	Lead: not more than 2 mg/kg
	Mercury: not more than 1 mg/kg

Table 6: Specifications for calcium sulphate (E 516) according to Commission Regulation (EU) No 231/2012 and JECFA (2006b)

	Commission Regulation (EU) No 231/2012	JECFA (2006a)
Synonyms	Gypsum; Selenite; Anhydrite	INS No 516
Definition	EINECS (EC) No: 231-900-3	CAS No: 7778-18-9
	Chemical name: calcium sulphate	Chemical name: calcium sulphate
	Chemical formula: $CaSO_4 \cdot nH_2O$ (n = 0 or 2)	Chemical formula: anhydrous: $CaSO_4$ dihydrate: $CaSO_4 \cdot 2H_2O$
	Molecular weight (g/mol): 136.14 (anhydrous), 172.18 (dihydrate)	Formula weight (g/mol): anhydrous: 136.14 dihydrate: 172.18

	Commission Regulation (EU) No 231/2012	JECFA (2006a)
	Assay: content not less than 99.0% on the anhydrous base	Assay: not less than 99.0% after drying
Description	Fine, white to slightly yellowish-white odourless powder	Fine, white to slightly yellow-white, odourless powder
Functional uses	—	Yeast food, dough conditioner, firming agent, sequestrant
Identification	Test for calcium: passes test	Test for calcium: passes test
	Test for sulphate: passes test	Test for sulphate: passes test
	Solubility: slightly soluble in water; insoluble in ethanol	Solubility: slightly soluble in water; insoluble in ethanol
Purity	Loss on drying: anhydrous: not more than 1.5% (250 C, constant weight) dihydrate: not more than 23% (250 C, constant weight)	Loss on drying: anhydrous: not more than 1.5% (250 C to constant weight) dihydrate: between 19% and 23% (250 C to constant weight)
	Fluoride: not more than 30 mg/kg	Fluoride: not more than 30 mg/kg
	Selenium: not more than 30 mg/kg	Selenium: not more than 30 mg/kg
	Arsenic: not more than 3 mg/kg	—
	Lead: not more than 2 mg/kg	Lead: not more than 2 mg/kg
	Mercury: not more than 1 mg/kg	—

The Panel noted that the differences in solubility of the calcium sulphate forms (i.e. anhydrous and dihydrate) are not indicated in the specifications.

Table 7: Specifications for ammonium sulphate (E 517) according to Commission Regulation (EU) No 231/2012

	Commission Regulation (EU) No 231/2012
Synonyms	—
Definition	EINECS (EC) No: 231-984-1
	Chemical name: ammonium sulphate
	Chemical formula: $(NH_4)_2SO_4$
	Molecular weight (g/mol): 132.14
	Assay: content not less than 99.0% and not more than 100.5%
Description	White powder, shining plates, or crystalline fragments
Functional uses	—
Identification	Test for ammonium: passes test
	Test for sulphate: passes test
	Solubility: freely soluble in water; insoluble in ethanol
Purity	Loss on ignition: not more than 0.25%
	Selenium: not more than 30 mg/kg
	Lead: not more than 3 mg/kg

The Panel noted that the molecular weight reported for sodium sulphate decahydrate in the Regulation Specifications must be corrected to 322.19 g/mol.

The Panel noted that the specification of the 'loss on ignition' test reported for ammonium sulphate (E 517) is equivocal in that the chemical decomposes at a temperature considerably lower than that canonically prescribed for the test (450–550°C) (http://www.fao.org/docrep/009/a0691e/a0691e00.htm): the 'not more than 0.25%' should rather be read as the result of a 'residue on ignition' test.

The Panel also noted that, according to EU specifications for the aforesaid food additives, impurities of the toxic elements arsenic, lead and mercury – eventually present in sulphuric acid and in sodium, potassium and calcium sulphates – are accepted up to concentrations of 3, 2 and 1 mg/kg, respectively; in ammonium sulphate, lead concentrations must not be higher than 3 mg/kg. Contaminations at such levels could have a significant impact on the exposure to these metals, for which the exposure already is

close to the health-based guidance values or benchmark doses (lower confidence limits) established by EFSA (EFSA CONTAM Panel, 2009, 2010, 2012a,b, 2014).

Analytical data provided by Interested Parties (Documentation provided to EFSA No. 1,2,3,4) concerning sodium hydrogen sulphate and sulphuric acid indicated that inorganic contaminants (As, Hg, Pb, Se) were well below the limits set by the Regulation, and frequently not detected based on sensitive methods. Analytical data on other inorganic contaminants including Cd for which levels are not set in the regulation were also reported by IPs (Documentation provided to EFSA No. 1,2,3,4,5).

3.1.3. Manufacturing process

Sulphuric acid (H_2SO_4) is generally manufactured by the sulphur trioxide (SO_3) contact process from sulphur-bearing raw materials; different process variants are employed depending on the raw material available (Documentation provided to EFSA No. 1, Müller, 2000, 2012); in some cases, sulphuric acid is obtained as a by-product of other processes (non-ferrous metal smelting). The contact process was introduced in the late 1800s; until the 1960s, it underwent minor changes primarily to reduce the atmospheric emissions of sulphur dioxide (SO_2), a key chemical in sulphuric acid production. In the 1970s and 1980s, production of the chemical from waste products and the increased value of energy led to a number of new modifications concerning both process and equipment. The principal raw materials employed are, in descending priority order: elemental sulphur, spent sulphuric acid and hydrogen sulphide (H_2S); the use of iron pyrites is substantially historical, at least in western countries.

Sodium sulphate (Na_2SO_4) can be produced by reacting sodium chloride with sulphuric acid (Mannheim process) or sulphur dioxide in the presence of oxygen (Hargreaves process), and then isolated from the solution by fractional crystallisation (EFSA ANS Panel, 2010; Butts and Bush, 1997):

$$2NaCl + H_2SO_4 \rightarrow Na_2SO_4 + 2HCl$$

$$4NaCl + 2SO_2 + O_2 + 2H_2O \rightarrow 2Na_2SO_4 + 4HCl$$

Sodium sulphate can also be mined from its natural mineral deposits and purified. In particular, it is common to use Glauber's salt (a mineral containing $Na_2SO_4{\cdot}10H_2O$) in an intermediate process step; Glauber's salt is then converted to anhydrous sodium sulphate, as required. Sodium sulphate is also obtained as a by-product of the manufacturing process of phenol by caustic fusion.

Sodium hydrogen sulphate ($NaHSO_4$) can be produced by reacting sodium chloride with sulphuric acid (Rao, 2010):

$$NaCl + H_2SO_4 \rightarrow NaHSO_4 + HCl$$

Chemicals are combined at elevated temperatures to produce molten sodium hydrogen sulphate. Once the reaction is complete, the molten sodium hydrogen sulphate is sprayed and cooled in order to form a solid beaded product.

Potassium sulphate (K_2SO_4) can be produced with processes similar to those described for sodium sulphate, that is by reacting potassium chloride with sulphuric acid (Mannheim process) or by heating a mixture of potassium chloride, sulphur dioxide, air and water (Hargreaves process) (EFSA ANS Panel, 2010; Freilich and Petersen, 2005). However, a large proportion of the world production of potassium sulphate is obtained by reacting potassium chloride with naturally occurring double salts containing magnesium sulphate – such as minerals schoenite ($K_2SO_4{\cdot}MgSO_4{\cdot}6H_2O$) or langbeinite ($K_2SO_4{\cdot}2MgSO_4$) – according to the following reactions:

$$K_2SO_4{\cdot}MgSO_4{\cdot}6H_2O + 2KCl \rightarrow 2K_2SO_4 + MgCl_2(aq)$$

$$K_2SO_4{\cdot}2MgSO_4 + 4KCl \rightarrow 3K_2SO_4 + 2MgCl_2$$

Where the mineral kieserite ($MgSO_4{\cdot}H_2O$) is readily available, this is generally first converted to schoenite by treatment with potassium chloride, as shown below; the production of potassium sulphate will then proceed as described above.

$$2(MgSO_4{\cdot}H_2O) + 4H_2O + 2KCl \rightarrow K_2SO_4{\cdot}MgSO_4{\cdot}6H_2O + MgCl_2$$

Information on the process utilised in the manufacture of potassium hydrogen sulphate ($KHSO_4$) was not available.

Calcium sulphate ($CaSO_4$) is mostly obtained from its mineral form, gypsum ($CaSO_4 \cdot 2H_2O$) (Lancia et al., 2011). Natural gypsum is rarely found in pure form: the dihydrate and anhydrous forms are usually found together; impurities typically include calcium and magnesium carbonates, silicon oxide (s), clays and small quantities of soluble salts. Commercial gypsum has generally a purity level not lower than 80%. By heat conversion, water can gradually be removed from gypsum, as per the following steps:

$$CaSO_4 \cdot 2H_2O \rightarrow CaSO_4 \cdot 0.5H_2O + 1.5H_2O$$

$$CaSO_4 \cdot 0.5H + 2O \rightarrow CaSO_4 + 0.5H_2O$$

The transition points of the forms dihydrate → hemihydrate and hemihydrate → anhydrite are indicated as 128 and 163°C, respectively. In the preparation of the diverse forms of calcium sulphate, temperature control is somewhat critical in all methods. In addition to the aforesaid methods, there are various chemical processes that produce calcium sulphate as a by-product at a volume level of commercial interest.

Ammonium sulphate ($(NH_4)_2SO_4$) is produced by reacting ammonia with sulphuric acid; it is also a co-product in the production of synthetic–fibre intermediates, such as caprolactam, acrylonitrile and methyl methacrylate, and in the production of formic acid and acrylamide (PubChem, 2019; Zapp, 2012). If sulphuric acid is in short supply, the chemical is generally obtained by reacting gypsum with ammonia and carbon dioxide (Merseburg process):

$$CaSO_4 \cdot 2H_2O + (NH_4)_2CO_3 \rightarrow (NH_4)_2SO_4 + CaCO + 3(aq)$$

Other production processes are available that are obsolete and have only a historical importance.

3.1.4. Methods of analysis in food

Sulphates in aqueous media can be measured by various standard test procedures (Stieg et al., 1997), among which the turbidimetric or gravimetric ones are a common choice (e.g. BS 6068-2.39, ISO 9280, PN-C-04566-10): sulphate ions in an acidic environment are precipitated with barium chloride to form barium sulphate; the resulting suspension is measured by a photometer at 420 nm or with a turbidity meter, or the sulphate precipitate is measured gravimetrically. For instance, the formed barium sulphate is measured gravimetrically in wine (AOAC 930.35 U), in vinegar (AOAC 950.55 U), in table salt after dilution in hot water (AOAC 925.55 F) and in baking powder after acidification and dilution in hot water (AOAC 920.46 I). Gravimetric and turbidimetric methods are suitable for sulphate (SO_4^{2-}) concentrations above 10 mg/L and over a sulphate range of 1−40 mg/L, respectively. The following methods are also used for determination of sulphates in water and wastewater: the ion chromatographic method and capillary ion electrophoresis, suitable for ulphate concentrations above 0.1 mg/L; the automated colorimetric methylthymol blue methods, suitable for analysing large numbers of samples for sulphate alone (over 30 samples per hour).

In Codex Alimentarius (2018), a number of standard analytical methods are recommended for the determination of sodium, potassium and calcium in a variety of foods, such as: special foods and infant formula, milk and dairy products, processed vegetables and fruit, fruit juices and nectars, table salt, and mineral waters. Methods are in general based on atomic emission spectroscopy (AES), flame atomic absorption spectrophotometry (F-AAS), inductively coupled plasma atomic emission spectroscopy (ICP-AES) (also known as inductively coupled plasma optical emission spectrometry (ICP-OES)) and complexometric titrimetry. The recommended standardised methods referred to above were developed by the following international organisations: Association of Official Analytical Chemists (AOAC) International, European Committee for Standardization (CEN), European Salt Producers' Association (EuSalt), International Dairy Federation (IDF), International Fruit and Vegetable Juice Association (IFU), International Organization for Standardization (ISO) and Nordic Committee on Food Analysis (NMKL). A method described by the World Health Organization (WHO), for sodium and potassium determination in natural mineral waters, is also mentioned.

3.1.5. Stability of the substance, and reaction and fate in food

Sulphuric acid and its sodium, potassium and ammonium salts are readily soluble in water (OECD, 2005; Müller, 2012): these substances are expected to dissolve in aqueous media into their respective

ions. Hydrous or anhydrous calcium sulphate is only slightly soluble in water (0.2−0.3 g/100 mL H_2O at 25°C) (Lancia et al., 2011): the solubilised fraction can also be expected to dissociate into calcium (Ca^{2+}) and sulphate (SO_4^{2-}) ions.

Sodium and potassium, as the other alkali metals, have a single *s* electron outside a noble gas core; as a result of the electronic structure and characteristics, their chemistry is principally that of the oxidation state M^{1+}; no other cations are known. The chemistry of the alkali metals is mainly that of their ionic salts in the solid state and solvated cations. The salts of the tetrahedral ammonium ion (NH_4^+) generally resemble those of potassium (K^+) as to solubilities and crystal structures. There are many quite stable crystalline salts of the ammonium ion, most of them water soluble: salts of strong acids are fully ionised, and their solutions are slightly acidic due to the hydrolytic reaction.

$$NH_4^+ + H_2O = NH_3 + H_3O^+ \; K_{25°C} = 5.5 \times 10^{-10}$$

Ammonium sulphate cannot be melted at atmospheric pressure without decomposition; however, the ammonia vapour pressure of pure, anhydrous ammonium sulphate is about zero up to 80°C (Zapp, 2012). Above 300°C, decomposition gives N_2, SO_2, SO_3 and H_2O in addition to ammonia.

Concentrated sulphuric acid is a strong and corrosive dibasic acid that reacts with most metals (Müller, 2012). The chemical is thermally stable: only at high temperatures, it is partially decomposed into its anhydride (SO_3) and water vapour. The reverse of this reaction is the overall route by which sulphuric acid is formed in the absorption section of a contact sulphuric acid plant. However, the Panel considered that, as it is used in food processing or as a food additive to adjust the pH, sulphuric acid is neutralised or buffered by the food to which it is added. The small amounts of acid that may persist in foods or drinks, would, in turn, be neutralised and buffered during ingestion and digestion, or after absorption.

Sodium sulphate is not reactive in aqueous solution at room temperature. Sodium hydrogen sulphate readily dissociates in water with an acidic reaction, resulting in hydrogen sulphate anions and sodium cations (OECD, 2005; ECHA, 2010): the hydrogen sulphate anion (pK_A = 1.99) partly dissociates further to sulphate anion and the hydrogen cation, which is responsible for the acidic reaction.

According to the information provided to EFSA (2009), sodium hydrogen sulphate is generally assumed to be stable in dry matrices; it is known to dissociate into ionic components in aqueous media:

$$NaHSO_4 \rightarrow Na^+ + H^+ + SO_4^{2-}.$$

Sodium and sulphate ions occur naturally (OECD, 2005; ECHA, 2010). Sodium ions are present ubiquitously in the environment and essential to all forms of life; sulphate ions also occur naturally, and can be considered to form part of the sulphur cycle, being readily utilised by bacteria, fungi and many aerobic and anaerobic prokaryotic species. Microbes play pivotal roles in the sulphur cycle: the sulphate moiety provides microorganisms with the possibility of carrying out sulphate reduction to derive their energy. Sodium sulphate will completely dissolve, ionise and distribute across the entire water compartment. Some sulphates may eventually be deposited; however, the majority of sulphates participate in the sulphur cycle in which natural and industrial sodium sulphate are not distinguishable.

3.2. Authorised uses and use levels

Maximum levels of sulphuric acid and its sodium, potassium and calcium salts (E 513, 514 (i), 514 (ii), 515 (i), 515 (ii) and 516) are defined in Annex II to Regulation (EC) No 1333/2008[12] on food additives, as amended. No maximum levels are defined in Annex II for ammonium sulphate (E 517). In this document, these levels are named maximum permitted levels (MPLs).

Sulphuric acid and its sodium, potassium and calcium salts (E 513, 514 (i), 514 (ii), 515 (i), 515 (ii) and 516) are authorised at *quantum satis* (QS) according to the Group I food categories (Table 8).

[12] 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.

Table 8: MPLs of sulphuric acid and its sodium, potassium and calcium salts (E 513, 514 (i), 514 (ii), 515 (i), 515 (ii) and 516) in foods according to Annex II to Regulation (EC) No 1333/2008

FCS category number	Food categories	Authoris.	Restrictions/ exception	MPL (mg/L or mg/kg as appropriate)
1.3	Unflavoured fermented milk products, heat-treated after fermentation	Group I		quantum satis
1.4	Flavoured fermented milk products including heat-treated products	Group I		quantum satis
1.6.3	Other creams	Group I		quantum satis
1.7.1	Unripened cheese excluding products falling in category 16	Group I	Except mozzarella	quantum satis
1.7.5	Processed cheese	Group I		quantum satis
1.7.6	Cheese products (excluding products falling in category 16)	Group I		quantum satis
1.8	Dairy analogues, including beverage whiteners	Group I		quantum satis
2.2.2	Other fat and oil emulsions including spreads as defined by Council Regulation (EC) No 1234/2007 and liquid emulsions	Group I		quantum satis
2.3	Vegetable oil pan spray	Group I		quantum satis
3	Edible ices	Group I		quantum satis
4.2.1	Dried fruit and vegetables	Group I		quantum satis
4.2.2	Fruit and vegetables in vinegar, oil or brine	Group I		quantum satis
4.2.4.1	Fruit and vegetable preparations excluding compote	Group I		quantum satis
4.2.5.4	Nut butters and nut spreads	Group I		quantum satis
4.2.6	Processed potato products	Group I		quantum satis
5.1	Cocoa and Chocolate products as covered by Directive 2000/36/EC	Group I	Only energy-reduced or with no added sugar	quantum satis
5.2	Other confectionery including breath freshening microsweets	Group I		quantum satis
5.3	Chewing gum	Group I		quantum satis
5.4	Decorations, coatings and fillings, except fruit-based fillings covered by category 4.2.4	Group I		quantum satis
6.2.2	Starches	Group I		quantum satis
6.3	Breakfast cereals	Group I		quantum satis
6.4.2	Dry pasta	Group I	Only gluten free and/ or pasta intended for hypoproteic diets in accordance with Directive 2009/39/EC	quantum satis
6.4.4	Potato gnocchi	Group I	Except fresh refrigerated potato gnocchi	quantum satis
6.4.5	Fillings of stuffed pasta (ravioli and similar)	Group I		quantum satis
6.5	Noodles	Group I		quantum satis
6.6	Batters	Group I		quantum satis
6.7	Pre-cooked or processed cereals	Group I		quantum satis
7.1	Bread and rolls	Group I	Except products in 7.1.1 and 7.1.2	quantum satis

FCS category number	Food categories	Authoris.	Restrictions/ exception	MPL (mg/L or mg/kg as appropriate)
7.2	Fine bakery wares	Group I		quantum satis
8.3.1	Non-heat-treated meat products	Group I		quantum satis
8.3.2	Heat-treated meat products	Group I	Except *foie gras, foie gras entier, blocs de foie gras, Libamáj, libamáj egészben, libamáj tömbben*	quantum satis
8.3.3	Casings and coatings and decorations for meat	Group I		quantum satis
9.2	Processed fish and fishery products including molluscs and crustaceans	Group I		quantum satis
9.3	Fish roe	Group I	Only processed fish roe	quantum satis
10.2	Processed eggs and egg products	Group I		quantum satis
11.2	Other sugars and syrups	Group I		quantum satis
12.1.2	Salt substitutes	Group I		quantum satis
12.2.2	Seasonings and condiments	Group I		quantum satis
12.3	Vinegars and diluted acetic acid (diluted with water to 4–30% by volume)	Group I		quantum satis
12.4	Mustard	Group I		quantum satis
12.5	Soups and broths	Group I		quantum satis
12.6	Sauces	Group I		quantum satis
12.7	Salads and savoury-based sandwich spreads	Group I		quantum satis
12.8	Yeast and yeast products	Group I		quantum satis
12.9	Protein products, excluding products covered in category 1.8	Group I		quantum satis
13.2	Dietary foods for special medical purposes defined in Directive 1999/21/EC (excluding products from food category 13.1.5)	Group I		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		quantum satis
13.4	Foods suitable for people intolerant to gluten as defined by Regulation (EC) No 41/2009	Group I	Including dry pasta	quantum satis
14.1.2	Fruit juices as defined by Directive 2001/112/EC and vegetable juices	Group I	Only vegetable juices	quantum satis
14.1.3	Fruit nectars as defined by Directive 2001/112/EC and vegetable nectars and similar products	Group I	Only vegetable nectars	quantum satis
14.1.4	Flavoured drinks	Group I		quantum satis
14.1.5.2	Other	Group I	Excluding unflavoured leaf tea; including flavoured instant coffee	quantum satis
14.2.3	Cider and perry	Group I		quantum satis
14.2.4	Fruit wine and made wine	Group I		quantum satis
14.2.5	Mead	Group I		quantum satis
14.2.6	Spirit drinks as defined in Regulation (EC) No 110/2008	Group I	Except whisky or whiskey	quantum satis

FCS category number	Food categories	Authoris.	Restrictions/ exception	MPL (mg/L or mg/kg as appropriate)
14.2.7.1	Aromatised wines	Group I		quantum satis
14.2.7.2	Aromatised wine-based drinks	Group I		quantum satis
14.2.7.3	Aromatised wine-product cocktails	Group I		quantum satis
14.2.8	Other alcoholic drinks including mixtures of alcoholic drinks with non-alcoholic drinks and spirits with less than 15% of alcohol	Group I		quantum satis
15.1	Potato-, cereal-, flour- or starch-based snacks	Group I		quantum satis
15.2	Processed nuts	Group I		quantum satis
16	Desserts excluding products covered in category 1, 3 and 4	Group I		quantum satis
17.1	Food supplements supplied in a solid form including capsules and tablets and similar forms, excluding chewable forms	Group I		quantum satis
17.2	Food supplements supplied in a liquid form	Group I		quantum satis
17.3	Food supplements supplied in a syrup-type or chewable form	Group I		quantum satis
18	Processed foods not covered by categories 1–17, excluding foods for infants and young children	Group I		quantum satis

MPL: maximum permitted level.
(a): Based on note of the legislation: 'The additives of categories 13.1.2 and 13.1.3 are applicable'.
(b): FC 17 refers to food supplements as defined in Directive 2002/46/EC of the European Parliament and of the Council excluding food supplements for infants and young children.

Sodium sulphates (E 514(i), E 514(ii)), potassium sulphates (E 515(i), E 515(ii)) and calcium sulphate (E 516) are also authorised according to Annex III, Part 1 (carriers in food additives at QS), Part 2 (food additive other than carrier added to food additives at QS), Parts 3 (food additives including carriers in food enzymes at QS), Part 4 (food additive added to food flavourings at QS) and Part 5 (food additives in nutrients section A at QS).

Sulphuric acid (E 513) is also authorised according to Annex III, Part 2 (food additive other than carrier added to food additives at QS), Part 3 (food additives including carriers in food enzymes at QS), Part 4 (food additive added to food flavourings at QS) and Part 5 (food additives in nutrients section A at QS).

Ammonium sulphate (E 517) is only authorised according to Annex III, Part 1 (carriers in food additives at QS) and Part 3 (food additives including carriers in food enzymes with the following maximum levels: 100,000 mg/kg in enzyme preparations, 100 mg/kg in final food except beverages and 50 mg/L in beverages).

3.3. Exposure data

3.3.1. Reported use levels of sulphuric acid and its sodium, potassium, calcium and ammonium salts (E 513, 514 (i), 514 (ii), 515 (i), 515 (ii), 516 and 517)

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 with an MPL at *QS*.

In the framework of Regulation (EC) No 1333/2008 on food additives and of Commission Regulation (EU) No 257/2010 regarding the re-evaluation of approved food additives, EFSA issued a public call[13] for occurrence data (usage level and/or concentration data) on sulphuric acid and its

[13] Call for food additives usage level and/or concentration data in food and beverages intended for human consumption. Published: 24 May 2016. Available online: https://www.efsa.europa.eu/en/data/call/160524

sodium, potassium, calcium and ammonium salts (E 513, 514 (i), 514 (ii), 515 (i), 515 (ii), 516 and 517). In response to these calls, usage levels on sodium sulphates, potassium sulphates and calcium sulphate (E 514, E 515, E 516) were submitted to EFSA by industry. No analytical data were made available by the Member States.

Summarised data on reported use levels in foods provided by industry

Industry provided use levels (n = 30) of sodium sulphates, potassium sulphates and calcium sulphate (E 514, E 515, E 516) in foods belonging to 8 out of the 67 food categories in which they are authorised according to Annex II to Regulation (EC) No 1333/2008 (Table 9). Two use levels related to the use of E 516 in an ingredient used as stuffing were not included in the exposure assessment because they refer to the non-authorised food category (FC) 8.2 Meat preparations. No use levels for sulphuric acid (E 513) and ammonium sulphate (E 517) were reported.

The use levels were provided by EUROGUM A/S and Food Drink Europe.

Four use levels of E 516 for FC 8.3 Meat products were provided by food additive producer EUROGUM A/S. Food additive producers do not directly use additives in food but may recommend food producers on the levels to be added to food. Therefore, use levels reported by these producers may differ from the actual levels used by the food industry. The use levels provided by EUROGUM were not used in the *refined exposure scenario* because of this reason. However, the levels were used in the *maximum level exposure assessment* scenario, because no other data for FC 8.3 were available from food producers and E 516 is authorised in this food category at *QS* (Table 8). In this way, the most complete exposure estimates were calculated for this scenario.

In addition, the Panel noted that seven use levels were reported on niche products for five food categories. Data on niche products are included in the *maximum level exposure assessment scenario*. These data are also considered in the *refined exposure scenario* if no use levels for more widely used products in the same food category are available. Use levels on more widely used products were available for four out of the five food categories. Use levels of niche products in these four food categories were therefore excluded from further analysis in the refined scenarios. Use levels of E 515 in F.C 14.1.4 and of E 516 in FC 12.6 referring to niche products were included in the refined exposure scenario (Appendix A and C).

According to the above exclusion criteria, nine use levels were excluded from further analysis in the refined scenarios, whereas none were excluded from the *maximum level exposure assessment* scenario.

Table 9: The number of use levels provided by industry, the number of food categories for which use levels were provided and the total number of authorised food categories according to Annex II to Regulation (EC) No 1333/2008 for sulphuric acid and its sodium, potassium, calcium and ammonium salts (E 513, E 514, E 515, E 516, E 517)

Number of	E 513	E 514	E 515	E 516	E 517*
Use levels (n)	0	3	1	26	0
Food categories covered	0	1	1	7	0
Authorised food categories	67	67	67	67	0

*: Only Annex III authorisation.

Appendix A provides data on the use levels of sodium sulphates, potassium sulphates and calcium sulphate (E 514, E 515, E 516) in foods as reported by industry.

3.3.2. Summarised data extracted from the Mintel's Global New Products Database

The Mintel's GNPD is an online database that monitors new introductions of packaged goods in the market worldwide. It contains information of over 2.5 million food and beverage products of which more than 900,000 are or have been available on the European food market. Mintel started covering EU's food markets in 1996, currently having 20 out of its 28 member countries and Norway presented in the Mintel's GNPD.[14]

[14] Missing Bulgaria, Cyprus, Estonia, Latvia, Lithuania, Luxembourg, Malta and Slovenia.

For the purpose of this Scientific Opinion, Mintel's GNPD[15] was used for checking the labelling of food and beverages products and food supplements for sulphuric acid and its sodium, potassium, calcium and ammonium salts (E 513, E 514, E 515, E 516, E 517) within the EU's food market as the database contains the compulsory ingredient information on the label.

Appendix B lists the number and percentage of the food products labelled with sulphuric acid and its sodium, potassium, calcium and ammonium salts (E 513, E 514, E 515, E 516, E 517) out of the total number of food products per food subcategory of the Mintel's GNPD food classification.

According to Mintel's GNPD, sulphuric acid or its sodium, potassium, calcium and ammonium salts (E 513, E 514, E 515, E 516, E 517) were labelled on 1,221 products between January 2014 and May 2019. These products represented 0.3% of all the products within the food subcategories of Mintel's GNPD food classification in which at least one food was labelled with the food additives.

Calcium sulphate (E 516) was labelled on foods across several food subcategories (n = 1037) with Meat substitutes representing 30% of all products. Sodium sulphates (E 514) were labelled on 138 products, whereas sulfuric acid (E 513), potassium sulphate (E 515) and ammonium sulphate (E 517) were only labelled on 1, 33 and 17 products, respectively. Sodium sulphates (E 514) were labelled as their generic form E 514 sodium sulphate (n = 77) or more specifically as E 514 (ii) sodium bisulphate (n = 36) and E 514(i) sodium sulphate (n = 26). Potassium sulphates were labelled as their generic form E 515 (n = 25) and more specifically as E 515 (i) potassium sulphate (n = 8).

The food subcategory with the highest number and percentage of products labelled with these additives was Meat Substitutes (8%). These products were all labelled to contain calcium sulphate (E 516) except one product labelled to contain potassium sulphate (E 515). No use level data were provided for foods belonging to this food subcategory. The corresponding Annex II food category is FC 12.9 Protein products, excluding products covered in category 1.8.

Based on information from the Mintel's GNPD, the Panel considered that sodium sulphates, potassium sulphates and calcium sulphate (E 514, E 515, E 516) are not likely to be used in combination in the same food product and, therefore, an exposure assessment was performed considering the highest reported use level for either E 514, E 515 or E 516 per food category. No use levels for sulphuric acid (E 513) and ammonium sulphate (E 517) were reported (Section 3.3.1).

3.3.3. Food consumption data used for exposure assessment

EFSA Comprehensive European Food Consumption Database

Since 2010, the EFSA Comprehensive European Food Consumption Database (Comprehensive Database) has been populated with national data on food consumption at a detailed level. Competent authorities in the European countries provide EFSA with data on the level of food consumption by the individual consumer from the most recent national dietary survey in their country (cf. Guidance of EFSA on the 'Use of the EFSA Comprehensive European Food Consumption Database in Exposure Assessment' (EFSA, 2011a). Consumption surveys added in the Comprehensive database in 2015 were also taken into account in this assessment.[16]

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 subjects' underreporting and/or misreporting of the consumption amounts. Nevertheless, the EFSA Comprehensive Database includes the currently best available food consumption data across Europe.

Food consumption data from infants, toddlers, children, adolescents, adults and the elderly were used in the exposure assessment. For the present assessment, food consumption data were available from 33 different dietary surveys carried out in 19 European countries (Table 10).

[15] http://www.gnpd.com/sinatra/home/ accessed on 27 May 2019.
[16] Available online: http://www.efsa.europa.eu/en/datexfoodcdb/datexfooddb.htm

Table 10: Population groups considered for the exposure estimates of sulphuric acid and its sodium, potassium, calcium and ammonium salts (E 513, E 514, E 515, E 516, E 517)

Population	Age range	Countries with food consumption surveys covering more than 1 day
Infants	From more than 12 weeks up to and including 11 months of age	Bulgaria, Denmark, Finland, Germany, Italy, UK
Toddlers[(a)]	From 12 months up to and including 35 months of age	Belgium, Bulgaria, Denmark, Finland, Germany, Italy, Netherlands, Spain, UK
Children[(b)]	From 36 months up to and including 9 years of age	Austria, Belgium, Bulgaria, Czech Republic, Denmark, Finland, France, Germany, Greece, Italy, Latvia, Netherlands, Spain, Sweden, UK
Adolescents	From 10 years up to and including 17 years of age	Austria, Belgium, Cyprus, Czech Republic, Denmark, Finland, France, Germany, Italy, Latvia, Netherlands, Spain, Sweden, UK
Adults	From 18 years up to and including 64 years of age	Austria, Belgium, Czech Republic, Denmark, Finland, France, Germany, Hungary, Ireland, Italy, Latvia, Netherlands, Romania, Spain, Sweden, UK
The elderly[(b)]	From 65 years of age and older	Austria, Belgium, Denmark, Finland, France, Germany, Hungary, Ireland, Italy, Romania, Netherlands, Sweden, UK

(a): The term 'toddlers' in the Comprehensive Database corresponds to 'young children' in Regulations (EC) No 1333/2008 and (EU) No 609/2013.
(b): The terms 'children' and 'the elderly' correspond, respectively, to 'other children' and the merge of 'elderly' and 'very elderly' in the Guidance of EFSA on the 'Use of the EFSA Comprehensive European Food Consumption Database in Exposure Assessment' (EFSA, 2011a).

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

Food categories considered in the exposure assessment of sulphuric acid and its sodium, potassium, calcium and ammonium salts (E 513, E 514, E 515, E 516, E 517) expressed as sulphate

The food categories in which the use of sodium sulphate, potassium sulphate and calcium sulphate (E 514, E 515, E 516) is authorised were selected from the nomenclature of the EFSA Comprehensive Database (FoodEx classification system), at the most detailed level possible (up to FoodEx Level 4) (EFSA, 2011b).

Overall, eight food categories were included in the *maximum level exposure scenario* for the exposure assessment of sodium sulphates, potassium sulphates and calcium sulphate expressed as sulphate (E 514, E 515, E 516) (Appendix C).

The same categories were included in the refined scenarios except for FC 8.3 Meat products. Use levels for this food category were provided by a food additive producer (Section 3.3.1). The maximum provided use level for this food category was attributed to the three underlying food categories (FC 08.3.1 Non-heat-treated meat products, 08.3.2 Heat-treated meat products and 08.3.3 Casings and coatings and decorations for meat) in the maximum level exposure scenario (Section 3.3.1).

The authorisation in FC 07.1 Bread and rolls excludes the subcategories FC 07.1.1 Bread prepared solely with the following ingredients: wheat flour, water, yeast or leaven, salt and FC 07.1.2 Pain courant français; Friss búzakenyér, fehér és félbarna kenyerek (Table 8). As foods are not referenced to this detail in the Comprehensive Database, the entire parent FC 07.1 Bread and rolls was used in the exposure assessment. This will have contributed to an overestimation of the exposure in all scenarios.

Exposure to ammonium sulphate (E 517) from its use as carrier in food enzymes could have been included in the *maximum level exposure assessment scenario* by attributing the MPL of 100 mg/kg to all foods and of 50 mg/kg to all beverages. This approach would have resulted in an unrealistically high estimate of the exposure as it is unlikely that all foods and beverages will contain E 517 at the level of the MPL. Thus, the Panel did not consider ammonium sulphate (E 517) from its use as a carrier in food enzymes.

3.4. Exposure estimate

3.4.1. Exposure to sulphuric acid and its sodium, potassium, calcium and ammonium salts (E 513, E 514, E 515, E 516, E 517) from their use as food additives

The Panel considered the highest reported use level for either E 514, E 515 or E 516 per food category in the exposure assessment (Section 3.3.2). The Panel noted that the highest reported use level in FC 14.1.4 flavoured drinks was related to a niche product. The Panel estimated the chronic dietary exposure to sulphate (see Section 1.1.3) derived from the exposure to the anion component of sodium sulphates, potassium sulphates or calcium sulphate (E 514, E 515, E 516) for the following population groups: infants, toddlers, children, adolescents, adults and the elderly. For this, the highest reported use level for sodium sulphates, potassium sulphates or calcium sulphate (E 514, E 515, E 516) per food category (Appendix C) was multiplied with the following conversion factors to obtain the use level related to sulphate: 0.82, 0.72 or 0.72, respectively. The resulting highest use level among the additives per food category was then used in the exposure assessment.

Dietary exposure was calculated by multiplying the highest use levels per food category with their respective consumed amount per kilogram body weight for each individual in the Comprehensive Database according to the scenarios described below. The exposure per food category was subsequently added to derive an individual total exposure per day. These exposure estimates were averaged over the number of survey days, resulting in an individual average exposure per day for the survey period. Dietary surveys with only 1 day per subject were excluded as they are not considered adequate to assess repeated exposure.

The exposure was calculated for all individuals per survey and per population group, resulting in distributions of individual exposure per survey and population group (Table 10). Based on these distributions, the mean and 95th percentile of exposure were calculated per survey and per population group. The 95th percentile of exposure could only be calculated for population groups with a sufficiently large sample size (EFSA, 2011a). Therefore, the 95th percentile of exposure for infants from Italy and for toddlers from Belgium, Italy and Spain was not estimated in the present assessment.

The exposure assessment to sodium sulphates, potassium sulphates and calcium sulphate (E 514, E 515, E 516) expressed as sulphate was carried out by the FAF Panel based on two different sets of concentration data: (1) maximum reported use levels and (2) typical reported use levels (defined as the *refined exposure assessment scenario*). These two scenarios are discussed in detail below.

These scenarios do not consider the intake through the consumption of food supplements. As no use levels had been provided for food supplements, this exposure source was not covered in additional scenarios.

A possible additional exposure from the use of sulfuric acid, sodium sulphates, potassium sulphates or calcium sulphate (E 513, E 514, E 515, E 516) in accordance with Annex III to Regulation (EC) No 1333/2008 was not considered in any of the exposure assessment scenarios, as no use level nor MPL was available.

Although MPLs were available, a possible additional exposure from the use of ammonium sulphate (E 517) in accordance with Annex III, Part 1 and 3 to Regulation (EC) No 1333/2008 was neither considered in any of the exposure assessment scenarios as no specific information about which foods and beverages were likely to contain ammonium sulphate (E 517) was available.

Maximum level exposure assessment scenario

Sodium sulphates, potassium sulphates and calcium sulphate (E 514, E 515, E 516) are authorised according to *QS* in all food categories (Table 8). Therefore, a *maximum level exposure assessment scenario* was performed based on the maximum of the reported maximum use levels provided by industry (food industry and food additive producers) for either E 514, E 515 or E 516 per food category. The use levels expressed as sulphate as used in this scenario are listed in Appendix C.

The Panel considers the exposure estimates based on this scenario as the most conservative, because it is assumed that the food additive is always present at the highest of the reported use levels for either E 514, E 515 or E 516 in all foods within the relevant food categories.

Refined exposure assessment scenario

The refined exposure assessment scenario was based on the highest (maximum or typical) use levels per food category for sodium sulphates, potassium sulphates or calcium sulphate (E 514, E 515,

E 516). Appendix C summarises the use levels of expressed as sulphate used in this scenario. Based on the available data set, the Panel calculated two refined exposure estimates based on two model populations:

- The brand-loyal consumer scenario: It was assumed that a consumer is exposed long-term to sodium sulphates, potassium sulphates or calcium sulphate (E 514, E 515, E 516) expressed as sulphate present at the highest maximum reported use level for one food category across the three additives. This exposure estimate is calculated as follows:
  - Combining consumption levels of the main contributing food category at the individual level with the highest reported maximum use level across the three additives.
  - Combining consumption levels of the remaining food categories with the mean of the highest reported typical use levels across the three additives.
- The non brand-loyal consumer scenario: It was assumed that a consumer is exposed long-term to sodium sulphates, potassium sulphates or calcium sulphate (E 514, E 515, E 516) present at the highest mean of the reported typical use levels in food across the three additives.

Dietary exposure to sulphuric acid and its sodium, potassium, calcium and ammonium salts (E 513, E 514, E 515, E 516, E 517) expressed as sulphate

Table 11 summarises the estimated exposure for sulphuric acid and its sodium, potassium, calcium and ammonium salts (E 513, E 514, E 515, E 516, E 517) from their use as a food additives expressed as sulphate in six population groups (Table 10) according to the different exposure scenarios (Section 3.4.1). Detailed results per population group and survey are presented in Appendix D.

Table 11: Summary of dietary exposure to sulphuric acid and its sodium, potassium, calcium and ammonium salts (E 513, E 514, E 515, E 516, E 517) from their use as a food additive in the maximum level exposure assessment scenario and in the refined exposure scenarios, in six population groups (minimum–maximum across the dietary surveys in mg sulphate/kg bw per day)

	Infants (12 weeks–11 months)	Toddlers (12–35 months)	Children (3–9 years)	Adolescents (10–17 years)	Adults (18–64 years)	The elderly (≥ 65 years)
Maximum level exposure assessment scenario						
• Mean	3–46	18–161	25–131	10–68	27–53	25–50
• 95th perc.	33–124	52–207	63–217	25–138	50–102	46–83
Refined exposure assessment scenario						
Brand-loyal scenario						
• Mean	1–32	5–71	3–65	1–36	13–24	15–24
• 95th perc.	14–82	15–117	10–129	4–69	29–49	28–46
Non brand-loyal scenario						
• Mean	0.4–13	4–35	2–33	1–16	5–11	6–10
• 95th perc.	14–35	14–68	9–67	3–30	12–22	12–18

In the *maximum level exposure assessment scenario*, mean exposure sulphuric acid and its sodium, potassium, calcium and ammonium salts (E 513, E 514, E 515, E 516, E 517) ranged from 3 mg/kg bw per day in infants to 161 mg/kg bw per day in toddlers expressed as sulphate. The 95th percentile of exposure ranged from 25 mg/kg bw per day in the adolescents to 217 mg/kg bw per day in children.

In the *refined estimated exposure scenario*, mean exposure ranged from 1 mg/kg bw per day in infants to 71 mg/kg bw per day in toddlers in the *brand-loyal scenario*. The 95th percentile of exposure ranged from 4 mg/kg bw per day in the adolescents to 129 mg/kg bw per day in children expressed as sulphate. In the *non brand-loyal scenario*, mean exposure ranged from 0.4 mg/kg bw per day in infants to 35 mg/kg bw per day in toddlers expressed as sulphate. The 95th percentile of exposure ranged from 3 mg/kg bw per day in the adolescents to 68 mg/kg bw per day in toddlers expressed as sulphate.

Main food categories contributing to exposure to sulphuric acid and its sodium, potassium, calcium and ammonium salts (E 513, E 514, E 515, E 516, E 517) expressed as sulphate

The main contributing food categories to the exposure to the three additives in all population groups from their use as food additives expressed as sulphate were FC 07.1 Bread and rolls, FC 07.2 Fine bakery wares and FC 08.3 Meat products in the *maximum level exposure scenario*.

In the *brand-loyal and non brand-loyal exposure scenarios,* the main contributing food categories to the exposure in all population groups were FC 07.1 Bread and rolls and FC 07.2 Fine bakery wares. FC 08.3 Meat products was excluded from these two refined scenarios.

For details on the contribution of each food category in the three scenarios, see Appendix E.

The Panel considered that the refined exposure assessment approach resulted in more realistic long-term exposure estimates compared to the *regulatory maximum level exposure assessment scenario*.

Sulphuric acid and its sodium, potassium, calcium and ammonium salts (E 513, E 514, E 515, E 516, E 517) are used as miscellaneous additives and they do not change the organoleptic properties of the final food. In addition, they are part of a large group of different additives having the same function which are available on the market.

For these reasons, the Panel considered the *non brand-loyal scenario* covering the general population as the most appropriate scenario for risk characterisation.

Uncertainty analysis

Uncertainties in the exposure assessment of sulphuric acid and its sodium, potassium, calcium and ammonium salts from their use as food additives (E 513, E 514, E 515, E 516, E 517) have been discussed above. In accordance with the guidance provided in the EFSA opinion related to uncertainties in dietary exposure assessment (EFSA, 2007), the following sources of uncertainties have been considered and summarised in Table 12.

Table 12: Qualitative evaluation of influence of uncertainties on the dietary exposure estimate of sulphuric acid and its sodium, potassium, calcium and ammonium salts from their use as food additives (E 513, E 514, E 515, E 516, E 517)

Sources of uncertainties	Direction[(a)]
Consumption data: different methodologies/representativeness/underreporting/misreporting/no portion size standard	+/–
Methodology used to estimate high percentiles (95th) of long-term (chronic) exposure based on data from food consumption surveys covering only a few days	+
Correspondence of reported use levels to the food items in the Comprehensive Database: uncertainties to which types of food the levels refer	+/–
Uncertainty in possible national differences in use levels of food categories	+/–
Food categories selected for the exposure assessment: inclusion of food categories without considering the restriction/exception (n = 2)	+
Use level data availability:	
– Use levels were available only for E514, E515 and E516	–
– use levels were available for 8 out of 67 (12%) authorised categories and the food categories included corresponded to 2%–59% of the amount (grams of foods by body weight) of food consumption documented in the Comprehensive Database (when no use level was available the food additive was considered as not used)	–
– E 516 was labelled on several foods belonging to the food subcategory Meat Substitutes in the Mintel database, but no use level had been provided	–
– use levels considered applicable to all foods within the entire food category	+
– use of these additives according to Annex III to Regulation (EC) No 1333/2008 was not considered	–
– Based on the highest (maximum or typical) reported use level across the three additives	+
– Inclusion of use levels of niche products	+
Maximum level exposure assessment scenario:	
– exposure calculations based on the maximum reported use levels (reported use from food industry and food additive producers)	+
Refined exposure assessment scenarios:	
– exposure calculations based on the maximum or mean reported use from food industry	+/–

Sources of uncertainties	Direction[(a)]
All scenarios for assessment: the co-occurrence of additives was dealt with by taking the highest use level per food category among those available for all additives	+

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

Sulphuric acid, sodium sulphates, potassium sulphates, calcium sulphate and ammonium sulphate (E 513, E 514, E 515, E 516, E 517) are all authorised as a Group I food additive in 67 food categories (Table 8). Use level data were provided on only very few categories by food industry as well as only for sodium sulphates, potassium sulphates and calcium sulphate (Table 9). This may be explained by their Group I authorisation. Due to this, the food additives may not necessarily be used in these food categories. The information from Mintel's GNPD supported this with the exception of the food subcategory Meat Substitutes (Appendix B).

Overall, the Panel considered the exposure to sulphuric acid, sodium sulphates, potassium sulphates, calcium sulphate and ammonium sulphate (E 513, E 514, E 515, E 516, E 517) from their use as food additives and expressed as sulphate, in European countries present in the Comprehensive Database to be an overestimation for the maximum and refined level exposure scenarios. This was due to the overall uncertainties (Table 12), and in particular that:

- all foods within a food category considered in the exposure assessment contained one of the additives.
- the additive was always present at the highest reported use level among those available for all food additives.

3.4.2. Exposure via other sources

Sodium and potassium sulphates are permitted as sources of sodium and potassium in food supplements according to Directive 2002/46/EC[17] and calcium sulphate is permitted as a source of calcium in food supplements, in foods in general and in foods for special nutritional purposes according to Regulation 1170/2009[18], Regulation 1925/2006[6] and Regulation 953/2009[19].

The majority of sulphate intake from the diet comes from protein-derived methionine and cysteine (Erdman, 2004), however, in areas with high levels of naturally occurring sulphate in the drinking water supply, drinking water may constitute the principal dietary source (WHO, 2004).

Sulphates (generally magnesium, sodium or calcium sulphate) are present in mineral water with concentration that can be higher than 200 mg/L in 'sulphate-rich' mineral water (Casado et al., 2015; Quattrini et al., 2016).

3.5. Biological and Toxicological data

When relevant, the dose of the test substance as a salt of sulphuric acid was calculated in mg of sulphate on the basis of the molecular weight of the corresponding salt of sulphuric acid in the anhydrous form.

SCF stated that the anions chloride, sulphate and carbonate are natural constituents of man, animals and plants, and therefore occur in foodstuffs. They, together with certain cations, constitute the major electrolytes present in all biological materials (SCF, 1991). No safety problems are likely to arise, provided the contributions from food do not disturb the homoeostatic mechanisms controlling the electrolyte balance of the body. Consequently, the Panel agreed with this statement and therefore primarily investigated the effects of these anions in human studies.

[17] Directive 2002/46/EC of the European Parliament and of the Council of 10 June 2002 on the approximation of the laws of the Member States relating to food supplements. OJ L 183 of 12.7.2002, p. 51–57.

[18] 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. (Text with EEA relevance). OJ L 314 of 1.12.2009, p. 36–42.

[19] Commission Regulation (EC) No 953/2009 of 13 October 2009 on substances that may be added for specific nutritional purposes in foods for particular nutritional uses (Text with EEA relevance). OJ L 269, 14.10.2009, p. 9–19.

3.5.1. Human data

Human studies

Diarrhoea and loose stools have been reported with high intakes of sulphate consumed in drinking water (Erdman, 2004). The soft stool or diarrhoea is an osmotic diarrhoea (i.e. one that results when the osmolality of the intestinal contents exceeds that of the interstitial fluids) where water is drawn across the intestinal membrane into the lumen, increasing the moisture content and volume of the faecal matter leading to an increased intestinal peristalsis and evacuation of the intestinal contents (US-EPA, 2003). Sodium sulphate is a well-known laxative and has as such been used medically as an osmotic laxative in doses of 300 mg/kg bw up to 20 g maximum for an adult (OECD, 2005). Such effects of sulphate observed only at high oral intakes are not considered relevant for the purpose of evaluating sulphates as food additives.

Sulphuric acid and sodium, potassium and calcium are used as acidity regulators in food and drinks, thus contributing to lowering pH in the oral cavity when these products are ingested. Low pH in the oral cavity can result in dental erosion. Dental erosion is defined as the pathological chronic loss of dental hard tissue because of the chemical influence of extrinsic and intrinsic acids. The critical pH for plaque fluid is approximately pH 5.5; however, the erosive potential is not just dependent on the pH in the food or drink but also strongly influenced other factors like buffering capacity, mineral content and calcium chelation. The greater the buffering capacity the longer time it takes to neutralise the acid in the oral cavity. Increased content of minerals like phosphate and calcium concentrations reduces the erosive potential (e.g. in yoghurt, the critical acidity is lowered to pH 4) while the calcium chelating properties of the acid/acids in the food can markedly increase the erosive potential by removing calcium from the tooth surface (Meurman and ten Cate, 1996; Lussi et al., 2011; Wang and Lussi, 2012).

Absorption, distribution, metabolism and excretion

The text below summarises common knowledge on the subject and was extracted from reports of the USA Institute of Medicine (2005) and US-EPA (2003).

Gastrointestinal absorption of sulphate in humans can occur in the stomach, small intestine and colon. Absorption is a sodium-dependent active process. When soluble sulphate salts (e.g. sodium, potassium and ammonium sulphate) are consumed, more than 80% of oral sulphate doses are absorbed, as shown by isotopic tracer studies. After absorption, inorganic sulphate is freely distributed in blood and does not accumulate in tissues. The normal serum level of sulphate found in humans is 29 mg/L. One of the important roles for inorganic sulphate is in the biosynthesis of 3′-phosphoadenosine-5′-phosphosulphate (PAPS), also known as active sulphate, which is used in the biosynthesis of many essential body compounds, some of which are not absorbed intact when present in foods. Sulphates are usually eliminated by renal excretion in free unbound form or as conjugates of various chemicals. Sulphate that is not absorbed in the upper gastrointestinal tract passes to the large intestine and colon, where it is either excreted in the faeces, reabsorbed or reduced by anaerobic bacteria to metabolites, such as hydrogen sulphide.

The most important studies evaluated in the EFSA (2004) and by JECFA (2000b), and the studies identified in the literature search are summarised below.

Serum concentration, urinary excretion and renal clearance of the sulphate ion were measured in a cross-over clinical trial after administration of sodium sulphate (Morris and Levy, 1983). Six men and two women (age: 26–35 years; weight: 45.5–97.7 kg and body surface area: 1.41–2.24 m^2) were administered a total of 9 g sodium sulphate decahydrate (two doses of 4.5 g/100 mL water an hour apart) or water. There were at least 4 days between interventions. On the days of intervention, administration of the first dose occurred 1–2 h after a light breakfast (hour 0). The subjects emptied their bladder at hour 1 and urine was collected from hour 1 to hour 3. Blood was drawn at hour 2 post-dosing. Sodium sulphate ingestion induced statistically significantly increase of inorganic sulphate concentrations in serum (mean ± SD: 0.51 ± 0.06 vs. 0.41 ± 0.04 mM) and in urinary excretion (mean ± SD: 2.36 ± 0.87 vs. 1.55 ± 0.46 mmol/1.73 m^2). Compared to the control level, the renal clearance of inorganic sulphate was greater after administration of sodium sulphate but did not reach statistical significance (mean ± SD: 38 ± 13 vs. 32 ± 10 mL/min per 1.73 m^2).

A total of five healthy men (25–36 years) received 18.1 g of sodium sulphate decahydrate (equivalent to 8 g of anhydrous sodium sulphate) in 50 mL of water on two occasions at least 1 week apart (Cocchetto and Levy, 1981). Prior to the intervention, all subjects had collected three separates 24-h urine samples for determination of baseline free sulphate output. After an overnight fast the

subjects consumed breakfast, emptied their bladder and ingested the dose of sodium sulphate either as a single dose or in four equally divided hourly doses. All urine was collected over 0–24, 24–48 and 48–72 h. Urinary free (inorganic) sulphate and total sulphate (the sum of free and organically bound sulphate) were determined. The cumulative amounts of free sulphate excreted in the urine 24, 48 and 72 h after sodium sulphate administration were statistically significantly larger than the amount of free sulphate excreted in the 24-h baseline samples ($p < 0.01$). The average urinary recovery of administered sulphate, calculated as the 72-h excretion of free sulphate minus the baseline excretion, averaged 53.4% from the single dose and 61.8% from the divided doses. The single bolus doses caused diarrhoea, while divided doses caused only mild or no diarrhoea.

Eight healthy male volunteers were administered 1 mL radioactive sulphate-35 (60–80 μCi ^{35}S/mL) in the oral cavity followed by 20–30 mL water (Bauer, 1976). Prior to the administration, all subjects were fasted and fluid restricted overnight until completion of the study. Blood was sampled at 10–60 min intervals for 4 h. A 24-h urine sample was collected from four subjects. According to the authors, radioactive ^{35}S demonstrated slow absorption from the gastrointestinal tract over a 10–30 min period, followed by a rapid absorption phase until peak plasma activity was achieved at 60–105 min. The mean ± SEM (n = 4) recovery of ^{35}S in 24-h urine was 79.9 ± 2.2%.

Eight healthy men consumed 0.58–0.78 mg sodium [^{34}S]sulphate/kg bw (n = 4) or 0.5 mg sodium [^{34}S]sulphate/kg bw (n = 4) (Hamadeh et al., 1999). The purity of sodium [^{34}S]sulphate was between 93 and 99%. Subjects were studied at 0700 h in the post absorptive state. Blood samples were drawn before and 30, 60, 90, 120, 180, 240 and 300 min after administration of sodium [^{34}S]sulphate. On average, sodium [^{34}S]sulphate reached a maximum in serum 2 h after oral administration.

Overall, absorption of sulphate from the gastrointestinal tract depends upon the amount of sulphate ingested as absorption of the sulphate ion occurs by active transport. After absorption sulphate is freely distributed in blood and does not accumulate in tissues. Sulphates are usually eliminated by renal excretion however at high doses, sulphate is also excreted in faeces.

3.5.2. Acute toxicity

Sprague–Dawley rats (minimum five animals/sex per group except for the highest dose group, which only included five males) were given single oral doses of 0, 1,750, 2,000, 2,250, 2,500, 3,000 or 3,500 mg/kg bw sodium hydrogen sulphate by gavage. Surviving animals were killed after 14 days. The oral median lethal dose (LD_{50}) was 2,800 mg/kg bw in males and > 2,500 mg/kg bw in females. Effects other than death observed during the study included weight loss, dehydration, scruffy coats and lethargy. Gross abnormalities observed in animals that died during the study included mottled red lungs, pale mottled livers and stomach lesions of ruptures (Northview-Pacific-Laboratories-Inc, 1990).

Wistar rats and ddy mice (three animals/sex per group) were orally treated with a single dose of 2,000 mg ammonium sulphate/kg bw (Yamanaka et al., 1990). The ammonium sulphate was dissolved in water. According to the authors, none of the animals died and an approximate LD_{50} for both rats and mice was established at > 2,000 mg ammonium sulphate/kg bw.

Overall, an LD_{50} value for sodium hydrogen sulphate > 2,500 mg/kg bw has been reported for rats and for ammonium sulphate > 2,000 mg/kg bw has been reported for rats and mice. The Panel considered sodium hydrogen sulphate and ammonium sulphate of low acute toxicity.

3.5.3. Short-term and subchronic toxicity

F344 rats (10 animals/sex per group) were fed a CRF-1 powder diet containing 0, 0.38, 0.75, 1.5 or 3% ammonium sulphate for 13 weeks (Takagi et al., 1999). Body weights and organ weights were recorded and haematological, serum biochemical and histopathological examinations were conducted. No effects were noticed, except for diarrhoea in males from the 3% group, which the Panel considered treatment-related but not as an adverse effect.

Based on the results, the Panel considered the 3% ammonium sulphate in the diet (equivalent to 2,700 mg/kg bw per day, corresponding to 2,025 mg sulphate kg bw/day) as the no observed adverse effect level (NOAEL), the highest dose tested.

3.5.4. Genotoxicity

In vitro

Potassium sulphate was tested in the Ames test with Salmonella Typhimurium TA100 and TA98 at concentrations 0.83, 1.66, 3.33 and 5 mg/plate and without metabolic activation and did not induce mutations (Kayraldiz et al., 2006).

Ammonium sulphate was tested for mutagenicity in an *in vitro* mammalian cell gene mutation assay (OECD Guideline 476; Good Laboratory Practice (GLP) compliant) using Chinese hamster V79 cells in two parallel cultures at concentrations 82.5; 165; 330; 660 or 1,320 μg/mL (Wollny, 2010). In one experiment, the treatment time was 4 h with or without metabolic activation while in the other experiment the treatment time was 4 h with metabolic activation and 24 h without metabolic activation. At the applied experimental conditions, sodium sulphate did not induce mutations in the hypoxanthine-guanine phosphoribosyl transferase (HPRT) locus in V79 cells.

Obe et al. (1986) studied induction of chromosomal aberrations by restriction endonuclease Alu I in human peripheral lymphocytes *in vitro*. The effect of Alu I on chromosomal aberrations was more pronounced in the presence of ammonium sulphate, whereas ammonium sulphate alone (single dose 3.2 M (432 mg/mL); 3-h exposure) did not induce structural chromosomal aberrations in isolated human peripheral lymphocytes.

In European Chemicals Agency (ECHA), dossiers are reported genotoxicity studies of ammonium and sodium sulphate that were not available to the Panel. In the bacterial reverse mutation assay with Salmonella Typhimurium, ammonium and sodium sulphate were negative. Sodium sulphate was negative in the vitro mammalian cell gene mutation assay with mouse lymphoma L5178Y cells and in the *in vitro* chromosomal aberration assay with Chinese hamster lung fibroblasts (as cited by ECHA, available at https://echa.europa.eu/registration-dossier/-/registered-dossier/15539/7/7/1 and https://echa.europa.eu/registration-dossier/-/registered-dossier/15571/7/7/1).

In summary, potassium sulphate did not show a genotoxic potential in the Ames test (Kayraldiz et al., 2006). Ammonium sulphate was not mutagenic in an *in vitro* gene mutation assay using Chinese hamster V79 cells (Wollny, 2010) and did not induce chromosomal aberration in primary peripheral lymphocytes (Obe et al., 1986). Ammonium and sodium sulphate are reported to be negative in the Salmonella Typhimurium reverse mutation assay and sodium sulphate is reported to be negative in the *in vitro* mammalian cell gene mutation assay and *in vitro* chromosomal aberration assay (as cited by ECHA).

Overall, the Panel considered that the available data do not indicate genotoxicity for potassium, ammonium and sodium sulphates. No data were found in the literature for sulphuric acid and calcium sulphate, but the Panel considered that genotoxic properties of these substances will not be essentially different from the salts for which data were available.

3.5.5. Chronic toxicity and carcinogenicity

Mice

CBAxC57B1 mice (30 males and 27 females per group) were given 0.2 mL of a 0.2% sulphuric acid water solution by gavage once a week for lifetime; the control group was not treated (Uleckiene and Griciute, 1997). The animals were observed for their entire life. Necropsy was performed on all animals, which were killed when moribund or found dead. Gross examination was performed on all organs. Histopathological examinations were performed on trachea, lungs, oesophagus, stomach, spleen, liver, kidney and all other organs in which pathological changes were identified. Hyperplasia of the epithelium, hyperkeratosis and acanthosis were frequently observed in the forestomach of treated mice, but there was no significant difference in the number of mice with benign or malignant tumours between the treated group and the untreated control.

The Panel noted that the control group was not treated with the vehicle (water) by gavage. The histopathological changes observed in the forestomach of the treated group may be related to the treatment by gavage and the strong acidity of sulphuric acid. The Panel also noted that these observations have no relevance for the evaluation of the safety of sulphuric acid as food additive, given the buffer capacity of foods.

Rats

Ammonium sulphate has been investigated for chronic toxicity and carcinogenicity in F344/DuCrj rats (Ota et al., 2006). In the chronic toxicity study, 10 animals/sex per group were given 0, 0.1, 0.6

or 3% ammonium sulphate in the diet (equivalent to 0, 50, 300 or 1,500 mg ammonium sulphate/kg bw per day or 0, 36, 218 or 1,090 mg sulphate/kg bw per day) for 52 weeks. In the carcinogenicity study, 50 animals/sex per group were given 0, 1.5 or 3% ammonium sulphate in the diet (equivalent to 0, 750 or 1,500 mg ammonium sulphate/kg bw per day or 0, 545 or 1,090 mg sulphate/kg bw per day) for 104 weeks. The Panel noted that the study was with two instead of three treatment groups and as such did not comply OECD TG 453. During the treatment period, clinical signs and mortality were observed daily, and body weight and food consumption were recorded every 2 weeks until week 10 and every 5 weeks thereafter. At the end of the treatment period (52 and 104 weeks, respectively), all survivors were sacrificed. In the chronic toxicity study, haematological parameters and clinical biochemistry parameters were examined by the end of the study period (52 weeks). Urinalysis was not performed. Organ weights were recorded for brain, lungs, heart, spleen, liver, adrenals, kidneys and testes. Histopathological examination was performed on organs and tissues from control and 3% group animals in the chronic toxicity study and from all groups in the carcinogenicity study. Macroscopically abnormal sites in the 0.1% and 0.6% group animals in the chronic toxicity study were also histopathologically examined. No mortality occurred in the chronic toxicity study. In the carcinogenicity study, the survival rates were 88/76%, 78/80% and 76/80% (males/females) of control, 1.5% and 3.0% groups, respectively. No clinical signs of toxicity were observed and no changes in body weight or food consumption were noted except for a tendency to increased food intake in the high-dose males (3% group) in the chronic toxicity study. No significantly dose-related changes were observed in any of the haematological or biochemical parameters in the chronic toxicity study. Statistically significant changes in relative organ weights included increased liver weight (males) and kidney weights (both sexes) at the highest dose level (3%) in the chronic toxicity study. According to the authors, there were no obvious macroscopic findings in any group in either the chronic toxicity or carcinogenicity studies. There were no significant differences in the incidences of non-neoplastic histopathological lesions between the groups in either the chronic toxicity study or in the carcinogenicity study, except for an increased incidence of chronic nephropathy in the kidney of males of the 1.5% and 3.0% groups in the carcinogenicity study (1.5%: 29/48 animals, statistically significant; 3.0%: 28/50 animals, not statistically significant). The incidence in the control group was 19/50. The Panel noted that chronic progressive nephropathy (CPN) is a spontaneous disease in laboratory rats that progresses with age and ultimately involves the whole kidney typically over 18 months of age. Males are more affected than females. CPN is a rodent-specific entity and is regarded as having no relevance for extrapolation in human risk assessment (Haschek and Rousseaux, 2013).

Neoplastic lesions in the carcinogenicity study included phaeochromocytomas of the adrenal in the male 3 % group and adenomas in the anterior pituitary in females of the 3% group. The Panel noted that phaeochromocytomas and pituitary adenomas occur spontaneously with high frequency in many strains of laboratory rats, including the F344 and Wistar rat. The incidence of benign phaeochromocytomas in 2-year-old F344 rats may be up to 20% in males and 4% in females, and varies considerably among studies (Haschek and Rousseaux, 2013). The high frequency of spontaneous pituitary adenomas in laboratory rats is a well-recognised phenomenon. There is a striking degree of strain variations in the incidence of pituitary tumours in rats which has been reported to range from 10% to more than 90%. In the F344 rat, adenomas were identified in up to 95% of the animals at 24 months of age. Moreover, phaeochromocytomas of the adrenal medulla and pituitary adenomas are considered not relevant for the human situation (Gold et al., 2001; Greim et al., 2009). Based on the results in the chronic toxicity and carcinogenicity studies and the aforementioned evaluations and considerations, the Panel considered 3% ammonium sulphates in the diet (equivalent to 1,500 mg ammonium sulphate/kg bw per day corresponding to 1,090 mg sulphate/kg bw per day) as the NOAEL, the highest dose tested.

Wistar rats (30 animals/sex per group) were given 0.5 mL 0.6% sulphuric acid water solution by gavage once a week for lifetime; the control group was not treated (Uleckiene and Griciute, 1997). The animals were observed for their entire life. Necropsy was performed on all animals, which were killed when moribund or found dead. Gross examination was performed on all organs. Histopathological examinations were performed on trachea, lungs, oesophagus, stomach, spleen, liver, kidney and all other organs in which gross changes were identified. The survival of treated animals was shorter than that of the control animals and the survival of treated males was shorter than that of treated females. The number of animals with tumours was statistically significantly higher in the treated group (38.8%) compared to the untreated control (22.8%). The only increase in tumour incidence over control was in the case of forestomach tumours. Hyperplasia of the epithelium of the forestomach, hyperkeratosis and acanthosis were frequently observed in the treated group. The Panel noted that the control group was not treated with the vehicle (water) by gavage. The histopathological changes observed in the

forestomach of the treated group may be related to the treatment by gavage and the strong acidity of sulphuric acid. The Panel also noted that these observations have no relevance for the evaluation of the safety of sulphuric acid as food additive, given the buffer capacity of foods.

Overall, based on the results of the chronic toxicity and carcinogenicity studies in rats, the Panel considered that ammonium sulphate is not carcinogenic and that the no observed adverse effect level (NOAEL) is 1,090 mg sulphate/kg bw per day, the highest dose tested (Ota et al., 2006).

3.5.6. Reproductive and developmental toxicity

Reproductive toxicity studies

Mice

Random bred ICR virgin female mice (10 animals per group) were given 0 (control), 0 (sodium control, sodium bicarbonate), 924, 1,848, 3,696 or 7,392 mg/L reagent grade sodium sulphate in water (equivalent to 0, 0, 139, 277, 554 and 1,109 mg/kg bw per day, respectively (Andres and Cline, 1989). The concentration of sodium was equal in all groups except for the control group (deionised, distilled water; sodium concentration 0 mg/L). After one week of administration, the female mice were mated with untreated males. Dams were allowed to have two litters and treatment was continued during each parity. Water consumption was measured daily during the 2nd and 3rd week of gestation and the 1st and 2nd week of lactation. At parturition, the dams were weighed, and litter size was recorded. The litters were subsequently standardised to 8 pups per litter. At day 21 postpartum the pups were weaned and the litters and dams were weighed individually. The dams were rebred at first oestrus following weaning. Only animals that littered during each parity were used in the analysis. All groups of animals given sodium sulphate drank less water than the sodium control group but more than the control group during both gestation and lactation (group size between 4 and 9 mice). Maternal body weight gains during gestation and lactation and litter size were comparable between the groups. The Panel noted that this study cannot be used for risk assessment due to the study design, low numbers of dams per groups and limitations in reporting.

Developmental studies

Mice

Pregnant ICR/SIM mice (28 animals per group) were dosed with sodium sulphate (2,800 mg/kg bw per day) or water by gavage on gestation days (GD) 8 through 12 (Seidenberg et al., 1986). All mice were weighed on GD 7 and 13 and postnatal day (PND)1. Neonates were examined, counted and weighed on PND 1 and 3. Dead neonates were externally examined for abnormalities. Dams that had not given birth by GD 21 or 22 were necropsied and their uteri were examined. The average neonatal weight at PND 1 was statistically significantly higher than that of controls (g $\pm$ SD: 1.8 $\pm$ 0.14 vs. 1.72 $\pm$ 0.13). No other statistically significant effects were observed in neonates or in dams. The Panel noted that only one dose group treated with sodium sulphate was included in the study and the study design was limited did not allow use this study for risk assessment.

Pigs

A total of 31 sows and 27 gilts of Hampshire X Yorkshire X Duroc breeding were randomly assigned to three treatments of sodium sulphate in water: control (local water supply containing 320 mg sulphate/L), low sulphate (1,790 mg/L) and high sulphate (3,298 mg/L) (Paterson et al., 1979). The water was available ad libitum from about 30 days post-breeding until 28 days after parturition. At parturition, the number of live and stillborn piglets was counted, and the average piglet weight was obtained. Litter weight was recorded at parturition and PND 14 and 28. Number of piglets and average piglet weight was also recorded at PND 28. There were no adverse effects of sodium sulphate in the drinking water observed on maternal body weight gain during gestation or lactation and number or body weight of piglets at birth or at weaning. Based on the results, the authors concluded that sulphate up to 3,298 mg/L in water had no significant effect on reproduction in the gilt or sow. In addition, the authors described a 28-day study in 4-week-old piglets. Nine groups, each group consisted of two 4-week-old pigs from the three treatment groups. These groups were randomly allotted to three replications of three treatments: (1) control water, (2) 3,000 mg sulphate/L as sodium sulphate and (3) 3,000 mg sulphate/L equally from magnesium and sodium sulphate. No statistically significant differences between body weight gains and feed efficiency were observed. Water consumption increased significantly in the sulphate-treated groups when compared to the control.

Faecal condition in the sulphate groups was statistically significant less firm compared to the control group. The Panel noted several limitations in the reporting of the study such as the number of sows and gilts which were initially used per group and the number of females that did not litter per group (sows or gilts).

Overall, no reproductive or developmental toxicity studies according to the current OECD Guidelines were available and the Panel considered the available studies not adequate for risk assessment.

3.5.7. Hypersensitivity, allergenicity and food intolerance

No data available.

3.6. Discussion

Sulphuric acid (E 513), sodium sulphates (E 514), potassium sulphates (E 515), calcium sulphate (E 516) and ammonium sulphate (E 517) are authorised as food additives in the EU, in accordance with Annex II and/or Annex III to Regulation (EC) No 1333/2008 and specific purity criteria have been defined in the Commission Regulation (EU) No 231/2012.

They were previously evaluated by JECFA several times, the latest in 2010 (JECFA, 2010b) and the SCF in 1991 (SCF, 1991). Both committees established a group ADI 'not specified' for sulphuric acid and its sodium, potassium, calcium and ammonium salts.

Specifications for sulphuric acid, sodium sulphate, sodium hydrogen sulphate, potassium sulphate, potassium hydrogen sulphate, calcium sulphate and ammonium sulphate have been defined in the EU in Commission Regulation (EU) No 231/2012 and in regard to sulphuric acid, sodium sulphate, sodium hydrogen sulphate, potassium sulphate and calcium sulphate also by JECFA (JECFA, 2006a,b, 2009a).

Absorption of sulphate from the gastrointestinal tract depends upon the amount of sulphate ingested as absorption of the sulphate ion occurs by active transport. After absorption sulphate is freely distributed in blood and does not accumulate in tissues. Sulphates are usually eliminated by renal excretion; however at high doses, sulphate is also excreted in faeces.

The Panel noted that sulphates are of low acute oral toxicity.

In a subchronic oral toxicity study in rats, no effects were noticed, except for diarrhoea in males at dose of 2,025 mg sulphate/kg bw/day, which the Panel considered treatment-related but not as an adverse effect. Based on the results, the Panel considered the 2,025 mg sulphate/kg bw/day as the NOAEL, the highest dose tested.

The Panel considered that the available data do not indicate genotoxicity for potassium, ammonium and sodium sulphates. No data were available for sulphuric acid and calcium sulphate, but the Panel considered that genotoxicity of these substances will not be essentially different from the salts for which data were available.

Based on the results of the chronic toxicity and carcinogenicity studies in rats, the Panel considered that ammonium sulphate is not carcinogenic and that the no observed adverse effect level (NOAEL) is 1,090 mg sulphate/kg bw per day, the highest dose tested.

No reproductive or developmental toxicity studies suitable for risk assessment were available. However, no effects on reproductive organs were observed in the repeated dose toxicity studies.

Based on information from the Mintel's GNPD, the Panel considered that sodium sulphates, potassium sulphates and calcium sulphate (E 514, E 515, E 516) are not likely to be used in combination in the same food product and, therefore, an exposure assessment was performed considering the highest reported use level for either E 514, E 515 and E 516 per food category. No use levels for sulphuric acid (E 513) and ammonium sulphate (E 517) were reported (Section 3.3.1).

Dietary exposure to sulphuric acid and its sodium, potassium, calcium and ammonium salts (E 513, E 514, E 515, E 516, E 517) from their use as food additives was calculated according to different exposure scenarios based on the provided use levels, as described in Section 3.4.1 and was expressed as sulphate. The Panel considered that the refined exposure assessment scenario resulted in more realistic long-term exposure estimates compared to the *maximum level exposure assessment scenario* which was considered very conservative.

Panel considered the *non brand-loyal scenario* covering the general population as the most appropriate scenario for risk characterisation (see Section 3.4.1).The Panel estimated that in the *refined estimated exposure non brand-loyal scenario*, mean exposure ranged from 0.4 mg sulphate/kg bw per day in infants to 35 mg sulphate/kg bw per day in toddlers. The 95th percentile of exposure ranged from 3 mg sulphate/kg bw per day in adolescents to 68 mg sulphate/kg bw per day in toddlers.

The Panel considered that the uncertainties in exposure assessment identified would, in general, result in an overestimation of the exposure to sulphate derived from the use of sulphuric acid and its sodium, potassium, calcium and ammonium salts (E 513, E 514, E 515, E 516, E 517) for all exposure scenarios.

The Panel noted that the exposure to sulphuric acid and its sodium, potassium, calcium and ammonium salts (E 513, E 514, E 515, E 516, E 517) from their use as food additives expressed as sulphate according the Annex III (Parts 1, 2, 3, 4 and 5A) was not considered in the exposure assessment.

The Panel also noted that the refined exposure estimates are based on information provided on the reported level of use of sulphuric acid and its sodium, potassium, calcium and ammonium salts (E 513, E 514, E 515, E 516, E 517). If actual practice changes, this refined estimate may no longer be representative and should be updated.

Data in humans indicated that sodium sulphate at 300 mg/kg bw and higher (corresponding to 207 mg sulphate/kg bw) induced laxative effect. The Panel noted that the exposure to sulphates at mean and 95th percentile in the *non brand-loyal scenario* as well as in the other scenarios, is far below this dose.

4. Conclusions

Sulphate is a natural constituent of human, animals and plants and is present in all biological materials, including foodstuffs. Based on the toxicological database available, the Panel concluded that the exposure to sulphuric acid (E 513), sodium sulphate (E 514), potassium sulphates (E 515), calcium sulphate (E 516) and ammonium sulphate (E 517) does not raise a safety concern at the reported uses and use levels and there is no need for a numerical ADI.

5. Recommendations

The Panel recommended that the European Commission considers lowering the current limits for toxic elements (arsenic, lead and mercury) in the EU specifications for sulphuric acid (E 513), sodium sulphates (E 514), potassium sulphates (E 515), calcium sulphate (E 516) and ammonium sulphate (E 517) in order to ensure that sulphuric acid (E 513), sodium sulphates (E 514), potassium sulphates (E 515), calcium sulphate (E 516) and ammonium sulphate (E 517) as a food additive will not be a significant source of exposure to those toxic elements in food.

Documentation provided to EFSA

1) EFSA-Q-2011-00662_Manufacturing process Submitted by LANXESS on 2017-11-22.
2) EFSA-Q-2011-00662_Analytical data Impurities_Sulphuric acid. Submitted by LANXESS on 2017-11-22.
3) Scientific Data for the Re-Evaluation of the Food Additive Sodium Hydrogen Sulphate (E 514ii). Submitted by Jones-Hamilton Co. December 2010.
4) Call for Data food additives-E 514ii Sodium hydrogensulphate. Submitted by Grillo-Werke Aktiengesellschaft March 2013.
5) Bundesamt für Verbraucherschutz und Lebensmittelsicherheit. Aufruf der EFSA-052/2012 zur Neubewertung diverser in der EU zugelassener Lebensmittelzusatzstoffe unterschiedlicher Funktionsklassen im Kontext der Verordnung (EG) Nr. 1333/2008 des Europäischen Parlaments und des Rates vom 16. Dezember 2008 über Lebensmittelzusatzstoffe. February 2012.
6) EFSA-Q-2011-00662 Submitted by Polish EFSA Focal Point, July 2012.
7) EUROGUM A/S, 2014. Data on usage levels of calcium sulphate (E 516) 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 (Batch 5). Submitted to EFSA on 30 September 2014.
8) FDE (Food Drink Europe), 2017. Data on usage levels of sodium sulphate (E 514), potassium sulphate (E 515) and calcium sulphate (E 516) 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 (Batch 5). Submitted to EFSA on 1 February 2017.
9) Pre-evaluation document prepared by DTU Food, 2/10/2014.

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Abbreviations

ADI	Acceptable Daily Intake
AES	atomic emission spectroscopy, inductively coupled plasma atomic emission spectroscopy (ICP-AES) (also known as)
bw	Body Weight
Ca	Calcium
CAS	Chemical Abstract Service
CPN	chronic progressive nephropathy
CHA	European Chemicals Agency
EINECS	European Inventory of Existing Commercial chemical Substances
F-AAS	flame atomic absorption spectrophotometry
F_1	First generation pups
F_2	Second generation pups
FAF	Food Additives and Flavourings
GD	Gestation Days
GLP	Good Laboratory Practice
GNPD	Global New Products Database
GMP	Good Manufacturing Practice
HPRT	hypoxanthine-guanine phosphoribosyl transferase
JECFA	Joint FAO/WHO Expert Committee on Food Additives
ICP-AES	inductively couple plasma atomic emission spectroscopy
ICP-OES	inductively coupled plasma optical emission spectrometry
IPCS	International Program on Chemical Safety
K	Potassium
LD_{50}	Lethal dose, 50% i.e. dose that causes death among 50% of treated animals
MPLs	maximum permitted levels
Na	Sodium
NOAEL	No-Observable-Adverse-Effect Level
OECD	Organisation for Economic Co-operation and Development
P_1	First generation adults
P_2	Second generation adults
P_3	Third generation adults
QS	*quantum satis*
SCF	Scientific Committee for Food
TemaNord	Nordic Council of Ministers
WHO	World Health Organization

Appendix A – Summary of reported use levels (mg/kg or mg/L as appropriate) of sodium, potassium and calcium sulphates (E514, E515, E516) provided by industry (no use level provided for E513 and E517)

Appendix B – Number and percentage of food products labelled with sulphuric acid and sodium, potassium, calcium and ammonium sulphates (E513, E514, E515, E516, E517) out of the total number of food products present in the Mintel GNPD per food subcategory between January 2014 and May 2019

Appendix C – Concentration levels of sulfuric acid and sodium, potassium, calcium and ammonium sulphates (E513, E514, E515, E516, E516) expressed as sulphate used in the exposure assessment scenarios (mg/kg or mL/kg as appropriate)

Appendix D – Summary of total estimated exposure of sulfuric acid and sodium, potassium, calcium and ammonium sulphates (E13, E514, E515, E516, E517) expressed as sulphate from their use as food additives for the maximum level exposure scenario and the refined exposure assessment scenarios per population group and survey: mean and 95th percentile (mg/kg bw per day)

Appendix E – Main food categories contributing to exposure to sulfuric acid and sodium, potassium, calcium and ammonium sulphates (E513, E514, E515, E516, E517) using the maximum level exposure assessment scenario and the refined exposure assessment scenarios (> 5% to the total mean exposure)

Appendices A–E can be found in the online version of this output ('Supporting information' section): https://doi.org/10.2903/j.efsa.2019.5868