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Re-evaluation of calcium silicate (E 552), magnesium silicate (E 553a(i)), magnesium trisilicate (E 553a(ii)) and talc (E 553b) as food additives

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Abstract

The EFSA Panel on Food Additives and Nutrient Sources added to Food (ANS) provides a scientific opinion re-evaluating the safety of calcium silicate (E 552), magnesium silicate (E 553a) and talc (E 553b) when used as food additives. In 1991, the Scientific Committee on Food (SCF) established a group acceptable daily intake (ADI) 'not specified' for silicon dioxide and silicates. The EFSA Panel on Food Additives and Nutrient Sources added to Food (ANS) recently provided a scientific opinion re-evaluating the safety of silicon dioxide (E 551) when used as a food additive. The Panel noted that the absorption of silicates and talc was very low; there was no indication for genotoxicity or developmental toxicity for calcium and magnesium silicate and talc; and no confirmed cases of kidney effects have been found in the EudraVigilance database despite the wide and long-term use of high doses of magnesium trisilicate up to 4 g/person per day over decades. However, the Panel considered that accumulation of silicon from calcium silicate in the kidney and liver was reported in rats, and reliable data on subchronic and chronic toxicity, carcinogenicity and reproductive toxicity of silicates and talc were lacking. Therefore, the Panel concluded that the safety of calcium silicate (E 552), magnesium silicate (E 553a(i)), magnesium trisilicate (E 553a(ii)) and talc (E 553b) when used as food additives cannot be assessed. The Panel considered that there is no mechanistic rationale for a group ADI for silicates and silicon dioxide and the group ADI established by the SCF is obsolete. Based on the food supplement scenario considered as the most representative for risk characterisation, exposure to silicates (E 552–553) for all population groups was below the maximum daily dose of magnesium trisilicate used as an antacid (4 g/person per day). The Panel noted that there were a number of approaches, which could decrease the uncertainties in the current toxicological database. These approaches include – but are not limited to – toxicological studies as recommended for a Tier 1 approach as described in the EFSA Guidance for the submission of food additives and conducted with an adequately characterised material. Some recommendations for the revision of the EU specifications were proposed by the Panel.

Keywords: calcium silicate, E 552, magnesium silicate, magnesium trisilicate, E 553°, Talc, E 553b

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Summary

Calcium silicate (E 552), magnesium silicate (E 553a) and talc (E 553b) are authorised as food additives according to Regulation (EC) No 1333/2008 on food additives and specifications have been defined in the Commission Regulation (EU) No 231/2012[1] for calcium silicate (E 552), magnesium silicate (E 553a(i)), magnesium trisilicate (E 553a(ii)) and talc (E 553b).

In 1991, the Scientific Committee on Food (SCF) established a group acceptable daily intake (ADI) 'not specified' for sodium silicate, silicon dioxide, calcium silicate, magnesium silicate and potassium silicate.

Although calcium silicate (E 552) and magnesium silicate (E 553(i)) may be described in terms of theoretical oxides, the Panel concluded that they are not mixtures of silicon dioxide and calcium or magnesium oxides; therefore, their definitions in the European Union (EU) specifications should be revised accordingly.

Information on particle size of calcium silicate analysed by laser diffraction (LD) and transmission electron microscopy (TEM) were provided. The Panel noted that these methods measure different particle characteristics, which are reflected in the different numerical size-values obtained. Taking into account the analysis by TEM provided by industry, calcium silicate falls under the definition of a nanomaterial according to the Commission Recommendation 2011/696/EU. However, the Panel considered that the dispersion method (sonication) of the sample before its analysis by TEM is not representative of the common use of calcium silicate as a food additive. Following an European Food Safety Authority (EFSA) request, no TEM data were provided for magnesium silicate (E 553a(i)) and magnesium trisilicate (E 553a (ii)). Scanning electron microscope (SEM) data for talc indicated a particle size distribution of 20–40 μm.

The Panel considered that crystalline silica, fluoride, aluminium and nickel may be present in associated minerals in talc (E 553b) and, then, they could be present also in the food additive E 553b. Therefore, maximum limits for them should be established in the EU specifications for talc (E 553b).

The Panel considered that silicate anion from both calcium silicate or magnesium trisilicate was absorbed to a limited extent in rats. No data were available for magnesium silicate.

Based on a 2-year study with calcium silicate in rats, the Panel considered that at high doses (up to 5,000 mg/kg body weight (bw) per day), there was evidence of silicon accumulation in the liver and kidney. The Panel considered that limited data in humans indicated that the silicate anion from magnesium trisilicate is absorbed to a limited extent, then excreted in the urine (as determined from urinary silicon measurements). No human data were available for calcium silicate or magnesium silicate; however, the Panel considered that a read-across approach was appropriate and considered that silicate anion from both calcium silicate or magnesium silicate would behave similarly.

The Panel noted that studies with synthetically produced talc in mice, rat and guinea pigs as well as talc (baby powder) in hamsters indicated that less than 2% talc was systemically available, with low levels seldom found in the liver.

The Panel considered that calcium silicate (E 552), magnesium silicate (E 553a(i)), magnesium trisilicate (E 553a(ii)) and talc (E 553b) dissociate to a limited extent in the gastrointestinal tract into silicates and their corresponding cations. The resulting low amounts of calcium and magnesium ions were considered not to disturb normal physiological processes and therefore, are not discussed further in this opinion.

The Panel considered that calcium silicate, magnesium silicate and talc have a low acute oral toxicity. No studies were available for magnesium trisilicate.

No adverse effects were observed in short-term toxicity studies in rats with calcium silicate, magnesium trisilicate or talc. The kidney effects observed in dogs were most probably related to the large amount of test compound consumed as a bolus dose by the animals. The effects on the kidney reported in guinea pigs could be due to higher concentrations of silicate in the primary urine as a consequence of lower glomerular filtration rates in guinea pigs (2.29 mL plasma/min per kg) as compared to rats (4.63 mL plasma/min per kg). The Panel noted that in humans the glomerular filtration rate (3.56 mL plasma/min per kg) is higher than in guinea pigs and, furthermore, kidney effects have not been found in humans in the EudraVigilance database despite the wide and long-term use of high doses of magnesium trisilicate (up to 4 g/person per day) as an antacid over decades.

The Panel considered that the available data did not raise concern with respect to genotoxicity of calcium silicate (E 552), magnesium silicate (E 553a(i)), magnesium trisilicate (E 553a(ii)) and talc (E 553b) when used as food additives.

[1] 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.

In a 2-year study in rats, not performed according to current standards, calcium silicate had no effect on mortality at a dose up to 5,000 mg/kg bw per day. No gross pathology or histopathological findings that could be attributed to calcium silicate were observed in the 500 and 2,500 mg/kg bw per day groups. However, in the absence of clinical chemistry data, given the respiratory infection of animals and only 15 animals/sex per group, the Panel considered that this study was too limited to conclude on the chronic toxicity of calcium silicate. However, the Panel noted that no carcinogenic effects were reported in this study. There were no data for oral chronic toxicity/carcinogenicity of talc.

No reproductive toxicity studies were available. Prenatal developmental toxicity studies with calcium silicate by gavage during organogenesis in mice, rats and hamsters, and with talc in mice and rats, up to 1,600 mg/kg bw per day (the highest dose tested), showed no dose-related developmental effects.

The Panel noted that cases of renal calculi were rarely reported considering the high number of exposed humans to magnesium trisilicate used as an antacid. The Panel applied the WHO algorithm for assessing the association between adverse events and drug intake, and found that the association between silicate antacid use and renal calculi was 'possible' but not 'definite', which does not exclude that the occurrence of renal calculi and intake of silicates would be a chance finding.

In the available data on subacute toxicity, genotoxicity and developmental toxicity studies, no adverse effects were reported for silicates and talc. From the only chronic toxicity study (with calcium silicate) available, there was no indication for carcinogenicity. However, due to the limitations of this study, it was not possible to draw a reliable conclusion on the chronic toxicity and carcinogenicity of calcium silicate. Furthermore, no subchronic and reproductive toxicity studies with silicates or talc were available.

The Panel noted that in 1991, the SCF established a group ADI 'not specified' for sodium silicate, silicon dioxide, calcium silicate, magnesium silicate and potassium silicate presumably on the basis that they share a common moiety. The Panel noted that more recent evidence suggested that this assumption might not be valid. Therefore, the Panel considered that on the evidence currently available, there is no mechanistic rationale for a group ADI for silicates and silicon dioxide. Therefore the Panel considered this group ADI obsolete.

Due to the limitations in the available toxicological database for individual silicates, the Panel was unable to derive ADIs for calcium silicate (E 552), magnesium silicate (E 553a(i)), magnesium trisilicate (E 553a(ii)) and talc (E 553b).

Silicates (E 552–553) are authorised in 28 food categories, including FC 0, according to Annex II to Regulation (EC) No 1333/2008. Their use in FC 0 means that they are 'permitted in all categories of foods excluding foods for infants and young children, except where specifically provided for'. Silicates (E 552–553) are also authorised according to Annex III to Regulation (EC) No 1333/2008 (Parts 1, 2 and 5 A) in food-improving agents and nutrients, except nutrients intended for foods for infants and young children. As such, silicates (E 552–553) can be found in many foods via carry-over. The industry provided use levels for silicates (E 552–553) for their use according to Annex II. No analytical data on the concentration of these food additives in foods were made available by the Member States.

Dietary exposure to silicates (E 552–553) from their use as food additives according to Annex II was calculated for different exposure scenarios based on the provided use levels. 98% of the reported use levels referred to the use of talc (E 553b). This was in line with the information from the Mintel's Global New Products Database (GNPD), showing that 89% of the foods labelled with silicates (E 552–553) were labelled to contain talc (E 553b). Therefore, the Panel noted that the calculated exposure reflects chiefly the exposure to talc (E 553b).

Additionally, 91% of the reported use levels were related to the use of silicates in food supplements. The Panel noted that the main food category labelled with silicates (E 552–553) in the Mintel GNPD was also food supplements (Appendix B). Therefore, the Panel considered the food supplements consumers only scenario as the most appropriate scenario for risk characterisation of silicates (E 552–553). Dietary exposure to silicates (E 552–553) via this exposure scenario was up to 31 mg/kg bw per day at the mean level in children and up to 46 mg/kg bw per day at the high (P95) level in the elderly.

The exposure assessment was hampered by several uncertainties. Overall, it was considered that the exposure was most likely overestimated due to the use levels used and assumptions made in the exposure assessment. Furthermore, the Panel noted that no foods belonging to an important contributing food category in all population groups, i.e. ripened cheese, were labelled to contain silicates (E 552–553) according to the Mintel GNPD.

The Panel noted that:

- the absorption of silicates and talc was very low;
- there was no indication for genotoxicity or developmental toxicity for calcium and magnesium silicate and talc;
- no confirmed cases of kidney effects have been found in the EudraVigilance database despite the wide and long-term use of high doses of magnesium trisilicate up to 4 g/person per day over decades.

However, the Panel considered that accumulation of silicon from calcium silicate in the kidney and liver was reported in rats, and reliable data on subchronic and chronic toxicity, carcinogenicity and reproductive toxicity of silicates and talc were lacking. Therefore, the Panel concluded that the safety of calcium silicate (E 552), magnesium silicate (E 553a(i)), magnesium trisilicate (E 553a(ii)) and talc (E 553b) when used as food additives cannot be assessed.

Based on the food supplement scenario considered as most representative for risk characterisation, exposure to silicates (E 552–553) for all population groups was below the maximum daily dose of magnesium trisilicate used as an antacid (4 g/person per day).

The Panel noted that there were a number of approaches which could decrease the uncertainties in the current toxicological database. These approaches include – but are not limited to – toxicological studies as recommended for Tier 1 approach as described in the EFSA Guidance for the submission of food additives (EFSA ANS Panel, 2012) and conducted with an adequately characterised material. Since the available data showed that nano particles are present in calcium silicate (E 552), the studies should be conducted with a material that contains a fraction of nanoparticles typical for silicates used as food additives.

The Panel recommended that:

- the European Commission considers the revision of the EU specifications for calcium silicate (E 552), magnesium silicate (E 553a(i)), magnesium trisilicate (E 553a(ii)) and talc (E 553b) in order to include better definitions, assays in line with the definitions, and characterisation of particle size distributions (using appropriate statistical descriptors (e.g. range, median, quartiles) as well as the percentages (in number and by mass) of particles in the nanoscale (with at least one dimension < 100 nm). With regard to the characterisation of the particle size distribution, the analytical methodologies applied should comply with those recommended in the EFSA Guidance on risk assessment of the application of nanoscience and nanotechnologies in the food and feed chain (EFSA Scientific Committee, 2018)).
- in first instance, toxicological studies as recommended for a Tier 1 approach as described in the EFSA Guidance for the submission of food additives (EFSA ANS Panel, 2012) should be conducted with adequately characterised material(s) in order to decrease the uncertainties in the current toxicological database.
- more data on the actual usage and use levels of silicates (E 552, E 553a(i)), E 553a(ii)) should be provided because most of the data submitted were for talc (E 553b).
- the European Commission considers lowering the current limits for toxic elements (arsenic, lead and mercury) in the EU specifications for calcium silicate (E 552), magnesium silicate (E 553a(i)), magnesium trisilicate, (E 553a(ii)) and talc (E 553b) in order to ensure that the food additives will not be a significant source of exposure to these toxic elements in food.
- the European Commission considers inclusion of maximum limits for aluminium, nickel, fluoride and crystalline silica (alpha-quartz) in the EU specifications for talc (E 553b).

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1. Introduction

The present opinion document deals with the re-evaluation of calcium silicate (E 552), magnesium silicate (E 553a(i)), magnesium trisilicate (E 553a(ii)) and talc (E 553b) when used as food additives.

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 the European Food Safety Authority (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 EFSA 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.

1.2. Information on existing authorisations and evaluations

Calcium silicate (E 552), magnesium silicate (E 553a) and talc (E 553b) are authorised as food additives according to Regulation (EC) No 1333/2008 on food additives and specifications have been defined in the Commission Regulation (EU) No 231/2012[1] for calcium silicate (E 552), magnesium silicate (E 553a(i)), magnesium trisilicate (E 553a(ii)) and talc (E 553b).

In 1991, the SCF established a group acceptable daily intake (ADI) 'not specified' for sodium silicate, silicon dioxide, calcium silicate, magnesium silicate and potassium silicate. The Committee argued that the available data confirmed the biological inertness of these compounds (SCF, 1991). The

[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.

SCF also concluded that: 'any silicate absorbed is excreted by the kidney without evidence of toxic accumulation in the body, except for the reported damage to dog kidney by magnesium trisilicate and sodium silicate'.

Silicates have been discussed by the Joint FAO/WHO Expert Committee on Food Additives (JECFA) on several occasions (JECFA, 1969, 1974, 1986, 1987). JECFA conducted its first toxicological evaluation of amorphous silicon dioxide, and aluminium, calcium, magnesium and sodium aluminosilicates (including talc and magnesium trisilicate) in 1969 (JECFA, 1969). In this evaluation, it was concluded that 'The available data on orally administered silica and silicates, including flumed silicate dioxide, appear to substantiate the biological inertness of these compounds.[...] This information taken together with human clinical experience and the ubiquitous occurrence of these compounds in the environment does not point to any significant toxic effects when these substances are used as food additives'. Therefore, the use of these substances as food additives was 'not limited except for good manufacturing practice' (JECFA, 1969). In 1974, the toxicological monograph was expanded to include new data (JECFA, 1974). This new evaluation concluded that the ADI for silicon dioxide and certain silicates, except magnesium silicate and talc, to be 'not limited', whereas for magnesium and talc concluded an ADI 'temporarily not limited'. Further studies on magnesium trisilicate elucidating the reported kidney damage in dogs, and long-term feeding studies on talc, specified as free from asbestos-like particles were requested by JECFA in 1974 (JECFA, 1974). In 1976, JECFA reiterated the need for a long-term study on talc (of an acceptable specification) before an acceptable daily intake (ADI) could be established. The committee requested short-term studies to differentiate between medicinal magnesium trisilicate and the insoluble magnesium silicate in food processing. Magnesium silicate was allocated an 'ADI not specified' (JECFA, 1976).

In 1980, JECFA extended the temporary ADI 'not specified' for talc and requested a long-term study by 1983 (JECFA, 1980). However, the study was not available and talc was therefore removed from the agenda in 1983. Owing to the revised specifications (satisfactory method for estimating asbestos and does not contain magnesium trisilicate) for talc by JECFA in 1986, the request for a long-term feeding study was withdrawn. An ADI 'not specified' was allocated for talc, provided that the talc used in food processing complied with the new specifications (JECFA, 1987).

The temporary ADI 'not specified' for magnesium silicate was extended to 1982 because the previously requested dog studies were not available (JECFA, 1980). In 1982, the requested studies were still not available, however the existing tentative specifications were revised excluding magnesium trisilicate and concluded that the ADI status should be reallocated as 'not specified' (JECFA, 1982). This ADI was confirmed in 1986 (JECFA, 1986).

The Nordic Council of Ministers (TemaNord) summarised the findings of JECFA and the SCF and concluded that 'an immediate re-evaluation is not needed but the next evaluation should include a proper carcinogenicity test' (TemaNord, 2002).

The ANS Panel evaluated calcium silicate and silicon dioxide/silicic acid gel added for nutritional purposes to food supplements and concluded that the proposed use and use levels of calcium silicate in food supplements (these vary depending on the formulation, but is normally the quantity necessary to supply not more than 100 mg silicon/day and up to 140 mg calcium/day) is of no safety concern, provided that it complies with the specifications set for its use as a food additive (EFSA ANS Panel, 2009).

The UK Expert Group on Vitamins and Minerals (2003) reviewed data relating to silicon and, although oral toxicity data were sparse, derived a 'Safe Upper Limit' of 25 mg silicon/kg body weight (bw) per day based on a carcinogenicity study that tested silicon dioxide (Takizawa et al., 1988).

The EFSA Panel on Food Additives and Nutrient Sources added to Food (ANS) provided a scientific opinion re-evaluating the safety of silicon dioxide (E 551) when used as a food additive (EFSA ANS Panel, 2018), not covering the silicates (E 552–553).

IARC monographs on silicates and talc were prepared in 1987, 1997 and 2010 (IARC, 1987, 1997, 2010). However, most of the data in these monographs relate to the inhalation toxicity and do not include any good quality oral chronic toxicity or carcinogenicity studies. Hence, the IARC monographs did not make a conclusion on the carcinogenic potential of silicates following oral ingestion.

The Cosmetic Ingredient Review Expert Panel has assessed the safety of talc for use in cosmetics and concluded that talc is safe for use in cosmetics using current practices of use and concentration. However, it was recommended that talc should not be applied to the skin when the epidermal barrier is missing or significantly disrupted (CIR, 2013; Fiume et al., 2015).

Calcium silicate, magnesium silicate, magnesium trisilicate and talc are permitted as ingredients in cosmetic products (European Commission database-CosIng[6]). Calcium silicate is included in the European Union Register[7] of feed additives (Regulation (EC) No 1831/2003[8]).

Calcium silicate (silicic acid, calcium salt; EC Number 215-710-8), magnesium silicate (silicic acid, magnesium salt; EC Number 215-681-1), magnesium trisilicate (dimagnesium trisilicon octaoxide, EC Number 329-076-7) and talc have been registered under the REACH Regulation 1907/2006[9] (ECHA, online).

2. Data and methodologies

2.1. Data

The ANS Panel was not provided with a newly submitted dossier. EFSA launched public calls for data[10,11] to collect information from interested parties.

The Panel based its assessment on information submitted to EFSA following the public calls for data, information from previous evaluations and additional available literature up to May 2018. 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 silicates (E 552–553) were derived from the EFSA Comprehensive European Food Consumption Database (Comprehensive Database[12]).

The Mintel's Global New Products Database (GNPD) was used to verify the use of calcium silicate (E 552), magnesium silicate (E 553a(i)), magnesium trisilicate (E 553a(ii)) and talc (E 553b) in food products. The Mintel's GNPD is an online database that contains the compulsory ingredient information present on the label of numerous food 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 ANS Panel assessed the safety of silicates (E 552–553) 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 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 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 (2000). In these cases, the daily intake was 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 silicates (E 552–553) from their use as food additives was estimated by combining the food consumption data available within the EFSA Comprehensive Database with the maximum permitted levels according to Annex II to Regulation (EC) No 1333/2008 and reported use levels submitted to EFSA following a call for data. The exposure was estimated according to different scenarios (see Section 3.4.1). Uncertainties in the exposure assessment were identified and discussed.

[6] Available online: http://ec.europa.eu/consumers/cosmetics/cosing/index.cfm?fuseaction=search.simple
[7] Available online: http://ec.europa.eu/food/food/animalnutrition/feedadditives/comm_register_feed_additives_1831-03.pdf
[8] Regulation (EC) No 1831/2003 of the European Parliament and the Council of 22 September 2003 on additives for use in animal nutrition. OJ L 268, 18.10.2003, 29–43.
[9] Regulation (EC) No 1907/2006 of the European Parliament and of the Council of 18 December 2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH). OJ L 396, 30.12.2006.
[10] Call for scientific data on miscellaneous food additives permitted in the EU and belonging to several functional classes. Published: 15 February 2012. Available online: https://www.efsa.europa.eu/sites/default/files/consultation/120215.pdf
[11] Call for food additives usage level and/or concentration data in food and beverages intended for human consumption (Batch 5). Published 24 May 2016. Available online: https://www.efsa.europa.eu/en/data/call/160524
[12] Available online: http://www.efsa.europa.eu/en/food-consumption/comprehensive-database

3. Assessment

3.1. Technical data

3.1.1. Identity of the substances

Calcium silicate (E 552)

According to Commission Regulation (EU) No 231/2012, the food additive calcium silicate (E 552) is defined as 'a hydrous or anhydrous silicate with varying proportions of CaO and SiO_2. The product should be free of asbestos'. No molecular formula or molecular weight is indicated. The EINECS/EC Number is 215-710-8 and its chemical name is calcium silicate.

Calcium silicate (E 552) is described in Commission Regulation (EU) No 231/2012 as a white to off-white free-flowing powder that remains so after absorbing relatively large amounts of water or other liquids.

According to industry (CEFIC, 2017a (Documentation provided to EFSA n. 4)), calcium silicate (E 552) is the silicic acid salt of calcium with CAS 1344-95-2 and EINECS No 215-710-8. While it can be described in terms of hypothetical oxides, it is not a mixture of silicon dioxide and calcium oxide. The Panel noted that X-ray diffraction data (CEFIC, 2017a (Documentation provided to EFSA n. 4)) confirmed that calcium silicate is not a mixture of silicon dioxide and calcium oxide.

According to the EC inventory (online),[13] the molecular formula for EC No 215-710-8 is CaO_3Si and the structural formula is shown in Figure 1.

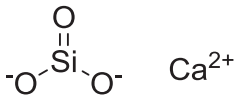


Figure 1: Structural formula for calcium silicate (EC inventory, online)[13]

Solubility: It is insoluble in water and in ethanol (JECFA, 2015) by following the solubility test described in Volume 4 (JECFA), which foresees a waiting time of 5 min.

In the REACH registration dossier, water solubility of calcium silicate has been reported to be in the region of 260 mg/L, using EU Method A.6 (which extends the measurement time for several days) (CEFIC, 2017a (Documentation provided to EFSA n. 4)).

According to industry (CEFIC, 2017a (Documentation provided to EFSA n. 4)), the time needed to achieve solubility equilibrium at room temperature is between 3 and 6 days based on studies made with synthetic amorphous silicon dioxide. The solubility of three commercial calcium silicates measured according to this approach varies between 220 and 330 mg/L, depending on the manufacturing parameters and calcium content (OECD 1054 method). However, the Panel noted that a solubility of 220–330 mg/L, equal to one part of substance dissolved in 4,545-3,030 parts of water, even when the equilibrium is reached, would classify the substance as 'very slightly soluble' according to the classification of the solubility by JECFA (2016).

Synonyms: silicic acid calcium salt (CEFIC, 2017a (Documentation provided to EFSA n. 4)).

Information on particle size

Industry (CEFIC, 2017a (Documentation provided to EFSA n. 4)) provided information on the particle size distribution of three types of commercial products of E 552 obtained from two different producers. Laser diffraction (LD) (ultrasonication in water for 1 or 2 min) was used as the method of measurement. The overall particle size distribution ranges (by volume) were: d50 (median) between 7.99 and 14.48 μm; d10 between 2.30 and 5.80 μm; d90 between 16.83 and 35.49 μm. No particles had sizes below 100 nm.

Using transmission electron microscopy (TEM), after dispersion the sample in a water–isopropanol mixture and ultrasonication for 3 min, the values (by number) were as follows: 24 nm for 1 type of commercial material and 12 nm for the second one (CEFIC, 2017a (Documentation provided to EFSA n. 4)). Using this method, 100% of particles had sizes below 100 nm, therefore, these two materials fall under the definition of nanomaterial according to the Commission Recommendation 2011/696/EU[14].

[13] Available online: https://echa.europa.eu/information-on-chemicals/ec-inventory

[14] Commission Recommendation of 18 October 2011 on the definition of nanomaterial. OJ L 275, 20.10.2011, p. 38–40.

Magnesium silicate (E 553a(i))

According to Commission Regulation (EU) No 231/2012, the food additive magnesium silicate (E 553a(i)) is defined as 'a synthetic compound of which the molar ratio of magnesium oxide to silicon dioxide is approximately 2:5'. No chemical formula, molecular weight and EINECS number indicated.

Physical description: It is a very fine, white, odourless powder, free from grittiness (Commission Regulation (EU) No 231/2012).

According to industry (CEFIC, 2017b (Documentation provided to EFSA n. 5)), magnesium silicate (E 553(i)) – CAS 1343-88-0 and an EINECS number 215-681-1 – has the name 'Synthetic amorphous magnesium silicate, with molar ratio (SiO_2:MgO) range of 1.4-4'. While it can be described in terms of hypothetical oxides, it is not a mixture of silicon dioxide and magnesium oxide. The Panel agreed with this conclusion.

According to the EC inventory (online),[13] the molecular formula for EC Number 215-681-1 is MgO_3Si and its structural formula is shown in Figure 2.

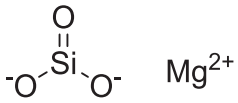


Figure 2: Structural formula for magnesium silicate (EC inventory, online)[13]

The Panel noted that, according to the definition given in the EU specifications, the food additive E 553a(i) has a molar ratio of magnesium oxide to silicon dioxide of approximately 2:5. This stoichiometry does not correspond with magnesium silicate (MgO_3Si) as presented in the EC inventory.[13]

According to industry, the time needed to achieve solubility equilibrium at room temperature is between 3 and 6 days based on studies made with synthetic amorphous silicon dioxide (CEFIC, 2017b (Documentation provided to EFSA n. 5)). The solubility of three non-food-grade commercial magnesium silicates by following this approach varied between 127 and 268 mg/L. However, the Panel noted that a solubility of 127–268 mg/L, equal to one part of substance dissolved in 4,874-3,731 parts of water, even when the equilibrium is reached, would classify the substance as 'very slightly soluble' according to the classification of the solubility by JECFA (2016).

Synonyms: silicic acid magnesium salt (CEFIC, 2017b (Documentation provided to EFSA n. 5)).

Information on particle size

Industry (CEFIC, 2017; Documentation provided to EFSA n. X) provided information on the particle size distributions of two types of commercial products of E 553a(i). LD in water (no ultrasonication) was used as the method of measurement. The particle size distribution ranges (by volume), for the first type of E 553a(i) were: d50 (median) between 60 and 80 μm, d10 ≥ 10 μm, d90 ≥ 120 μm; and for the second type: d50 (median) between 5 and 20 μm, d10 ≥ 2 μm, d90 ≥ 20 μm.

No data measured by TEM were provided following a request from EFSA.

Magnesium trisilicate (E 553a(ii))

According to Commission Regulation (EU) No 231/2012, the food additive magnesium trisilicate (E 553a(ii)) is identified as:

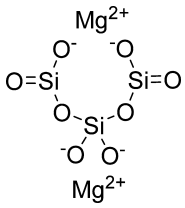
Chemical name: magnesium trisilicate
EINECS Number: 239-076-7
Chemical formula: $Mg_2Si_3O_8 \cdot nH_2O$
Description: fine, white powder, free from grittiness.

The Panel noted that the EINECS Number reported in EU specifications corresponds to the CAS Number 14987-04-3 (anhydrous form), while the chemical formula given in the EU specifications refers to an hydrated form.

Solubility: It is insoluble in water and ethanol (Elmore, 2003)

Synonyms: dimagnesium trisilicon octaoxide (EC inventory, online)[13]

Structural formula is shown in Figure 3.



[a]https://pubchem.ncbi.nlm.nih.gov/compound/5311266#section=2D-Structure

Figure 3: Structural formula for anhydrous magnesium trisilicate[a]

Information on particle size

Industry (CEFIC, 2017; Documentation provided to EFSA n. X) provided information on the particle size distributions of one type of commercial product of E 553a(ii). LD (80 s ultrasonication in a 0.1% solution of tetrasodium pyrophosphate in water) was used as the method of measurement. The particle size distribution ranges (by volume) were: d50 (median) between 10 and 20 μm, d10 ≥ 3 μm, d90 ≥ 20 μm.

No data measured by TEM were provided following a request from EFSA.

Talc (E 553b)

According to Commission Regulation (EU) No 231/2012, the food additive talc (E 553b) is defined as 'naturally occurring form of hydrous magnesium silicate containing varying proportions of such associated minerals as alpha-quartz, calcite, chlorite, dolomite, magnesite, and phlogopite' and is identified as:

Chemical name: Magnesium hydrogen metasilicate
EINECS Number: 238-877-9
Chemical formula: $Mg_3(Si_4O_{10})(OH)_2$
Molecular weight: 379.22 g/mol
Description: It is a light, homogeneous, white or almost white powder, and greasy to the touch.

The Panel noted that the chemical formula and molecular weight indicated in the EU specifications refer to the pure mineral magnesium hydrogen metasilicate.

The EINECS Number indicated in the EU specifications for E 553b corresponds to CAS number 14807-96-6.

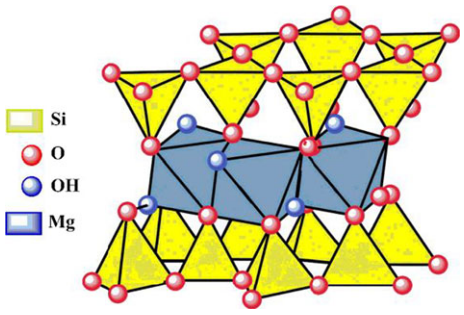


Figure 4: Schematic structure of talc (© SAGE Publications, Fiume et al., 2015)

Solubility: It is insoluble in water and ethanol (Commission Regulation (EU) No 231/2012). It is soluble in hot concentrated phosphoric acid (Fiume et al., 2015). According to Rashid et al. (2011), it is practically insoluble in water and in 'dilute' mineral acids, but it dissolves practically at concentrations up to 3 M of the acid and dissociates under these conditions to magnesium cations and silicic acid. The Panel assumed that, when talc dissociates, the associated water molecules are liberated in the solution.

Synonyms: talcum

According to industry (EUROTALC, 2012 (Documentation provided to EFSA n. 10)), a commercial brand of talc is a mixture of 75% (w/w) talc, 9% (w/w) chlorite (no further information on the variety of chlorite), 9% (w/w) dolomite ($CaMg(CO_3)_2$)[15] and 7% (w/w) magnesite ($MgCO_3$).[15]

[15] Chemical formula extracted from www.geology.com

Chlorite minerals have a general chemical composition of $[(X,Y)_{4-6}(Si,Al)_4O_{10}(OH,O)_8$. The 'X' and 'Y' in the formula represent ions, which might include: Fe^{2+}, Fe^{3+}, Mg^{2+}, Mn^{2+}, Ni^{2+}, Zn^{2+}, Al^{3+}, Li^{1+} or Ti^{4+}].[15] Among chlorites, there are minerals with specific composition, e.g. donbassite, $Al_{13}(Al_3Si_9O_{30})(OH)_{24}$, or nimite $(Ni,Mg,Al)_6(Si,Al)_4O_{10}(OH)_8$.[15]

The Panel noted that in the case of the possible presence of donbassite (the chlorite with highest aluminium content), the aluminium content is 27.5%, and consequently, the aluminium content in the food additive talc (E 553b) could be up to 2.47% when assuming that 9% of the food additive contain chlorite (donbassite).

The Panel noted that in the case of the possible presence of nimite (the chlorite with highest nickel content), the nickel content is 29.9% and consequently the nickel content in the food additive talc (E 553b) could be up to is 2.7% in the hypothesis that 9% of the food additive contain chlorite (nimite).

According to industry (EUROTALC, 2012 (Documentation provided to EFSA n. 10)), a commercial brand of talc is a natural association of talc and chlorite at greater than or equal to 95% where chlorite is defined as $(Mg.Fe)_5$ $Al[AlSi_3O_{10}][OH]_8$ (CAS No 1318-59-8). In this chlorite, the aluminium content is 6.5%. There is no information on the proportion of chlorite in the commercial talc.

According to industry, another commercial brand of talc contains at least 94% of talc $[Mg_3(Si_4O_{10})(OH)_2]$.

According to EU specifications for talc (E 553b), phlogopites can also be present as associated minerals. Some phlogopites with specific composition (e.g. fluorophlogopite $KMg_3(AlSi_3O_{10})F_2$) may contain up to 9% of fluorine.[16]

The Panel noted that the various proportions chlorite or phlogopite, which can be present in talc, largely influence the amounts of impurities such as nickel or aluminium, in the food additive.

Information on particle size

Industry (EUROTALC, 2012 (Documentation provided to EFSA n. 10)) provided information on the particle size distribution of two lots of talc (E 553b). LD was used as measuring method of suspensions dispersed in water. The particle size distributions ranges (by volume) were as follows: d50, 13.94–14.32 μm; d10, 3.26–3.76 μm; d90, 36.79–39.64 μm.

Additional information on talc (E 553b) analysed with a scanning electron microscope (SEM) indicated that the particles have an irregular shape and are non-porous and exist as two different particle sizes of 40 and 20 μm. The specific surface area (MSSA) of the finest E 553b is between 5 and 7 m^2/g (corresponding to VSSA of 14–19.6 m^2/cm^3, using talc density 2.8 g/cm^3) (EUROTALC, 2018b; (Documentation provided to EFSA n. 12)).

3.1.2. Specifications

The specifications for calcium silicate (E 552), magnesium silicate (E 553a(i)), magnesium trisilicate, (E 553a(ii)) and talc (E 553b) as defined in the Commission Regulation (EU) No 231/2012 and by JECFA (2015) are listed in Tables 1, 2, 3 and 4.

Table 1: Specifications for calcium silicate (E 552) according to Commission Regulation (EU) No 231/2012 and JECFA (2015)

	Commission Regulation (EU) No 231/2012	JECFA (2015)
Definition	Calcium silicate is a hydrous or anhydrous silicate with varying proportions of CaO and SiO_2. The product should be free of asbestos	Calcium silicate is an inorganic substance that is a hydrous or anhydrous substance with varying proportions of calcium as calcium oxide, and silicon as silicon dioxide. It is prepared by various reactions between siliceous material (e.g. diatomaceous earth) and calcium compounds (e.g. lime, calcium hydroxide)

[16] http://www.minerals.net/mineral/phlogopite.aspx

	Commission Regulation (EU) No 231/2012		JECFA (2015)
Assay	Content on the anhydrous basis: • as SiO_2 not less than 50% and not more than 95% • as CaO not less than 3% and not more than 35%		Not less than 50% and not more than 95% of silicon dioxide (SiO_2) and not less than 3% and not more than 35% of calcium oxide (CaO), calculated on the ignited basis
Description	White to off-white free-flowing powder that remains so after absorbing relatively large amounts of water or other liquids		Very fine, white or off-white powder with low bulk density and high physical water absorption
Identification	Test for silicate	Passes test	Passes test [test for silicon]
	Test for calcium	Passes test	Passes test
	pH	–	8.4–12.5 (5% slurry)
	Gel formation	Forms a gel with mineral acids	–
	Solubility	–	Insoluble in water and ethanol
Purity			
Loss on drying	Not more than 10% (105°C, 2 h)		Not more than 10% (105°, 2 h)
Loss on ignition	Not less than 5% and not more than 14% (1,000°C, constant weight)		5.0–14.0% on the dried basis (1,000°C, constant weight)
Sodium	Not more than 3%		–
Fluoride	Not more than 50 mg/kg		Not more than 50 mg/kg
Arsenic	Not more than 3 mg/kg		Not more than 3 mg/kg
Lead	Not more than 2 mg/kg		Not more than 5 mg/kg
Mercury	Not more than 1 mg/kg		–

The Panel noted that in the JECFA specifications, a test for silicon is used as a surrogate for the identification of silicate in calcium silicate, whereas a test for silicate is required in the EU specifications. The Panel also noted that there is no reference to solubility in EU specifications, where there is one in JECFA specifications.

The Panel noted that, according to the assay proposed in the EU specifications, silicon dioxide (SiO_2) can be up to 95%; this means that calcium oxide would be 5% which represents 9.7% as calcium silicate in the final product. Additionally if the content calcium oxide is at the minimum permitted of 3%, 7.2% of calcium silicate would be in the final product. The Panel noted that the limits in the assay should be reviewed in order to clarify the purity of calcium silicate as such in the food additive.

Table 2: Specifications for magnesium silicate (E 553a(i)) according to Commission Regulation (EU) No 231/2012 and JECFA (2011)

	Commission Regulation (EU) No 231/2012		JECFA (2011)
Definition	Magnesium silicate is a synthetic compound of which the molar ratio of magnesium oxide to silicon dioxide is approximately 2:5		Magnesium silicate (synthetic) is manufactured by the precipitation reaction between sodium silicate and a soluble magnesium salt. The aqueous suspension of the precipitate is filtered and the collected solid washed, dried, classified for particle size and packaged. The finest material is intended for use as an anticaking agent and the coarser particles are for use as a filtering aid. The moisture content of the material meant for use as an anticaking agent is kept to less than 15%. Although magnesium silicate is of variable composition, the molar ratio of MgO to SiO2 is approximately 2:5
Assay	Content not less than 15% of MgO and not less than 67% of SiO_2 on the ignited basis		Not less than 15% of MgO and not less than 67% of SiO_2, calculated on the ignited basis
Description	Very fine, white, odourless powder, free from grittiness		Very fine, white, odourless powder, free from grittiness
Identification	Test for magnesium	Passes test	Passes test
	Test for silicate	Passes test	Passes test
	Solubility	–	Insoluble in water
	pH	7–10.8 (10% slurry)	7–11 (1 in 10 slurry)
Purity			
Loss on drying	Not more than 15% (105°C, 2 h)		Not more than 15% (for material used as an anticaking agent (105°C, 2 h))
Loss on ignition	Not more than 15% after drying (1,000°C, 20 min)		Not more than 15% on the dried basis (900/1,000°C, 20 min)
Fluoride	Not more than 10 mg/kg		Not more than 10 mg/kg
Water-soluble salts	Not more than 3%		Not more than 3%
Free alkali	Not more than 1% (as NaOH)		Not more than 1% (as NaOH)
Arsenic	Not more than 3 mg/kg		–
Lead	Not more than 5 mg/kg		Not more than 5 mg/kg
Mercury	Not more than 1 mg/kg		–

The Panel also noted that there is no reference to solubility in EU specifications, where there is one in JECFA specifications.

Table 3: Specifications for magnesium trisilicate (E 553a(ii)) according to Commission Regulation (EU)

	Commission Regulation (EU) No 231/2012	
Definition		
Assay	Content not less than 29.0% of MgO and not less than 65.0% of SiO_2 both on the ignited basis	
Description	Fine, white powder, free from grittiness	
Identification	Test for magnesium	Passes test
	Test for silicate	Passes test
	pH	6.3–9.5 (5% slurry)
Purity		
Loss on ignition	Not less than 17% and not more than 34% (1,000°C)	
Water-soluble salts	Not more than 2%	

	Commission Regulation (EU) No 231/2012
Free alkali	Not more than 1% (as NaOH)
Fluoride	Not more than 10 mg/kg
Arsenic	Not more than 3 mg/kg
Lead	Not more than 5 mg/kg
Mercury	Not more than 1 mg/kg

Table 4: Specifications for talc (E 553b) according to Commission Regulation (EU) No 231/2012 and according to JECFA (2006)

	Commission Regulation (EU) No 231/2012		JECFA (2006)
Definition	Naturally occurring form of hydrous magnesium silicate containing varying proportions of such associated minerals as alpha-quartz, calcite, chlorite, dolomite, magnesite, and phlogopite. The product should be free of asbestos		Powdered, natural, hydrated magnesium silicate containing varying proportions of such associated materials as alpha-quartz, calcite, chlorite, dolomite, magnesite and phlogopite
Assay	–		–
Description	Light, homogeneous, white or almost white powder, greasy to the touch		Odourless, very fine, white or greyish white crystalline powder; unctuous, adheres readily to the skin, free from grittiness
Identification	Infrared absorption spectrum	Characteristic peaks at 3,677, 1,018 and 669 cm^{-1}	Major peaks of a potassium bromide dispersion of the sample at 3,677, 1,018 and 669 cm^{-1}
	X-ray diffraction	Peaks at 9.34/4.66/3.12 Å	Pattern of a random powder sample exhibits reflections at d values of 9.34, 4.66 and 3.12 Å
	Solubility	Insoluble in water and ethanol	Insoluble in water and ethanol
Purity			
Loss on drying	Not more than 0.5% (105°C, 1 h)		Not more than 0.5% (105°C, 1 h)
Acid soluble matter	Not more than 6%		Not more than 2.5%
Water-soluble matter	Not more than 0.2%		Not more than 0.2%
Acid soluble iron	Not detectable		Not detectable
Arsenic	Not more than 10 mg/kg		–
Lead	Not more than 2 mg/kg		Not more than 2 mg/kg
Asbestos	(a)		Free from asbestos as demonstrated by the test for amphiboles and serpentines

(a): The provision for asbestos in the EU specifications is included in the definition of the food additive.

The Panel noted that according to Regulation 231/2012 calcium silicate (E 552), magnesium silicate (E 553(i)) and magnesium trisilicate (E 553(ii)) are defined as silicates with varying proportions of oxides and silicon dioxide. The Panel considered that, in fact, silicates are not a mixture of oxides and silicon dioxide. The Panel considered that this should be clarified in the EU specifications.

The Panel noted that no minimum limit for hydrous magnesium silicate in E 553b is specified in the EU specifications. According to Fiume et al. (2015), talc used in cosmetics consists of a minimum of 90% hydrous magnesium silicate with the rest consisting of naturally associated minerals such as calcite, chlorite, dolomite, kaolin and magnesite (but no alpha-quartz or phlogopite, as in the EU specifications for E 553b).

The Panel noted that impurities of the toxic elements arsenic, lead and mercury are accepted up to concentrations of 3, 2 and 1 mg/kg according to the EU specifications for calcium silicate (E 552), up to concentrations of 3, 5 and 1 mg/kg for magnesium silicate (E 553a(i)) and magnesium trisilicate, (E 553a(ii)). For talc (E 553b), arsenic and lead are accepted up to concentrations of 10 and 2 mg/kg. Contamination at such levels could have a significant impact on the exposure to these metals, which is

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

Considering the information presented in Section 3.1.1, the Panel considered that maximum limit for aluminium, nickel and fluoride should be included in the EU specifications for talc (E 553b).

The Panel noted that crystalline silica (alpha-quartz) may also be present as an associated mineral, according to the EU specifications for talc (E 553b). The Panel noted that crystalline silica is a class 1 carcinogen by inhalation (IARC, 1997) and no maximum limit for quartz has been established in the EU specifications for talc (E 553b).

3.1.3. Manufacturing process

Calcium silicate (E 552)

According to industry, the manufacturing process for calcium silicate (E 552) comprises the following stages: dilution of raw materials, mixing and precipitation, solid–liquid filtration/washing, drying and packaging. Optionally, after the drying step, the product can be milled and/or granulated. The substance is, manufactured either batchwise or via a continuous process. The starting materials for the production of E 552 are diluted calcium chloride or calcium hydroxide and sodium silicates (e.g. waterglass composed of Na_2O:SiO_2) (CEFIC, 2017a (Documentation provided to EFSA n. 4)).

When using calcium chloride and sodium silicate (waterglass) as starting materials, calcium silicate is formed as a precipitate.

When using calcium hydroxide as a starting material, the calcium hydroxide is added to a slurry of silicon dioxide, before or after the filtration step. Calcium hydroxide reacts *in situ* in aqueous media with silicon dioxide forming calcium silicate.

The calcium silicate suspension is filtered and the filtrate is washed to remove salts (e.g. sodium chloride or sodium sulfate). Drying is performed according to different processes depending on the characteristics required for the final product.

After drying, the product is milled. During milling the particle size distribution and sieve residue characteristics of the product are controlled.

Magnesium silicate (E 553a(i)) and magnesium trisilicate (E 553 a(ii))

According to information provided (CEFIC, 2017b (Documentation provided to EFSA n. 5)), both magnesium silicate (E 553a(i) and magnesium trisilicate E 553a(ii) are manufactured either batchwise or via a continuous process. The production steps include raw material preparation, synthesis, drying, packaging, storage and shipment. After the drying step, the products may further be milled or granulated.

The raw materials for the production of E 553a(i) and E 553a(ii) are magnesium salts (e.g. magnesium sulfate, magnesium chloride) and aqueous alkali metal solution (sodium silicate solution).

In the reaction of magnesium salt with sodium silicate (waterglass), magnesium silicate is formed in a process-controlled, double replacement reaction in water.

The suspension obtained after reaction is filtered using various solid/liquid filters. After filtration, salts are washed-out. The silicate is dried, and further processed by milling or granulation depending on the required properties of the final product.

Talc (E 553b)

Talc is a naturally occurring substance. Deposits of talc are found in several countries, including China, United States, India, Brazil and France; different types of deposit occur depending on the way in which the talc was formed, and each type contains a different group of associated minerals (IARC, 1997).

The purity of commercial products can be improved by either dry or wet processing. In both cases, talc ore is crushed and ground to a fine material before being mixed with water and a frothing agent (often a low-molecular-weight alcohol). Air is bubbled through the suspension which results in flotation and sequestration of talc particles and therefore removal of hydrophilic non-talc impurities. This process may be repeated several times to increase talc purity. Magnetic separation or acid washing may be used to remove iron-bearing minerals, soluble salts and metals. Finally, the talc is filtered, washed and dried, and may be heat sterilised (CIR, 2013; Fiume et al., 2015).

Talc (E 553b) is a white mineral powder produced after grinding talc that has been mined (EUROTALC, 2018b (Documentation provided to EFSA n. 12)).

3.1.4. Methods of analysis in food

The Panel noted that silicates may be determined in food via measuring the total silicon. Analytical methods for measuring total silicon in food were described in the EFSA opinion on the re-evaluation of silicon dioxide (E 551) (EFSA ANS Panel, 2018). Nevertheless, when this principle is followed, it cannot be differentiated whether the measured silicon content originates from the added silicates, silicon dioxide or the naturally occurring silicon in food.

General methods for the analysis of silicates were reviewed by (Rashid et al., 2011). These relate mainly to the analysis of aqueous samples.

Information on a method for the detection of talc (E 553b) in food or beverage samples was submitted by industry (EUROTALC, 2012 (Documentation provided to EFSA n. 10)). This involves burning a sample of the food/beverage in a furnace for 1 h at 500°C to remove organic components, followed by X-ray diffraction examination of a sample of the ash to identify and quantify the talc. No information on the limit of detection of the method has been provided.

The Panel noted that no specific analysis for the presence of silicates or their particles in food have been reported in the literature.

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

According to industry (CEFIC, 2017a (Documentation provided to EFSA n. 4)), calcium silicate is formed by replacing protons (H^+) of silanol groups with calcium ions (Ca^{2+}) in alkaline conditions. This is a reversible reaction and in acidic conditions silanol groups are re-formed and Ca^{2+} ions released.

3.2. Authorised uses and use levels

Maximum levels of calcium silicate (E 552), magnesium silicate (E 553a), talc (E 553b) and for the group 'silicon dioxide-silicates (E 551-553)' have been defined in Annex II to Regulation (EC) No 1333/2008 on food additives, as amended. In this document, these levels are named maximum permitted levels (MPLs).

Currently, calcium silicate (E 552), magnesium silicate (E 553a) and talc (E 553b) are authorised food additives in the EU with MPLs ranging from 5,400 to 30,000 mg/kg in 13 food categories and at *quantum satis* (*QS*) in 15 food categories as listed in Table 5.

In this opinion, exposure to calcium silicate (E 552), magnesium silicate (E 553a) and talc (E 553b) as a group 'silicates (E 552–553)' was calculated.

Table 5: MPLs of calcium silicate (E 552), magnesium silicate (E 553a(i)), magnesium trisilicate (E 553a(ii)) and talc (E 553b) in foods according to the Annex II to Regulation (EC) No 1333/2008

Food category number	Food categories name	E-Number/ group	Name	Restrictions/ exceptions	MPL (mg/L or mg/kg as appropriate)
0	Food additives permitted in all categories of foods	E 551–553	Silicon dioxide – silicates	Only foods in dried powdered form (i.e. foods dried during the production process, and mixtures thereof), excluding foods listed in table 1 of Part A of Annex II	10,000
0	Food additives permitted in all categories of foods	E 551–553	Silicon dioxide – silicates	Only foods in tablet and coated tablet form, excluding the foods listed in table 1 of Part A of Annex II	*Quantum satis*
01.7.2	Ripened cheese	E 551–553	Silicon dioxide – silicates	Only sliced or grated cheese hard and semi-hard cheese	10,000

Food category number	Food categories name	E-Number/ group	Name	Restrictions/ exceptions	MPL (mg/L or mg/kg as appropriate)
01.7.5	Processed cheese	E 551–553	Silicon dioxide – silicates		10,000
01.7.6	Cheese products (excluding products falling in category 16)	E 551–553	Silicon dioxide – silicates	Only sliced or grated hard and semi-hard products	10,000
01.8	Dairy analogues, including beverage whiteners	E 551–553	Silicon dioxide – silicates	Only sliced or grated cheese analogues and processed cheese analogue; beverage whiteners	10,000
02.2.2	Other fat and oil emulsions including spreads as defined by Council Regulation (EC) No 1234/2007 and liquid emulsions	E 551–553	Silicon dioxide – silicates	Only tin greasing products	30,000
02.3	Vegetable oil pan spray	E 551–553	Silicon dioxide – silicates	Only tin greasing products	30,000
05.2	Other confectionery including breath refreshening microsweets	E 551–553	Silicon dioxide – silicates	Surface treatment only	*Quantum satis*
05.3	Chewing gum	E 552	Calcium silicate	Surface treatment only	*Quantum satis*
05.3	Chewing gum	E 553a	Magnesium silicate	Surface treatment only	*Quantum satis*
05.3	Chewing gum	E 553b	Talc		*Quantum satis*
05.4	Decorations, coatings and fillings, except fruit based fillings covered by category 4.2.4	E 551–553	Silicon dioxide – silicates	Surface treatment only	*Quantum satis*
06.1	Whole, broken, or flaked grain	E 553b	Talc	Only rice	*Quantum satis*
08.2	Meat preparations as defined by Regulation (EC) No 853/2004	E 553b	Talc	Only surface treatment of sausages	*Quantum satis*
08.3.1	Non-heat-treated meat products	E 553b	Talc	Only surface treatment of sausages	*Quantum satis*
08.3.2	Heat–treated meat products	E 553b	Talc	Only surface treatment of sausages	*Quantum satis*
10.2	Processed eggs and egg products	E 553b	Talc	Only on the surface of unpeeled coloured boiled eggs	5,400
11.1	Sugars and syrups as defined by Directive 2001/111/EC	E 551–553	Silicon dioxide – silicates	Only dried powdered foods	10,000
11.1	Sugars and syrups as defined by Directive 2001/111/EC	E 551–553	Silicon dioxide – silicates	Only foods in tablet and coated tablet form	*Quantum satis*

Food category number	Food categories name	E-Number/ group	Name	Restrictions/ exceptions	MPL (mg/L or mg/kg as appropriate)
11.4.2	Table top sweeteners in powder form	E 551–553	Silicon dioxide – silicates		10,000
11.4.3	Table top sweeteners in tablets	E 551–553	Silicon dioxide – silicates		*Quantum satis*
12.1.1	Salt	E 551–553	Silicon dioxide – silicates		10,000
12.1.2	Salt substitutes	E 551–553	Silicon dioxide – silicates		20,000
12.2.2	Seasonings and condiments	E 551–553	Silicon dioxide – silicates	Only seasoning	30,000
17.1[(a)]	Food supplements supplied in a solid form including capsules and tablets and similar forms, excluding chewable forms	E 551–553	Silicon dioxide – silicates		*Quantum satis*
17.2[(a)]	Food supplements supplied in a liquid form	E 551–553	Silicon dioxide – silicates		*Quantum satis*
17.3[(a)]	Food supplements supplied in a syrup-type or chewable form	E 551–553	Silicon dioxide – silicates		*Quantum satis*

MPL: maximum permitted level.
(a): FCS 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.

According to Annex III, Part 1, calcium silicate (E 552) is authorised as a carrier in emulsifiers and colours at *QS*, and talc (E 553b) is authorised as a carrier in colours at a maximum level of 50 mg/kg in the colour preparation.

According to Annex III, Part 2 of Regulation (EC) No 1333/2008, calcium silicate (E 552) is authorised as a food additive other than a carrier in dry powdered preparations of emulsifiers at a maximum level of 50,000 mg/kg in the preparation. Calcium silicate (E 552), magnesium silicate (E 553a) and talc (E 553b) are authorised as food additives in food additives only in dry powdered preparations of polyols at a maximum level of 10,000 mg/kg in the preparation.

In addition, according to Annex III, Part 5, Section A of Regulation (EC) No 1333/2008, calcium silicate (E 552) is authorised as a food additive in dry powdered preparations of all nutrients, except nutrients intended to be used in foods for infant and young children as listed in point 13.1 of Part E of Annex II, at a maximum level of 50,000 mg/kg in the dry preparation (singly or in combination with silicon dioxide (E 551)).

The Panel noted that calcium silicate (E 552), magnesium silicate (E 553a(i)), magnesium trisilicate (E 553a(ii)) and talc (E 553b) are authorised mainly for use in dried products or as a surface treatment.

3.3. Exposure data

3.3.1. Reported use levels or data on analytical levels of calcium silicate (E 552), magnesium silicate (E 553a(i)), magnesium trisilicate (E 553a(ii)) and talc (E 553b)

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, which are authorised according at *QS* in all or part of the authorised food categories.

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(s)[17] for occurrence data (usage level and/or analytical data) on calcium silicate (E 552), magnesium silicate (E 553a(i)), magnesium trisilicate (E 553a(ii)) and talc (E 553b). In response to this public call, updated information on the actual use levels of these food additives in foods was made available to EFSA by industry. No analytical data on the concentration of these additives in foods were made available by the Member States.

Summarised data on reported use levels in foods provided by industry

Industry provided EFSA with data on use levels (n = 292) of calcium silicate (E 552), magnesium silicate (E 553a(i)), magnesium trisilicate (E 553a(ii)) and talc (E 553b) in foods for 7 out of the 28 food categories in which these food additives are authorised. Most of the data provided to EFSA referred to talc (E 553b) (n = 287).

Updated information on the actual use levels of silicates (E 552–553) in foods was made available to EFSA by Dr Loges Naturheilkunde neu entdecken, Grupo AC MARCA, European Snacks Association/ SNACMA (ESA), Association of the European Self-Medication Industry (AESGP), Specialised Nutrition Europe (SNE), Food Drink Europe (FDE), Food Supplements Europe (FSE), International Chewing Gum Association (ICGA) and EUROTALC.

The Panel noted that two use levels on food supplements referred to niche products. Since other use levels were available for this food category, the Panel excluded them from further analysis.

Appendix A provides the data on the use levels of silicates (E 552–553) 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 which 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 GNPD.[18]

For the purpose of this Scientific Opinion, THE Mintel's GNPD[19] was used for checking the labelling of food and beverages products and food supplements for silicates (E 552–553) within the EU's food market as the database contains the compulsory ingredient information on the label.

According to the Mintel's GNPD, silicates (E 552–553) were labelled on more than 1,000 products between January 2013 and January 2018. In 89% of the foods, the food additive labelled was talc (E 553b). The main food category labelled with one of these food additives is food supplements.

Appendix B lists the percentage of the food products labelled with silicates (E 552–553) out of the total number of food products per food subcategory according to the Mintel's GNPD food classification. The percentages ranged from less than 0.1% in most of food subcategories up to 8% in the Mintel's GNPD food subcategory 'Vitamins & Dietary Supplements'. The average percentage of foods labelled to contain calcium silicate (E 552), magnesium silicate (E 553a(i)), magnesium trisilicate (E 553a(ii)) and talc (E 553b) was 0.2%. For five food categories authorised to contain silicates (E 552–553) and found to be labelled with these food additives in the Mintel's GNPD, no data were submitted (meat products, sugar and syrups, and seasonings).

For ripened cheese and processed cheese, which are food categories authorised to contain silicates, no food items were found in the Mintel's GNPD, but data were submitted to EFSA.

For other food categories authorised to contain silicates (rice, table-top sweeteners, dairy analogues, other fat and oil emulsions, vegetable oil pan spray, processed eggs and egg products and salt substitutes), no foods were found in the Mintel's GNPD nor were data submitted to EFSA.

[17] http://www.efsa.europa.eu/sites/default/files/consultation/160524.pdf
[18] Missing Bulgaria, Cyprus, Estonia, Latvia, Lithuania, Luxembourg, Malta and Slovenia.
[19] http://www.gnpd.com/sinatra/home/ accessedon 4/1/2018.

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.[20]

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 the following population groups were used for the exposure assessment: infants, toddlers, children, adolescents, adults and the elderly. For the present assessment, food consumption data were available from 33 different dietary surveys carried out in 19 European countries (Table 6).

Table 6: Population groups considered for the exposure estimates of silicates (E 552–553)

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): 'Toddlers' in the EFSA 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. In practice, the FoodEx food codes were matched to the FCS food categories.

Food categories considered for the exposure assessment of silicates

The food categories in which the use of silicates (E 552–553) 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).

Some food categories for which MPLs were available and/or use levels were submitted are not referenced in the EFSA Comprehensive Database and could therefore not be taken into account in the exposure assessment. This was the case for five food categories (Appendix C) and may have resulted

[20] Available online: http://www.efsa.europa.eu/en/datexfoodcdb/datexfooddb.htm

in an underestimation of the exposure. The food categories which were not taken into account were (in ascending order of the FCS codes):

- 01.7.6 Cheese products (excluding products falling in category 16)
- 02.2.2 Other fat and oil emulsions including spreads as defined by Council Regulation (EC) No 1234/2007 and liquid emulsions, only tin greasing products
- 02.3 Vegetable oil pan spray, only tin greasing products
- 10.2 Processed eggs and egg products, only on the surface of unpeeled coloured boiled eggs
- 12.1.2 Salt substitutes.

For the following food categories, the restrictions/exceptions which apply to the use of silicates (E 552–553) could not be taken into account, and therefore the whole food category was considered in the exposure assessment. This applied to four food categories (Appendix C) and may have resulted in an overestimation of the exposure:

- 01.7.2 Ripened cheese, only sliced or grated cheese hard and semi-hard cheese. The full food category was taken into account because the restriction could represent a large part of the consumed food category.
- 01.8 Dairy analogues, including beverages whiteners, only sliced or grated cheese analogues and processed cheese analogue; beverages whiteners. The full food category was taken into account because the restriction could represent a large part of the consumed food category.
- 11.1 Sugars and syrups as defined by Directive 2001/111/EC, only dried powdered foods.
- 11.1 Sugars and syrups as defined by Directive 2001/111/EC, only foods in tablet and coated tablet form.

These last two food categories represent most of the foods belonging to FC 11.1 and were therefore considered completely. This uncertainty was furthermore only relevant for the *regulatory maximum level exposure assessment* scenario. In the refined scenarios, three of these four food categories were not included (except FC 01.7.2), due to lack of use levels (Appendix A).

The FCs 17.1/17.2/17.3 Food supplements, in solid, liquid, syrup-type or chewable form, the form cannot be differentiated and the same use level was applied to the whole FC 17. The FCs were taken into account only in the specific scenario on food supplements and were not included in the regulatory exposure scenario.

It has to be noted that silicates (E 552–553) are authorised in FC 0, meaning in 'all categories of foods excluding foods for infants and young children, except where specifically provided for'. In the case of silicates, two restrictions apply to this food category:

- only foods in dried powdered form (i.e. foods dried during the production process, and mixtures thereof), excluding foods listed in Table 1 of Part A of Annex II,
- only foods in tablet and coated tablet form, excluding the foods listed in Table 1 of Part A of Annex II.

Use levels of E 552 were provided for FC 15 Ready-to-eat savouries and snacks, and 'coated peanut cracker' despite not being authorised in this FC. However, its use in FC 15 can be explained by its authorisation in FC 0. This was also true for the use level provided for 'chocolate bar'. These use levels were respectively mapped to the consumption of FCs 15.1, 15.2 and chocolate coating (FC 05.4) in all exposure scenarios. This is in line with Mintel's GNPD as nuts and snacks were found to be labelled with silicates (Appendix B).

Four food categories (06.1, 08.2, 08.3.1 and 08.3.2) could not be taken into account as they are authorised at *QS* and no use levels were reported by industry.

Considering all, in total 16 food categories were included in the *regulatory maximum level exposure assessment* scenario.

Considering only the food categories for which use levels were provided, nine food categories were included in the refined exposure assessment to silicates (E 552–553), including the two FCs 15.1 and 15.2 and excluding exposure via food supplements (Appendix C).

Compared to the refined scenario, three additional food categories (in total 12) were considered in the food supplements scenario.

For the remaining food categories, the refinements considering the restrictions/exceptions as set in Annex II to Regulation No 1333/2008 were applied.

3.4. Exposure to silicates from their use as food additives

The Panel estimated the chronic dietary exposure to silicates (E 552–553) for the following population groups: infants, toddlers, children, adolescents, adults and the elderly. Dietary exposure to silicates was calculated by multiplying concentrations of silicates (E 552–553) per food category (Appendix C) with their respective consumption amount per kilogram body weight for each individual in the Comprehensive Database. The exposure per food category was subsequently added to derive an individual total exposure per day. These exposure estimates were averaged over the number of survey days, resulting in an individual average exposure per day for the survey period. Dietary surveys with only one day per subject were excluded as they are considered as not adequate to assess repeated exposure.

This was carried out for all individuals per survey and per population group, resulting in distributions of individual exposure per survey and population group (Table 6). On the basis of these distributions, the mean and 95th percentile of exposure were calculated per survey and per population group. The 95th percentile of exposure was only calculated for those population groups with a sufficiently large sample size (EFSA, 2011a). Therefore, in the present assessment, the 95th percentile of exposure for infants from Italy and for toddlers from Belgium, Italy and Spain were not estimated.

Exposure assessment to silicates (E 552–553) was carried out by the ANS Panel based on two different sets of concentration data: (1) MPLs as set down in the EU legislation (defined as the *regulatory maximum level exposure assessment scenario*) and maximum reported use level for food categories with a permitted use at *QS*; and (2) 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 of food supplements. This exposure source is covered in an additional scenario detailed below (*food supplements consumers only scenario*).

A possible additional exposure from the use of silicates as food additives in food additives and nutrients in accordance with Annex III to Regulation (EC) No 1333/2008 (Parts 1, 2 and 5A) was not considered in any of the exposure assessment scenarios.

3.4.1. Regulatory maximum level exposure assessment scenario

The *regulatory maximum level exposure assessment* scenario is based on the MPLs as set in Annex II to Regulation (EC) No 1333/2008 and listed in Table 2. For silicates, the MPLs used in the assessment are listed in Table 5. For the food categories authorised at *QS*, the maximum reported use levels when available was used (Appendix C).

The Panel considers the exposure estimates derived with this scenario as the most conservative since it is assumed that that the population will be exposed to food additives present in food at the MPL/maximum reported use level over a longer period of time.

3.4.2. Refined exposure assessment scenario

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

Appendix C summarises the concentration levels of silicates (E 552–553) used in the refined exposure assessment 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 silicates (E 552–553) present at the maximum reported use level for one food category. This exposure estimate was calculated as follows:
  - Combining food consumption with the maximum of the reported use levels for the main contributing food category at the individual level.
  - Using the mean of the typical reported use levels for the remaining food categories.
- The non-brand-loyal consumer scenario: It was assumed that a consumer is exposed long-term to silicates present at the mean reported use levels in food. This exposure estimate was calculated using the mean of the typical reported use levels for all food categories.

3.4.3. Food supplement consumers only scenario

Silicates are authorised in FC 17 (Food supplements as defined in Directive 2002/46/EC excluding food supplements for infants and young children). As exposure via food supplements may deviate largely from that via food, and the number of food supplement consumers may be low depending on populations and surveys, an additional scenario was calculated in order to reflect additional exposure to silicates from the intake of food supplements. This additional exposure was estimated assuming that consumers of food supplements were exposed to silicates present at the maximum reported use levels in food supplements on a daily basis. For the remaining food categories, the mean of the typical reported use levels of silicates was used.

As FC 17 does not consider food supplements for infants and toddlers as defined in the legislation, exposure to silicates from food supplements was not estimated for these two population groups.

This scenario included 12 food categories (Appendix C).

3.4.4. Dietary exposure to silicates

Table 7 summarises the estimated exposure to silicates (E 552–553) from their use as food additives in six population groups (Table 6) according to the different exposure scenarios. Detailed results per population group and survey are presented in Appendix D.

Table 7: Summary of dietary exposure to silicates (E 552–553) from their use as food additives in the regulatory maximum level exposure assessment scenario and in the refined exposure scenarios, in six population groups (minimum–maximum across the dietary surveys in mg/kg bw 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)
Regulatory maximum level exposure assessment scenario						
• Mean	2.1–16.2	9.1–24.9	4.1–34.6	2.7–24.3	2.0–14.6	2.6–10.0
• 95th percentile	9.3–39.2	27.0–72.9	14.6–113.8	9.1–73.2	6.9–51.8	7.1–18.4
Refined estimated exposure assessment scenario						
Brand-loyal scenario						
• Mean	0.1–10.5	2.2–19.9	1.1–27.5	0.7–17.8	0.3–11.7	0.7–6.7
• 95th percentile	0–21.4	12.9–65.0	4.5–110.4	3.9–64.9	1.7–46.6	3.0–14.7
Non-brand-loyal scenario						
• Mean	0.1–10.5	1.0–18.4	0.6–13.2	0.6–9.4	0.2–6.9	0.5–4.7
• 95th percentile	0–21.4	4.9–27.3	2.7–41.9	2.9–24.1	1.3–18.4	2.2–11.9

In the *regulatory maximum level exposure assessment* scenario, the mean exposure to silicates (E 552–553) from their use as food additives ranged from 2 mg/kg bw per day in adults to 34.6 mg/kg bw per day in toddlers. The 95th percentile of exposure to silicates (E 552–553) ranged from 6.9 mg/kg bw per day in adults to 113.8 mg/kg bw per day in children.

In the *brand-loyal* scenario, the mean exposure to silicates (E 552–553) from their use as food additives ranged from 0.1 mg/kg bw per day in infants to 27.5 mg/kg bw per day in children. The high exposure to silicates ranged from 0 mg/kg bw per day in infants to 110 mg/kg bw per day in children. In the *non-brand-loyal* scenario, the mean exposure to silicates (E 552–553) from their use as food additives ranged from below 0.1 mg/kg bw per day in infants to 18.4 mg/kg bw per day in toddlers. The 95th percentile of exposure to silicates (E 552–553) ranged from below 0 mg/kg bw per day in infants to 41.9 mg/kg bw per day in children.

For the food supplements consumers only scenario, the mean exposure to silicates (E 552–553) from their uses as food additives ranged between 5 mg/kg bw per day for adults and the elderly to 31 mg/kg bw per day for children. The 95th percentile of exposure to silicates ranged between 14 and 46 mg/kg bw per day for the elderly (Appendix F).

Main food categories contributing to exposure to silicates for the general population

In the *regulatory maximum level exposure assessment scenario*, the main contributing food categories to the total mean exposure to silicates (E 552–553) were FC 01.7.2 Ripened cheese and FC 11.1 Sugars and syrups for all population groups.

For infants, adults and the elderly, the main contributing food categories in both the brand-loyal and non-brand-loyal scenario were FC 01.7.2 Ripened cheese and FC 01.7.5 Processed cheese.

For toddlers, the main contributing food categories in both the brand-loyal and non-brand-loyal scenario were FC 01.7.2 Ripened cheese, FC 01.7.5 Processed cheese and FC 05.1 Cocoa and Chocolate products as covered by Directive 2000/36/EC. In the brand-loyal scenario also FC 05.2 Other confectionery including breath freshening microsweets was an important contributing food category.

For children, the main contributing food categories in the brand-loyal were FC 01.7.2 Ripened cheese, FC 05.2 Other confectionery including breath freshening microsweets and FC 05.3 Chewing gum. In the non-brand-loyal, the main contributing food categories were FC 01.7.2 Ripened cheese, FC 05.1 Cocoa and Chocolate products as covered by Directive 2000/36/EC and FC 05.3 Chewing gum.

For adolescents, the main contributing food categories in the brand-loyal scenario were FC 01.7.2 Ripened cheese and FC 05.3 Chewing gum. In the non-brand-loyal, the main contributing food categories were FC 01.7.2 Ripened cheese, FC 01.7.5 Processed cheese and FC 05.3 Chewing gum.

Appendix E summarises the contributing food categories for the *regulatory maximum level* and *the refined exposure assessment scenario*.

3.4.5. Uncertainty analysis

Uncertainties in the exposure assessment of silicates (E 552–553) 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 8.

Table 8: Qualitative evaluation of influence of uncertainties on the dietary exposure estimate of silicates (E 552–553)

Sources of uncertainties	Direction[a]
Consumption data: different methodologies/representativeness/underreporting/misreporting/no portion size standard	+/–
Use of data from food consumption surveys covering only a few days to estimate high percentiles (95th) long-term (chronic) exposure	+
Correspondence of reported use levels to the food items in the EFSA Comprehensive Food Consumption Database: uncertainties to which types of food the levels refer	+/–
Uncertainty in possible national differences in use levels within food categories	+/–
Concentration data: • use levels considered applicable to all foods within the entire food category, whereas on average 0.2% of the foods (according to the Mintel's GNPD), belonging to food categories with foods labelled with silicates (E 552–553), was labelled with at least one of these additives	+
Food categories selected for the exposure assessment: exclusion of food categories with MPLs and/or use levels due to missing FoodEx linkage (n = 5/28 food categories authorised according to Annex II)	–
Food categories selected for the exposure assessment: inclusion of food categories without considering the restriction/exception (n = 4 food categories authorised according to Annex II in the regulatory maximum level exposure assessment scenario and n = 1 in the refined exposure assessment scenario)	+
Food categories selected for the exposure assessment: no concentration data for certain food categories which were therefore not considered in the exposure estimates (n = 4 for the regulatory scenario/13 food categories for refined scenario)	–
Foods which may contain the food additive according to Annex III to Regulation (EC) No 1333/2008 not taken into account	–

Sources of uncertainties	Direction[a]
Regulatory maximum level exposure assessment scenario:	
• exposure calculations based on the MPL/maximum reported use levels according to Annex II to Regulation (EC) No 1333/2008	+
Refined exposure assessment scenarios:	
• exposure calculations based on the maximum or mean levels (reported use from industries)	+/–

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

Silicates (E 552–553) are authorised in 28 food categories (Table 2). Reported use levels were only available for seven food categories in the refined scenario.

The Panel noted that information from the Mintel GNPD (Appendix B) showed that the main food subcategories, categorised according to the Mintel GNPD nomenclature (i.e. Vitamins & Dietary Supplements, confectionary, chewing gums), labelled to contain silicates (E 552–553) were included in the current exposure assessment. On the other hand, some foods in which the use of silicates (E 552–553) is authorised but for which no data were submitted, were labelled to contain silicates (E 552–553) according to the Mintel's GNPD (e.g. meat products, sugar and syrups). This represents at the maximum 2.5% of all food products within the food category (Appendix B).

The Panel also noted that no foods belonging to the main contributing food category in all population groups i.e. ripened cheese, were labelled according to the Mintel GNPD. Only one use level was reported for ripened cheese.

Furthermore, the Mintel's GNPD showed that the maximum percentage of foods per food subcategory labelled to contain silicates (E 552–553) was 8.4% for 'Vitamins & Dietary Supplements'. The average percentage of foods labelled to contain silicates (E 552–553) was 0.2%. In the assessment, it was assumed that all foods belonging to the considered food categories contained silicates (E 552–553) as food additives.

Given that the information from the Mintel's GNPD reflects the use levels reported by industry to a large extent, and that it was assumed that all foods belonging to the considered food categories contained silicates (E 552–553), the Panel considered overall that the uncertainties identified would, in general, result in an overestimation of the exposure to silicates (E 552–553) from their use as food additives according to Annex II in all scenarios in European countries considered in the EFSA European database. The Panel noted that food categories which may contain silicates (E 552–553) due to carry-over (Annex III, Part 1, 2, 5) were not considered in the current exposure assessment.

3.4.6. Exposure to silicates from other sources

The Panel noted that magnesium trisilicate may be used with other ingredients to treat ulcer dyspepsia and non-erosive gastroesophageal reflux as an over-the-counter therapeutic (Martindale online). A single tablet of 'magnesium trisilicate mixture' (250 mg magnesium trisilicate, 250 mg magnesium carbonate, 250 mg sodium hydrogen carbonate) may be taken as a single dose up to 1,000 mg magnesium trisilicate (14.3 mg/kg bw per dose). However, it may be taken *ad libitum* since no maximum dose is indicated.

Calcium silicate, magnesium silicate, magnesium trisilicate and talc are permitted as ingredients in cosmetic products and as an excipient for drugs.

Data to calculate the exposure via all these sources were not available to the Panel and therefore the exposure resulting from these other sources could not be taken into account in this opinion.

3.5. Biological and Toxicological data

The Panel noted that:

- Some silicates are known to have effects on the lungs when inhaled (IARC 1997). This route of exposure is not representative of the exposure of consumers to a food additive and therefore these data were not considered in this evaluation.
- Data obtained with test samples that contained asbestos fibres were not considered in this evaluation because asbestos must not be present in the food additives (E 552, E 553b) according to the current EU specifications and therefore these data were considered not relevant.

- Data regarding the effect of 'talc' on the incidence of ovarian cancer were not considered in this evaluation because they are associated with exposure to talc via a route of exposure (topical) which is not representative of its use as a food additive.

The Panel noted that in some studies (especially those conducted in the 1960–1970s) while the authors reported analysis of 'silica' or 'silicon dioxide' content, analytical methods available at the time were only capable of measuring silicon. The Panel considered that while this was expressed as silica or silicon dioxide by the authors, it was not possible to determine whether it was silica or silicon that was measured.

The Panel noted that many toxicity studies on calcium silicate reported in this opinion have been performed in the 1960s using Silene EF, described as hydrated calcium silicate consisting of 64% silicon dioxide, 18% calcium oxide; 0.6% aluminium oxide; 0.1% magnesium oxide; and 1.5% sodium chloride with an average particle size of 30 nm (Columbia-Southern Chemical Corporation, 1953 (Documentation provided to EFSA n. 8)). According to industry (CEFIC, 2018b (Documentation provided to EFSA n. 7)), Silene EF was not sold for use as a food additive at that time and is not produced any longer. Although a complete characterisation was not available, the percentage of calcium silicate- expressed as silicon dioxide and calcium oxide- complied with the EU specifications for E 552. Therefore, the Panel considered that the available toxicity studies could be used for the assessment of calcium silicate.

3.5.1. Absorption, distribution, metabolism and excretion

Animal studies

Calcium silicate

No information on absorption, metabolism and excretion was available; however some information on distribution and accumulation could be obtained from a 2-year feeding study using Carworth Farm rats (6 animals/sex per group; 3 weeks old). Animals were fed 1.0%, 5.0%, 7.5% or 10% (w/w) (equivalent to 500, 2,500, 3,750 and 5,000 mg/kg bw per day) calcium silicate (Silene EF) in their diets (Hazelton Laboratory, 1956 (Documentation provide to EFSA n 18)). At the end of the dosing period, animals were sacrificed and tissue samples from the kidney, liver, spleen, cardiac muscle, skeletal muscle and testes of three of the animals were sampled and pooled. There was a dose-related increase of 'silicon dioxide' in the liver (5% concentration: males, 2-fold background; females, no or slight increase; 10% concentration: males and females, 3-fold background), and in the kidney (5% concentration: males, 3-fold background; females, no or slight increase; 10% concentration: males, 20-fold background; females, 15-fold background), but not in the other organs tested.

Magnesium silicate

No studies were available.

Magnesium trisilicate

Urinary excretion of silicon following oral ingestion of magnesium trisilicate has been investigated in male Sprague–Dawley Cox rats (3 animals per group) (Benke and Osborn, 1979). Following a 17- to 18-h fasting period, the animals were dosed by gavage with a single dose of 0, 40, 200 or 1,000 mg/kg bw of magnesium trisilicate. Control animals (4–6 animals; 240–260 g) were administered water. Urine was collected for four consecutive 24-h periods. Silicon excretion was most rapid during the first 24 h after dosing. The total amount of silicon excreted as a proportion of the total dose was 16.8% in the group administered 40 mg magnesium trisilicate/kg bw. This decreased to 5.1% in the 200 mg/kg bw group, and 1.5% in the 1,000 mg/kg bw group. According to the authors, the excretion of silicon from magnesium trisilicate was limited, suggesting that either the process of absorption or excretion became saturated. The Panel agreed with this conclusion.

Talc

Mice

Mice of the LACA strain (4 female animals; age not stated) were given a single oral dose (40 mg/kg bw per day) of ^{3}H-labelled talc (synthetically produced magnesium hydrogen metasilicate) by gavage (Phillips et al., 1978). Two animals were then killed at 6 and 24 h after dosing. Urine and faeces were collected, and the radioactivity was determined in the urine, combined faeces and large intestine, combined stomach and small intestine, and in the carcass. The entire radioactivity was detected in the

gastrointestinal tract and faeces at 6 and 24 h. No radioactivity was detected in the remainder of the carcass including the liver and the kidneys.

Rats

Wistar rats (3 male animals; age not stated) were given a single oral dose (50 mg/kg bw) of ^{3}H-labelled talc (synthetically produced magnesium hydrogen metasilicate) by gavage (Phillips et al., 1978). Urine and faeces samples were collected at 24 h intervals for 4 days and then on day 10 following administration. Animals were sacrificed and the liver, kidneys and the gastrointestinal tract were removed. Radioactivity in urine, faeces and tissues were determined. Three additional male rats were administered a daily oral dose of ^{3}H-labelled talc (50 mg/kg bw per day) for 6 consecutive days. The animals were sacrificed 10 days after the final dosing and radioactivity determined in urine, faeces and tissues. Following the single dose of ^{3}H-labelled talc, approximately 75% and 95.8% of radioactivity was found in the faeces within the first 24 h, and 96 h, respectively. By 24 h after administration, only 0.08% of the dose remained in the gastrointestinal tract. A total of less than 2% of the administered radioactivity was found in the urine. There was no radioactivity in the liver or kidneys 10 days following administration of ^{3}H-labelled talc. Furthermore, after 10 days, no radioactivity was detected in the faeces or the livers of animals which were administered 6 consecutive daily doses of ^{3}H-labelled talc. Less than 0.02% of the total administered radioactivity was found in the kidneys.

Hamsters

The oral absorption of talc (baby powder, no more details on composition) was investigated using Syrian golden hamsters (6 females; 10 weeks old) (Wehner et al., 1977). Irradiated (neutron-activated) talc was suspended in physiological saline solution and 1 mL of the suspension was administered to the animals by gavage. Control animals (4 females; 10 weeks old) received 1 mL of saline solution. The animals were housed in metabolism cages for 24 h, then, the animals were killed and the skinned carcass, gastrointestinal tract, lungs, liver, kidneys and collected urine and faeces were analysed for radioactive isotopes using gamma-ray spectrometry. Overall, approximately 74.5% of the administered dose was found in the faeces, 23.5% in the gastrointestinal tract and 1.9% in the carcass, but not in the lungs, liver or kidneys. The authors estimated that no more than a further 1% would be absorbed from the gut. The Panel agreed with the authors.

Guinea pigs

Dunkin/Hartley guinea pigs (3 female animals) were given a single oral dose (25 mg/kg bw) of ^{3}H-labelled talc (synthetically produced magnesium hydrogen metasilicate) by gavage (Phillips et al., 1978). Urine and faeces were collected at 24 h intervals for 4 days. After 10 days, the animals were sacrificed, and the liver, kidney and gastrointestinal tract removed for determination of radioactivity. Approximately 32% of the radioactivity was detected in the faeces within the first 24 h, and 94.6% was present within 96 h. By day 10, less than 0.03% of the administered dose was detected in the gastrointestinal tract. Very little (< 0.2%) of the total radioactivity was present in the urine up to 4 days following administration.

Human studies

Calcium silicate

No studies were available.

Magnesium silicate

No studies were available.

Magnesium trisilicate

Twenty-four-hour excretion of urine was collected at several-day intervals and the 'silica' content (expressed as silicon dioxide, method of determination not stated) was quantitatively determined for each 24-h period in five healthy young males (no further details provided) (Page et al., 1941). The mean average daily excretion of five normal subjects on a regular diet was 16.2 mg SiO_2. Synthetic hydrated magnesium trisilicate was then given to each subject in the form of 0.5 g compressed products suspended in water. Five grams were given daily in five spaced doses of 1 g each for four consecutive days. On the second day, urine was collected and contained 172, 178 and 162 mg SiO_2 on the second, third and fourth days, respectively. Two days after magnesium trisilicate had been

stopped, the excretion had fallen to 24.5 mg and reported by the authors to be within the normal excretion range of these subjects.

The 24-h urinary excretion of silicon was determined by atomic absorption spectroscopy in a healthy adult male and healthy adult female on a normal diet, in four consecutive urine collections (Dobbie and Smith, 1982). Then, a single dose of magnesium trisilicate (2 g for the male; 2.5 g for the female) was ingested by the participants at the beginning of the second 24-h collection period. These studies were repeated with higher doses (5 and 10 g for the male; 5, 7.5 and 10 g for the female). There was a significant increase above basal levels in urinary silicon in the 24-h urinary in both subjects at all doses after ingestion. Maximum excretion occurred in the first 24 h after ingestion and amounts greater than in the predose collections (mean of 0.31 mmoles (8.7 mg) in females) continued to be excreted on the subsequent 2 days in some instances. The amounts excreted after a 5 g dose were greater than following the 2 g and 2.5 g doses. Little further increase in urinary silicon resulted from raising the dose to 7.5 or 10 g.

Urinary excretion of silicon was studied in healthy adults (no further information given) on either a low silicon diet, normal diet or after ingestion of 5 g magnesium trisilicate (Dobbie and Smith, 1986). The excretion of silicon in urine was dependent on the amount of silicon in the diets, being lower in individuals on the low silicon diet and higher in individuals that received continuous antacid therapy. Urinary samples from individuals on a normal diet were collected for 2 months. These samples showed that there are minor daily fluctuations in silicon urinary excretion. In individuals who received 5 g magnesium trisilicate antacid, urinary excretion of silicon increased 3- to 38-fold in the first 24 h after magnesium trisilicate ingestion and remained elevated for a further 2 days. In two other healthy subjects (no further details), frequent, simultaneous measurements of urinary and serum silicon concentrations were made for 24 h following ingestion of 5 g magnesium trisilicate. Peak urinary and serum concentrations of silicon were reached after 1–2 h (10.68 mmol/L and 2- to 3-fold above the baseline of approximately 30 μmol/L, respectively). This study also demonstrated the importance of the kidney in the excretion of silicon by comparing the excretion of silicon in healthy adults and in patients with chronic renal failure. It was shown that in healthy individuals, serum silicon concentrations are maintained within a narrow range, but that hypersilicaemia can develop in individuals with kidney disease.

Silicon absorption from magnesium trisilicate was studied in healthy volunteers with normal kidney function and not taking silicon supplements or any medication (Sripanyakorn et al., 2009). Blood samples were collected at 30 min intervals for the first 2 h, then at 1-h intervals for a further 4 h. Urine was collected in two 3-h collections. The mean baseline fasting serum silicon concentration for all participants reported in this study was 113.9 μg/mL. There was a statistically significant increase in urinary silicon over the 6-h collection period following ingestion of magnesium trisilicate ($p < 0.001$), with urinary silicon greatest in the second 3-h collection period. The proportion of the dose excreted in urine was 3.7% for magnesium trisilicate. According to the authors, slow absorption of magnesium trisilicate is related to its buffering activity. As the initial disaggregation of magnesium trisilicate may require acid digestion, silicate dissolution would be slow and relatively short-lived; therefore, the percentage absorption from antacids would be of small magnitude.

Overall, the Panel considered that the silicate anion from calcium silicate or magnesium trisilicate is absorbed to a limited extent in rats with evidence that absorption is saturable. No data were available for magnesium silicate.

Based on a 2-year study with calcium silicate incorporated in the diet in rats, the Panel considered that at high doses (up to 5,000 mg/kg bw per day), there is evidence of silicon accumulation in the liver and kidney.

The Panel considered that data in humans with magnesium trisilicate indicated that silicate anion is absorbed to a limited extent (less than 5%) similarly to rodents, becomes systemically available and silicon is excreted in the urine. No human data were available for calcium silicate or magnesium silicate.

The Panel considered that a read-across approach from magnesium trisilicate was appropriate and considered that silicate anion from both calcium silicate or magnesium silicate would be absorbed and excreted similarly in man.

The Panel noted that studies with synthetically produced talc in mice, rat and guinea pigs as well as talc (baby powder) in hamsters indicated that less than 2% of talc was systemically available with low levels found in the liver.

The Panel considered that calcium silicate (E 552), magnesium silicate (E 553a(i)), magnesium trisilicate (E 553a(ii)) and talc (E 553b) dissociate to a limited extent in the gastrointestinal tract into silicates and their corresponding cations. The resulting amounts of calcium and magnesium ions released were considered too low to disturb normal physiological processes and therefore, the

consequence of ingesting them from the use of the food additives E 552, E 553a and E 553b are not discussed further in this opinion.

3.5.2. Acute toxicity

Calcium silicate

A series of experiments with male Sprague–Dawley rats were reported by Litton Bionetics Inc (1974a).

Ten male rats (average weight 250 g) were administered a single oral dose of calcium silicate (Silene EF) (5,000 mg/kg bw) suspended in 0.85% saline by gavage. All of the animals died within 24 h. At necropsy, bloody stomach mucosa with distension, pleural fluid present and lung congestion was reported (Litton Bionetics Inc, 1974a).

Rats (5 males/group, average weight 250 g) were administered a single oral dose of calcium silicate (Silene EF) (0, 100, 500, 1,000, 2,000, 3,000 or 4,000 mg/kg bw) suspended in 0.85% saline by gavage. All animals were necropsied following a 10-day observation period. There were no deaths up to 1000 mg/kg bw, and 1/5, 2/5, and 3/5 deaths in the 2,000, 3,000, and 4,000 mg/kg bw groups, respectively. The necropsy findings in the animals that died receiving 2,000, 3,000 and 4,000 mg calcium silicate/kg bw during the 10-day observation period were bloody stomach mucosa with distension, pleural fluid present and lung congestion. The LD_{50} was determined by the authors to be 3,400 mg/kg bw (Litton Bionetics Inc, 1974a).

In another experiment, 10 male rats (average weight 385 g) were administered a single oral dose of 5,000 mg/kg bw calcium silicate (Silene EF) (as a 24.1% w/v suspension in saline) and were observed for the following 7 days (Litton Bionetics Inc, 1974a). There were no deaths, no signs of toxicity or abnormal necropsy findings. The LD_{50} was concluded by the authors to be greater than 5,000 mg/kg bw.

Magnesium silicate

In the Hill Top Biolaps (1989 (Documentation provide to EFSA n 19)) study (GLP-compliant), five females and five males Harlan Sprague–Dawley rats received 5,000 mg/kg bw of magnesium trisilicate in distilled water. No deaths occurred during the observation period.

In the Tox Monitor Laboratories, Inc (2000 (Documentation provide to EFSA n 28)) study (GLP-compliant), five females and five males Harlan Sprague–Dawley rats received by gavage 5,000 mg/kg bw of magnesium trisilicate in distilled water. No deaths occurred during the observation period.

From these two studies, the authors concluded that the LD_{50} for magnesium silicates in rats was higher than 5,000 mg/kg bw.

Magnesium trisilicate

No studies were available.

Talc

Ten male Sprague–Dawley CD rats (average weight 250 g) were administered a single oral dose of talc (5,000 mg/kg bw) suspended in 0.85% saline by gavage. All of the animals died within 24 h. At necropsy, impacted stomach, patchy liver and bloody fluid in the stomach and intestine were reported (Litton Bionetics Inc, 1974b).

Sprague–Dawley CD rats (5 males/group, average weight 250 g) were administered a single oral dose of talc (0, 50, 100, 500, 1,000, 2,000 or 3,000 mg/kg bw) suspended in saline by gavage. All animals were necropsied following a 10-day observation period. There were no deaths or adverse necropsy findings in the groups that received 50 or 100 mg/kg bw. In the 500, 1,000, 2,000 and 3,000 mg/kg bw groups, the numbers of deaths were 1/5, 3/5, 4/5 and 5/5, respectively. The necropsy findings in the animals that died receiving 500, 1,000, 2,000 or 3,000 mg talc/kg bw during the 10-day observation period were impacted stomach, patchy liver and bloody fluid in the stomach and intestine. The LD_{50} was determined by the authors to be 920 mg/kg bw (Litton Bionetics Inc, 1974b).

In a second experiment, 10 male Sprague–Dawley CD rats (average weight 219 g) were administered a single oral dose of 5,000 mg/kg bw talc (as a 18.3% w/v suspension in saline) and were observed for the following 7 days. There were no deaths, no signs of toxicity or abnormal necropsy findings. The LD_{50} was concluded by the authors to be greater than 5,000 mg/kg bw (no further details were available on this study) (Litton Bionetics Inc, 1974b).

Overall, based on the available studies the Panel considered that calcium silicate, magnesium silicate and talc have a low acute oral toxicity. No studies were available for magnesium trisilicate;

however, the Panel considered that a read-across approach was appropriate and that it would also have a low acute toxicity.

3.5.3. Short-term and subchronic toxicity

Calcium silicate

Calcium silicate (Silene EF) was added at levels of 0%, 1%, 5%, 10% and 20% (equivalent to 0, 1,200, 6,000, 12,000 or 24,000 mg/kg bw per day) to the feed and given to male and female Carworth Farms strain rats (n = 15 per group) for 4 weeks (Hazelton Laboratory, 1956 (Documentation provide to EFSA n 18)). After 2 weeks, the rats receiving 10% and 20% in the diet exhibited very poor weight gain, unthrifty appearance and severe signs of respiratory infections and were killed. In order to avoid the dusty and alkalinity nature of the test material, calcium silicate was mixed with gelatine and the doses received by the animals of the previous 1% and 5% groups were elevated at 10% and 20% for the remaining 2 weeks. At termination of the study, no gross pathology could be attributed to the ingestion of the test material; only hard faecal pellets were found in the large intestine of the animals having received doses of 5% for 2 weeks and then 20% for the 2 following weeks.

Magnesium silicate

No studies were available.

Magnesium trisilicate

Rats

Charles River rats (15 animals/sex per group; age not specified) were fed semi-synthetic diets containing magnesium trisilicate (1,800 mg/kg bw per day) (Newberne and Wilson, 1970). Control animals received untreated diet. All animals were examined daily and weighed weekly. Urinary specific gravity, and urinary protein and glucose concentrations were measured before dosing began, and then at weekly intervals. Total and differential white blood cell counts, packed cell volume, prothrombin time, serum concentrations of haemoglobin and urea nitrogen were all measured before dosing began, and then at weekly intervals. At the end of the 4-week dosing period, all animals were sacrificed and necropsied. Organ weights were determined and a complete set of tissues preserved for histopathological examination (tissues and organs examined not specified). The only clinical findings were occasional polydipsia, polyuria and soft stools seen intermittently in a few animals, clinical parameters were within normal limits. No adverse histopathological findings were reported.

Guinea pigs

Guinea pigs (6 males, strain not specified; age and weight not stated) were given a suspension of magnesium trisilicate in their drinking water for 4 months (5 days/week) (Dobbie and Smith, 1982). The dose of magnesium trisilicate in water was estimated by the study author to be 50–100 mg magnesium trisilicate/kg bw per day. Normal tap water was given to the control group throughout, and on 2 days/week for the test group. According to the authors, tap water in their study had a silicon concentration of 0.2 mg/L, and a soluble silicon concentration of 10 μmol/L. After 4 months, all animals were killed and a necropsy examination of the kidneys conducted (no other organs were examined). Kidney sections were examined microscopically for a birefringent material using crossed prisms. There were no kidney lesions in control animals. All six animals treated with magnesium trisilicate developed renal lesions with a similar distribution pattern and severity, which predominantly affected the distal nephron. The affected segments showed dilatation or cystic change, and some tubules were 'plugged' with 'proteinaceous material'. In the regions of the affected tubules, the interstitium was expanded by chronic inflammatory infiltrate and an excess of collagen fibres. There were no abnormal findings involving the glomeruli. The Panel also noted that the magnesium trisilicate used in this study was prepared by the authors by crushing and milling in order to obtain particles ranging from 0.5 to 40 μm.

Dogs

Pure bred Beagle dogs (6–9 animals/sex per group; approximately 6 months old) were fed diets containing magnesium trisilicate (1,800 mg/kg bw per day) for 4 weeks. The protocol was the same as the one used for the rat study described above (Newberne and Wilson, 1970). A few of the dogs had polydipsia and polyuria, and most of the treated animals had occasional soft faeces discoloured by unabsorbed test substance. All animals developed gross cortical lesions of the kidney. Histopathological

examination revealed hypertrophy of tubular epithelium (with or without degenerative changes), inflammatory cell infiltration into the interstitium and dilatation of some and collapse of other tubules. These findings were observed with varying severity within localised areas of the kidney. Occasional crystalline deposits characteristic of mineralisation were observed in degenerated tubular epithelium. The glomeruli were not affected. The author of the study concluded that the observed renal effects were due to irritation followed by degenerative and regenerative changes, accompanied by inflammatory cell infiltration into the interstitium. However, impairment of renal function was not detected by any of the clinical tests in urine and serum. The authors suggested that a study of longer duration could have revealed that kind of impairment of renal function.

Talc

Rats

Talc was tested in a 5-day toxicity study in Sprague–Dawley rats (10 males; 10–12 weeks old, average weight 367 g)) (Litton Bionetics Inc, 1974b). The animals were administered by gavage with 5,000 mg/kg bw per day for 5 days and observed for 14 days. The authors reported animals showing slightly rough fur, decreased activity and light-coloured faeces; no adverse pathological findings were reported.

Singh et al. treated 6 male/female Wister rats (not further specified) with 0.14 mg talc/kg bw per day (talc not characterised) for 16 weeks (Singh et al., 2014) or 20 weeks (Singh et al., 2016) and observed a significant increase in blood glucose and triglyceride levels accompanied by a decrease in blood insulin levels, which according to the authors suggested that oral exposure to talc may cause diabetes and insulin resistance (Singh et al., 2016).

Two groups (5 animals/group) of male albino Wistar rats (100–125 g) were orally administered talc (provided by Siddhartha Institute of Pharmacy) 10 mg/kg bw per day in saline or saline control for 21 days (Afzal et al., 2018). Administration of talc resulted in a significant increase in body weight (140 ± 23.17 g) compared to saline control (103 ± 5.56 g). At termination, blood levels of glucose in talc-treated animals were 194.0 ± 9.48 mg/dL compared to 79.4 ± 5.49 mg/dL in saline controls. Blood creatinine and urea were statistically significantly increased in talc-treated animals 1.3- and 2.1-fold, respectively. Serum cholesterol and triglycerides were also statistically significantly increased in talc-treated animals 2.4- and 9.7-fold, respectively, whereas serum HDL was statistically significantly decreased (0.73-fold) in talc-treated animals. Talc administration also resulted in a slight increase in serum ALT and AST of 1.4- and 1.3-fold, respectively. However, although statistically significant, the Panel considered these changes in liver serum enzyme not of toxicological significance.

The Panel noted the very low levels of talc used in the studies of Singh et al. (2014, 2016) and Afzal et al. (2018) as compared to 5,000 mg/kg bw per day in the study of Litton Bionetics Inc (1974b). Additionally, the Panel noted that the talc used for the studies of Singh et al. (2014 and) Singh et al. (2016) and Afzal et al. (2018) was not characterised and, according to Singh et al. (2016), 'may contain a variety of elements such as nickel and iron' (not further specified). The Panel considered that it was unclear how talc (E 553b), which is known to be hardly absorbed, could induce such a significant increase in body weight and diabetes in rats, and particularly at such low doses. Therefore, the Panel considered that the results of these studies could not be used for the hazard characterisation of talc (E 553b).

Overall, no adverse effects were observed in limited short-term and subchronic toxicity studies in rats. The kidney effects observed in dogs when treated with magnesium trisilicate were most probably related to the large amount of test compound administered as a bolus dose. The effects on the kidney reported in guinea pigs treated with magnesium trisilicate could be due to higher concentrations in the primary urine as a consequence of lower glomerular filtration-rates in guinea pigs (2.29 mL plasma/min per kg; Neiberger, 1992) as compared to rats (4.63 mL plasma/min per kg; Pestel et al., 2007).

3.5.4. Genotoxicity

In vitro

Calcium silicate

In the study by Litton Bionetics Inc (1974a), calcium silicate (Silene EF) was assessed for its mutagenicity in the reverse mutation assay using *Salmonella* Typhimurium strains TA1530 and G-46 and for induction of mitotic gene conversion in *Saccharomyces cerevisiae* (strain D3) and no

genotoxicity was observed. However, the Panel noted that the results from the bacterial gene mutation assay are limited due to the inadequate number of *S.* Typhimurium tester strains used and missing information on the use of metabolic activation and concentrations of test substance employed. In addition, the Panel noted that the gene conversion assay with *S. cerevisiae* has not been validated and it does not belong to the assays recommended for regulatory purposes (EFSA Scientific Committee, 2011). On this basis, the results were considered to be of low relevance.

In the study by (Aslam et al., 1993), the potential of calcium silicate (three different samples with a reported purity of approximately 97% with a different percentage of calcium oxide and silica oxide) to induce chromosomal aberrations and sister chromatid exchanges (SCE's) was investigated in purified Ficoll–Hypaque human lymphocytes obtained from a healthy 30-year-old male volunteer donor in the absence of S9 metabolic activation. Peripheral blood lymphocyte cultures were incubated (in the presence of 5-bromo-2′-deoxyuridine (BrdUrd) to detect SCE's) with each of the three samples of calcium silicate suspension at concentrations of 0.1, 1.0, 10 or 100 μg/mL. All cultures were then incubated in the dark at 37°C for 48 or 72 h to study chromosomal aberrations and SCE's respectively. Results obtained indicated that all three samples induced significant increases of both aberrant cells and SCE's at the two higher concentrations of 10 and 100 μg/mL compared with the concurrent untreated controls. For chromosomal aberrations, this result was only obtained when the gaps were included in the statistical analyses. The authors also indicate a significant reduction of third division metaphase cells at the highest doseblevel (100 μg/mL). The Panel noted that 'gaps' should be recorded and reported separately but not included in the total aberration frequency,z and therefore not evaluated in the subsequent statistical analyses as indicated in the relevant OECD Guideline TG 473. In the present case, the Panel also noted that 'gaps' were likely to be induced by BrdUrd, used to detect SCE's and normally not employed in the chromosome aberration studies. For SCE's, despite the reported statistically significant increases their frequencies never doubled the baseline frequency observed in the concurrent untreated control which is a common criteria for considering a result as positive. In addition, biological relevance of SCEs is unclear and the test for induction of sister chromatid exchanges does not belong to the assays recommended for regulatory purposes (EFSA Scientific Committee, 2011). Overall, the Panel considered that the study had some shortcomings, however, it does not indicate any genotoxic potential of calcium silicate.

Concentrations (1, 10 and 100 μg/mL) of calcium silicate were tested for their potential to cause chromosomal aberrations in human embryonic lung (WI-38) cell cultures observed in anaphase in the absence of S9 metabolic activation only (Litton Bionetics Inc, 1974a). At 24 h following addition of the test substance, 100 cells in anaphase from each culture were analysed for chromosomal aberrations and no cytogenetic effects were observed. However, the Panel noted that this assay has not been validated and does not belong to the assays recommended for regulatory purposes (EFSA Scientific Committee, 2011).

Magnesium silicate

In the study by Prival et al. (1991), magnesium silicate[21] was assessed for its mutagenicity in the reverse mutation assay using the *Salmonella* Typhimurium strains TA1535, TA1537, TA1538, TA98, TA100 and the *E. coli* strain WP2 according to the method of Ames by the plate incorporation method both in the absence and presence of S9 metabolic activation and no induction of mutations was observed. The Panel noted that this study was essentially performed in compliance with the OECD guideline no. 471.

Magnesium trisilicate

No studies were available.

Talc

In the study by Litton Bionetics Inc (1974b) talc was assessed for its mutagenicity in the reverse mutation assay using *S.* Typhimurium strains TA1530 and G-46 and for induction of mitotic gene conversion in *S. cerevisiae* (strain D3) and no genotoxicity was observed. However, the Panel noted that the results from the bacteria gene mutation assay are limited due to the inadequate number of *S.* Typhimurium tester strains used and missing information on the use of metabolic activation and concentrations of test substance employed. In addition, the Panel noted that the gene conversion

[21] The Panel noted that the test substance used by the authors was given as CAS Number 15702-53-1.

assay with *S. cerevisiae* has not been validated and does not belong to the assays recommended for regulatory purposes (EFSA Scientific Committee, 2011).

Concentrations (2, 20 and 200 μg/mL) of talc were tested for their potential to cause chromosomal aberrations in human embryonic lung (WI-38) cell cultures observed in anaphase in the absence of S9 metabolic activation only (Litton Bionetics Inc, 1974b). At 24 h following addition of the test substance, 100 cells in anaphase from each culture were analysed for chromosomal aberrations and no cytogenetic effects were observed. However, the Panel noted that this assay has not been validated and does not belong to the assays recommended for regulatory purposes (EFSA Scientific Committee, 2011).

In the study by Endo-Capron et al. (1993), the genotoxicity of talc was evaluated in rat pleural mesothelial cells using the unscheduled DNA synthesis (UDS) and SCE's assays. For the induction of UDS, three different samples of talc with particle size in the respirable range were incubated with the cells for 24 h. Each talc sample was tested at a concentration of 50, 100 and 250 μg/mL in the medium and each concentration was replicated six times. Anatase was tested as the negative control and did not increase UDS. Crocidolite and chrysotile were used as the positive controls and both showed enhancement of UDS. None of the talc samples increased UDS. For the induction of SCE's, samples of talc were treated at 2, 5, 10 or 15 μg/mL and incubated for 48 h at 37°C in the dark. No induction of SCE's was observed with any talc sample at any concentration tested. Similarly, negative control particles, attapulgite and anatase did not induce SCE's. Positive controls mitomycin C and potassium chromate induced statistically significant increases of SCE's while crocidolite did not show consistent positive result. On this basis, the authors concluded that equivocal results for the positive control crocidolite weakened the strength of the study. The Panel agreed with this conclusion and noted that the biological relevance of SCE is unclear and that the assay does not belong to those recommended for regulatory purposes (EFSA Scientific Committee, 2011).

In vivo

Calcium silicate

In a host-mediated assay, groups of 10 male IBR mice were administered calcium silicate (Silene EF) by gavage at 15, 150 and 1,500 mg/kg either once (acutely) or on five consecutive days 24 h apart (Litton Bionetics Inc, 1974a). Negative and positive control animal groups were also included. The highest dose level of calcium silicate (1,500 mg/kg) corresponded to the calculated LD_5. The indicator organisms used in this study were: (i) two histidine auxotrophs (his G-46, TA-1530) of *S.* Typhimurium for induction of reverse mutation and (ii) a diploid strain (D-3) of *S. cerevisiae* for the induction of mitotic gene conversion. Both for the acute and subacute studies, within 30 min from the last administration, all animals received 2 mL of the indicator organism, intraperitoneally, each mL containing 3.0×10^8 cells for *Salmonella* and 5.0×10^8 cells for *Saccharomyces*. Three hours after the injection of the indicator organism, the mice were sacrificed and the host cells were aseptically washed out of the peritoneum of each animal and plated under standard conditions. A second experiment was additionally performed under the same experimental conditions with only one dose level of calcium silicate but at 5,000 mg/kg. Results obtained in both experiments indicated that calcium silicate did not show genotoxic activity in any of the indicator organisms and dose levels employed. The Panel noted that the host mediated assay does not belong to those recommended for regulatory purposes (EFSA Scientific Committee, 2011).

In an *in vivo* cytogenetic assay, the induction by calcium silicate (Silene EF) of chromosomal aberrations in bone marrow cells of rats was investigated (Litton Bionetics Inc, 1974a). Groups of five male albino rats were administered with test substance by gavage acutely at 15, 150 and 1,500 mg/kg bw or subacutely on five consecutive days, 24 h apart, at the same dose levels employed for the acute treatment. Negative and positive control animal groups were also included. For the acute treatment, sampling of bone marrow cells was performed at 6, 24 and 48 h from the last administration, while in the subacute study, sampling was only performed at 6 h from the last administration. A second experiment was additionally performed under the same experimental conditions with only one dose-level of calcium silicate at 5,000 mg/kg. Results obtained indicated that calcium silicate induced no increases in the incidence of chromosomal aberrations in the bone marrow cells following both acute and subacute administration, at any of the dose level employed. The Panel noted that this study, essentially complies with the OECD Guideline 475 requirements, although it was performed before this Guideline was established.

In a dominant lethal assay, calcium silicate (Silene EF) was administered by gavage to groups of ten male albino rats acutely at 15, 150 and 1,500 mg/kg bw or subacutely on five consecutive days,

24 h apart, at the same dose levels employed for the acute treatment (Litton Bionetics Inc, 1974a). Negative and positive control animal groups were also included. Following treatment, the males were sequentially mated to two females per week for 8 weeks (7 weeks in the subacute study) and housed separately until sacrifice. A second experiment was additionally performed under the same experimental conditions with only one dose level of calcium silicate but at 5,000 mg/kg. Fertility index, total implants (live fetuses plus early and late fetal deaths), total dead (early and late fetal deaths), dead implants per total implants and preimplantation loss (calculated as the difference between the total *corpora lutea* and total implant counts) were evaluated and according to the authors, the results did not raise concern with respect to genotoxicity. The Panel agreed with this conclusion.

Magnesium silicate

No studies were available.

Magnesium trisilicate

No studies were available.

Talc

In a host-mediated assay, groups of 10 male IBR mice were administered talc by gavage at 30, 300 and 3,000 mg/kg either once (acutely) or on five consecutive days 24 h apart (Litton Bionetics Inc, 1974b). Negative and positive control animal groups were also included. The highest dose level of talc (3,000 mg/kg) corresponded to the calculated LD_5. The indicator organisms used in this study were: (i) two histidine auxotrophs (his G-46, TA-1530) of *S.* Typhimurium for induction of reverse mutation and (ii) a diploid strain (D-3) of *S. cerevisiae* for the induction of mitotic gene conversion. Both for the acute and subacute studies, within 30 min from the last administration, all animals received 2 mL of the indicator organism, intraperitoneally, each mL containing 3.0×10^8 cells for *Salmonella* and 5.0×10^8 cells for *Saccharomyces*. Three hours after the injection of the indicator organism, the mice were sacrificed and the host cells were aseptically washed out of the peritoneum of each animal and plated under standard conditions. A second experiment was additionally performed under the same experimental conditions with only one dose-level of talc but at 5,000 mg/kg. Results obtained in both experiments indicated that talc did not show genotoxic activity in any of the indicator organisms and dose-levels employed. The Panel noted that the host mediated assay does not belong to those recommended for regulatory purposes (EFSA Scientific Committee, 2011).

In an *in vivo* cytogenetic assay, the induction by talc of chromosomal aberrations in bone marrow cells of rats was investigated (Litton Bionetics Inc, 1974b). Groups of five male albino rats were administered with talc by gavage acutely at 30, 300 and 3,000 mg/kg bw or subacutely on five consecutive days, 24 h apart, at the same dose levels employed for the acute treatment. Negative and positive control animal groups were also included. For the acute treatment, sampling of bone marrow cells was performed at 6, 24 and 48 h from the last administration, while in the subacute study sampling was only performed at 6 h from the last administration. A second experiment was additionally performed under the same experimental conditions with only one dose level of talc but at 5,000 mg/kg. Results obtained indicated that talc induced no increases in the incidence of chromosomal aberrations in the bone marrow cells following both acute and subacute administration, at any of the dose level employed. The Panel noted that this study, essentially complies with the OECD Guideline 475 requirements, although it was performed before this Guideline was established.

In a dominant lethal assay, talc was administered by gavage to groups of 10 male albino rats acutely at 15, 150 and 1,500 mg/kg bw or subacutely on five consecutive days, 24 h apart, at the same dose levels employed for the acute treatment (Litton Bionetics Inc, 1974b). Negative and positive control animal groups were also included. Following treatment, the males were sequentially mated to two females per week for 8 weeks (7 weeks in the subacute study) and housed separately until sacrifice. A second experiment was additionally performed under the same experimental conditions with only one dose level of talc but at 5,000 mg/kg. Fertility index, total implants (live fetuses plus early and late fetal deaths), total dead (early and late fetal deaths), dead implants per total implants and preimplantation loss (calculated as the difference between the total *corpora lutea* and total implant counts) were evaluated. Results obtained indicated that talc induced significant decreases in *corpora lutea* at week 5 in the acute treatment and significant increases in the average resorption and in dead implants at week 6. However, these effects revealed no dose–response or time-trend pattern. No effects were observed at 5,000 mg/kg for the acute treatment. The author concluded that talc does not induce dominant lethal mutations under the reported experimental

condition. The Panel agreed with this conclusion and further noted that the number of animals employed for this study was low.

Overall, the Panel considered that the available data did not raise concern with respect to genotoxicity of calcium silicate (E 552), magnesium silicate (E 553a(i)), magnesium trisilicate (E 553a (ii)) and talc (E 553b).

3.5.5. Chronic toxicity and carcinogenicity

Carworth rats (15 male and 15 female weanlings/group) were fed a diet containing 0, 1%, 5%, 7.5% or 10% (equivalent to 0, 500, 2,500, 3,750 and 5,000 mg/kg bw per day, respectively) calcium silicate (Silene EF) as a gelatine mix (Hazelton Laboratory, 1956 [Documentation provided to EFSA No xx). The groups fed 7.5% and 10% were initially treated with diet containing 5% calcium silicate for the first 4 weeks followed by diet containing 7.5% calcium silicate to acclimatise the animals to the diet. The highest dose group was fed a diet containing 10% calcium silicate from 11 weeks. Control animals were fed diet containing gelatine only. Blood counts were made on 10 male and 10 female rats selected at random at the beginning of the study. Three male and three female rats from each group were randomly selected at weeks 13, 52 and 104 and blood counts performed. During week 104, five male and five female rats from each group were randomly selected and urinary pH determined. Pooled faeces were collected prior to termination for the determination of silicon dioxide content. The study was terminated at 104 weeks, and liver, kidney and spleen wet weights determined. Silicon dioxide levels were determined in the liver, spleen, kidney, skeletal muscle and cardiac muscle tissues (organs from three animals of each sex were pooled; six animals in total/sex were used in these determinations). Silicon dioxide levels were also determined in the testes (three animals were pooled; six animals in total were used in this determination). The thyroid, lung, heart, liver, stomach, large and small intestines, pancreas, spleen, kidney, adrenal, urinary bladder, gonads, bone marrow and skeletal muscle were collected from six male and six female rats/group, fixed and examined histopathologically. The appearance and behaviour of the rats were comparable in all groups. The faeces of rats in the 7.5% and 10% calcium silicate were hard and lighter in colour than the control groups and the majority of rats in these groups exhibited signs of mild constipation. Average silicon dioxide contents in organs showed a dose-dependent increase in the liver and kidney, with the highest levels found in the kidney. During the first year, both male and female rats in the 7.5% and 10% calcium silicate groups exhibited significant growth retardation. However, from 78 weeks, this retardation was only apparent in the 10% calcium silicate group. No significant difference in blood haemoglobin, total red and white cell counts or differential count throughout the study. The average urinary pH values of all experimental groups were not significantly increased over control values for both sexes. There was no effect on mortality. No gross pathology or histopathological findings that could be attributed to calcium silicate were observed in rats of the 1% and 5% calcium silicate groups. Dilated hepatic portal veins and bile ducts, and cholangitis were noted in 3 males and one female of the 7.5% and in two males of the 10% groups. The authors reported that at necropsy of animals that died during the study, 'the primary cause of death was an overwhelming respiratory infection'. The Panel noted that although the authors reported that 'silicon dioxide was determined in faeces and in a series of organs', the methodology used for this determination measured in fact total silicon as silicates; in addition, phosphorus strongly interferes in this method and has to be removed before measurement of silicates. The Panel considered that this study was not conducted according to the current standard. Particularly, only 15 animals per sex per group were used, no reliable clinical chemistry and haematological evaluation was conducted and animals had respiratory infection. The Panel noted that there was no indication on carcinogenicity; however, due to further limitations (histopathological examination was performed on only six animals per sex per group and on a limited number of organs and tissues) it was not possible to conclude on the chronic toxicity of calcium silicate.

There was no data for oral chronic toxicity/carcinogenicity of talc.

3.5.6. Reproductive and developmental toxicity

Reproductive toxicity studies

No studies were available.

Developmental studies

Calcium silicate

Mice

Pregnant CD-1 mice (20–23 animals/group) were treated with calcium silicate (Silene EF) by gavage once daily from gestation day (GD) 6 to 15 with doses of 16, 74, 350 and 1,600 mg/kg bw per day in water (1 mL/kg bw) (FDRL, 1972 (Documentation provide to EFSA n 15)). The control group was dosed with 1 mL corn oil/kg bw. At necropsy on GD 17, the surviving dams appeared to be completely normal and the number of implantations, and live fetuses were comparable to the control group. Doses up to 1,600 mg calcium silicate/kg bw per day had no noticeable effects on implantation nor on maternal and fetal survival. The numbers of live or dead fetuses, resorptions and implantations, as well as the fetal weights did not differ among the groups. The sex distribution of fetuses was not affected by the treatment. The number of abnormalities seen in either soft tissues or skeletons at fetal pathological examination of the calcium silicate-treated groups, did not differ from the number in vehicle-treated dams of the control group.

Rats

Pregnant Wistar rats (20–22 animals/group) were treated with calcium silicate (Silene EF) by gavage once daily from GD 6 to 15 with doses of 16, 74, 350 and 1,600 mg/kg bw per day in water (1 mL/kg bw) (FDRL, 1972 (Documentation provide to EFSA n 15)). The control group was dosed with 1 mL corn oil/kg bw. At necropsy on GD 20, animals that had received doses up to 1,600 mg calcium silicate/kg bw per day appeared to be completely normal and had no noticeable effects on implantation nor on maternal and fetal survival. The numbers of live or dead fetuses, resorptions, implantations and fetal weights did not differ among the groups. The sex distribution of fetuses was not affected by the treatment. The number of abnormalities seen in either soft tissues or skeletons at fetal pathological examination of the calcium silicate-treated groups did not differ from the number in vehicle-treated dams of the control group.

Hamsters

Pregnant Golden hamsters (19–22 animals/group) were treated with calcium silicate (Silene EF) by gavage once daily from GD 6 to 10 of gestation with doses of 0, 16, 74, 350 or 1,600 mg/kg bw per day in water (1 mL/kg bw) (FDRL, 1972 (Documentation provide to EFSA n 15)). The control group was dosed with 1 mL corn oil/kg bw. At necropsy on GD 14, animals that had received doses up to 1,600 mg calcium silicate/kg bw per day appeared to be completely normal and showed no noticeable effects on implantation nor on maternal and fetal survival. The numbers of live or dead fetuses, resorptions, implantations or fetal weights did not differ amongst the groups. The sex distribution of fetuses was not affected by the treatment. The number of abnormalities seen in either soft tissues or skeletons at fetal pathological examination of the calcium silicate-treated groups, did not differ from the number in vehicle-treated dams of the control group.

Rabbits

Artificially inseminated Dutch-belted rabbits (15–33 animals/group) were treated with calcium silicate (Silene EF) by gavage once daily from GD 6 to 18 with doses of 0, 16, 74, 350 or 1,600 mg/kg bw per day in water (8, 11, 12, 10 or 11 pregnant surviving females/group, respectively) (FDRL, 1973a). The mortality in this study was 3, 6, 3, 2 and 9 does in the respective groups. In addition, many animals per group were non-pregnant (5, 9, 11, 14 and 15 does in the respective groups). At necropsy on GD 20, animals that had received doses up to 1,600 mg calcium silicate/kg bw per day appeared to be completely normal and had no noticeable effects on implantation nor on maternal and fetal survival. The numbers of live or dead fetuses, resorptions, implantations and fetal weights did not differ amongst the groups. The sex distribution of fetuses was not affected by the treatment. The number of abnormalities seen in either soft tissues or skeletons at fetal pathological examination of the calcium silicate-treated groups, did not differ from the number in vehicle-treated dams of the control group. The Panel noted that due to the high mortality and the low pregnancy rate, this study cannot be used for hazard assessment.

Magnesium silicate

No studies were available.

Magnesium trisilicate

No studies were available.

Talc

Mice

Pregnant CD-1 mice (21–22 animals/group) were treated by gavage once daily from GD 6 to 15 with doses of 0, 16, 74, 350 and 1,600 mg talc/kg bw per day suspended in corn oil (dose volume not described) (FDRL, 1973b). At necropsy on GD 17, the surviving dams appeared to be completely normal and the number of implantations, and live fetuses were comparable to the control group. Doses up to 1,600 mg talc/kg bw per day had no noticeable effects on implantation nor on maternal and fetal survival. The numbers of live or dead fetuses, resorptions, implantations and also fetal weights did not differ among the groups. The sex distribution of fetuses was not affected by the treatment. The number of abnormalities seen in either soft tissues or skeletons at fetal pathological examination of the treated groups did not differ from the number in vehicle-treated dams of the control group.

Rats

Pregnant Wistar rats (20–23 animals/group) were treated by gavage once daily from GD 6 to 15 with doses of 0, 16, 74, 350 and 1,600 mg talc/kg bw per day suspended in corn oil (dose volume not described) (FDRL, 1973b). At necropsy on GD 20, animals that had received doses up to 1,600 mg talc/kg bw per day appeared to be completely normal and had no noticeable effects on implantation nor on maternal and fetal survival. The numbers of live or dead fetuses, resorptions, implantations and fetal weights did not differ amongst the groups. The sex distribution of fetuses was not affected by the treatment. The number of abnormalities seen in either soft tissues or skeletons at fetal pathological examination of the talc-treated groups did not differ from the number in vehicle-treated dams of the control group.

Hamsters

Pregnant Golden hamsters (19–21 animals/group) were treated by gavage once daily from GD 6 to 10 with doses of 0, 12, 56, 260 or 1,200 mg talc/kg bw per day suspended in corn oil (dose volume not described) (FDRL, 1973b). Does of the high-dose group lost weight from GD 6 to 8. At necropsy on GD 14, animals that had received doses up to 1,200 mg talc/kg bw per day appeared to be completely normal and showed no noticeable effects on implantation nor on maternal and fetal survival. The numbers of live or dead fetuses, resorptions, implantations or fetal weights did not differ amongst the groups. The sex distribution of fetuses was not affected by the treatment. The number of abnormalities seen in either soft tissues at fetal pathological examination of the talc-treated groups, did not differ from the number in vehicle-treated dams of the control group. Fetuses of the 1,200 mg/kg bw per day group showed skeletal retardation, which is most likely due to decreased body weights of the does.

Rabbits

Artificially inseminated Dutch-belted rabbits (14–29 animals/group) were treated by gavage once daily from GD 6 to 18 with doses of 0, 9, 42, 195 or 900 mg talc/kg bw per day suspended in corn oil (7, 11, 10, 10 or 11 pregnant surviving females/group, respectively) (FDRL, 1973c). Dose volume in the control and high-dose groups was 4 mL corn oil/kg bw per day and in the other groups 1 mL corn oil/kg bw per day. The mortality in this study was 2, 5, 4 and 7 including one aborted, two does in the respective groups. In addition, many animals per group were non-pregnant (6, 10, 11, 15 and 2 in the respective groups). At necropsy on GD 20, animals that had received doses up to 900 mg talc/kg bw per day appeared to be completely normal and had no noticeable effects on implantation nor on maternal and fetal survival. The numbers of live or dead fetuses, resorptions, implantations and fetal weights did not differ among the groups. The sex distribution of fetuses was not affected by the treatment. The number of abnormalities seen in either soft tissues or skeletons at fetal pathological examination of the talc-treated groups, did not differ from the number in vehicle-treated dams of the control group. The Panel noted that due to the high mortality and the low pregnancy rate, this study cannot be used for hazard assessment.

Overall, no reproductive study was available. Prenatal developmental toxicity studies with calcium silicate by gavage during organogenesis in mice, rats and hamsters (FDRL, 1972 (Documentation

provide to EFSA n 15)) and with talc (FDRL, 1973b) in mice and rats up to 1,600 mg/kg bw per day (the highest dose tested), showed no dose-related developmental effects.

3.5.7. Other studies

Human studies

A case report involving a patient with a history of renal colic who had taken the equivalent of 2 g magnesium trisilicate (as an antacid) with every meal for many years was available (Joekes et al., 1973). The 68-year-old male was first examined in 1971, at which point he had a history of two episodes of presumed renal colic. The patient had passed several bladder stones through the 1960s. The authors of the study commented that the patient was not certain how long he had been ingesting magnesium trisilicate, but it could have been from 1940, when renal colic was first diagnosed. Analysis of stones passed in urine in 1971 revealed that they predominantly consisted of opaline silica. The author of this study did not consider the intake of magnesium trisilicate to be excessive, and that if the stones were due to magnesium trisilicate then more silica stones should have be reported. However, the authors also reported that stone analysis in hospitals was limited, so the composition of the stones might not be accurate.

Treatment with silicate antacid drugs such as magnesium trisilicate resulting in urinary silicate calculi (Lee et al., 1993) are seldom found in humans (0.1–0.2% of all urinary stones). They are mostly found in adults but they have also been described in rare cases in children (Tasdemir et al., 2017), where they were associated with consumption of milk thickener containing 5.5% silicates in one case of a 6-month-old boy (Ulinski et al., 2004), or milk powder dissolved in silicate-rich mineral water (estimated daily intake of about 200 mg silicate) in a 10 month old boy (Nishizono et al., 2004).

The Panel noted that cases of renal calculi were rarely reported in the EudraVigilance database (online) considering the high number of exposed humans to magnesium trisilicate used as antacid. The Panel applied the WHO algorithm for assessing the association between adverse events and drug intake (Edwards and Biriell, 1994) and found that the association between silicate antacid use and renal calculi was 'possible' but not 'definite', which does not exclude that the occurrence of renal calculi and intake of silicates would be a chance finding.

3.6. Discussion

In previous evaluations, calcium silicate (E 552) and magnesium silicate (E 553a) have been combined with silicon dioxide (E 551). However, the ANS Panel provided a separate scientific opinion re-evaluating the safety of silicon dioxide (E 551) when used as a food additive, therefore not covering the silicates (E 552–553). The present opinion describes the re-evaluation of calcium silicate (E 552), magnesium silicate (E 553a(i)), magnesium trisilicate (E 553a(ii)) and talc (E 553b) when used as food additives.

According to Commission Regulation (EU) No 231/2012, the food additive calcium silicate (E 552) is defined as 'a hydrous or anhydrous silicate with varying proportions of CaO and SiO_2'; magnesium silicate (E 553a(i)) is defined as 'a synthetic compound of which the molar ratio of magnesium oxide to silicon dioxide is approximately 2:5' Although calcium silicate (E 552) and magnesium silicate (E 553(i)) may be described in terms of theoretical oxides, the Panel considered that they are not mixtures of silicon dioxide and calcium or magnesium oxides and, therefore, their definitions in the EU specifications should be revised accordingly. No definition for magnesium trisilicate (E 553a(ii)) is included in the EU specifications.

The water solubility of calcium silicate has been reported to be about 260 mg/L, though this requires a method which extends the measurement time for several days (CEFIC, 2017a (Documentation provided to EFSA n. 4)). The Panel considered this solubility indicates that calcium silicate and magnesium silicate are 'very slightly soluble' at equilibrium. According to Commission Regulation (EU) No 231/2012, magnesium trisilicate is insoluble in water and ethanol; however the Panel considered that a similar behaviour to calcium silicate and magnesium silicate would be expected at equilibrium for magnesium trisilicate. This assumption is also supported by the literature (Rashid et al., 2011). According to Commission Regulation (EU) No 231/2012 and information from industry (EUROTALC, 2018; Documentation provided to EFSA n. X), talc is insoluble in water.

Following an EFSA request, LD and TEM data for calcium silicate were provided. The Panel noted that these methods measure different particle characteristics, which are reflected in the different numerical size-values obtained. Taking into account the analysis by TEM provided by industry, calcium

silicate falls under the definition of nanomaterial according to the Commission Recommendation 2011/696/EU. However, the Panel considered that the dispersion method (sonication) of the sample before its analysis by TEM is not representative of the common use of calcium silicate as a food additive. Following an EFSA request, no TEM data were provided for magnesium silicate (E 553a(i)) and magnesium trisilicate (E 553a(ii)). SEM data for talc indicated a range of particle size distribution of 20–40 μm (EUROTALC, 2018; Documentation provided to EFSA n. X).

The Panel noted that crystalline silica (alpha-quartz) may be present as an associated mineral, according to the EU specifications for talc (E 553b). Crystalline silica is a class 1 carcinogen by inhalation (IARC, 1997) and no maximum limit for quartz has been established in the EU specifications for talc (E 553b). The Panel also noted that no maximum limit has been set for fluoride, while phlogopite (contains fluorine) is another possible associated mineral in talc (E 553b) according to the EU specifications. Therefore, the Panel considered that maximum limit for crystalline silica and fluoride should be included in the EU specifications for talc (E 553b).

The Panel considered that silicates may be determined in food via measuring the total silicon; however, under these conditions, it cannot be differentiated whether the measured silicon content originates from the added silicates or from other sources of silicon. The Panel also noted that no specific analysis for the presence of silicates or their particles in food have been reported in the literature.

General methods for the analysis of silicates are available but they relate mainly to the analysis of aqueous samples. Talc may be quantified through burning a sample of food/beverage in a furnace for 1 h at 500°C to remove organic components, followed by detection by X-ray diffraction.

The Panel considered that calcium silicate (E 552), magnesium silicate (E 553a(i)), magnesium trisilicate (E 553a(ii)) and talc (E 553b) are stable in food when used as food additives.

The Panel considered that in some biological studies, authors reported analysis of 'silica' or of 'silicon dioxide' content while analytical methods available at the time were only capable of measuring total silicon either measured as such or as silicate anion after transformation. Therefore, it was not possible for the Panel to determine whether it was silica, silicates or silicon that was measured.

The Panel considered that silicate anion from both calcium silicate or magnesium trisilicate was absorbed to a limited extent in rats. No data were available for magnesium silicate.

Based on a 2-year study with calcium silicate in rats, the Panel considered that at high doses (up to 5,000 mg/kg bw per day), there was evidence of silicon accumulation in the liver and kidney. The Panel considered that limited data in humans indicated that the silicate anion from magnesium trisilicate is absorbed to a limited extent, then excreted in the urine (as determined from urinary silicon measurements). No human data were available for calcium silicate or magnesium silicate; however, the Panel considered that a read-across approach was appropriate and considered that silicate anion from both calcium silicate and magnesium silicate would behave similarly.

The Panel noted that studies with synthetically produced talc in mice, rat and guinea pigs as well as talc (baby powder) in hamsters indicated that less than 2% talc was systemically available, with low levels seldom found in the liver.

The Panel considered that calcium silicate (E 552), magnesium silicate (E 553a(i)), magnesium trisilicate (E 553a(ii)) and talc (E 553b) dissociate to a limited extent in the gastrointestinal tract into silicates and their corresponding cations. The resulting low amounts of calcium and magnesium ions were considered not to disturb normal physiological processes and, therefore, the properties of the corresponding cations are not discussed further in this opinion.

The Panel considered that calcium silicate, magnesium silicate and talc have a low acute oral toxicity. No studies were available for magnesium trisilicate.

No adverse effects were observed in limited short-term and in subchronic toxicity studies in rats. The kidney effects observed in dogs were most probably related to the large amount of test compound consumed as a bolus dose by the animals. The effects on the kidney reported in guinea pigs could be due to higher concentrations of silicate in the primary urine as a consequence of lower glomerular filtration rates in guinea pigs (2.29 mL plasma/min per kg) as compared to rats (4.63 mL plasma/min pe kg). The Panel noted that in humans the glomerular filtration rate (3.56 mL plasma/min per kg) is higher than in guinea pigs and, furthermore, kidney effects have not been found in humans in the EudraVigilance database despite the wide and long-term use of high doses of magnesium trisilicate (up to 4 g/person per day) as an antacid over decades.

The Panel considered that the available data did not raise concern with respect to genotoxicity of calcium silicate (E 552), magnesium silicate (E 553a(i)), magnesium trisilicate (E 553a(ii)) and talc (E 553b).

In a 2-year study in rats, not performed according to current standards, calcium silicate (Silene EF) had no effect on mortality at a dose up to 5,000 mg/kg bw per day. No gross pathology or histopathological findings that could be attributed to calcium silicate were observed in the 500 and 2,500 mg/kg bw per day groups. However, in the absence of clinical chemistry data, given the respiratory infection of animals and only 15 animals/sex per group, the Panel considered that this study was too limited to conclude on the chronic toxicity of calcium silicate. However, the Panel noted that no carcinogenic effects were reported in this study.

There was no data for oral chronic toxicity/carcinogenicity of talc.

No reproductive toxicity studies were available. Prenatal developmental toxicity studies with calcium silicate (Silene EF) by gavage during organogenesis in mice, rats and hamsters (FDRL, 1972) and with talc (FDRL, 1973b) in mice and rats up to 1,600 mg/kg bw per day (the highest dose tested), showed no dose-related developmental effects.

Treatment with silicate antacid drugs such as magnesium trisilicate resulting in urinary silicate calculi (Lee et al., 1993) are seldom found in humans (0.1–0.2% of all urinary stones). They are mostly found in adults but they have also been described in rare cases in children (Tasdemir et al., 2017), where they were associated with consumption of milk thickener containing 5.5% silicates in one case of a 6-month-old boy (Ulinski et al., 2004), or milk powder dissolved in silicate-rich mineral water (water containing 172 mg silicate/L; estimated daily intake of about 200 mg silicate) in a 10 month old boy (Nishizono et al., 2004). The Panel noted that cases of renal calculi were rarely reported considering the high number of exposed humans to magnesium trisilicate used as an antacid. The Panel applied the WHO algorithm for assessing the association between adverse events and drug intake and found that association between silicate antacid use and renal calculi was 'possible' but not 'definite', which does not exclude that the occurrence of renal calculi and intake of silicates would be a chance finding.

In the available data on subacute toxicity, genotoxicity and developmental toxicity studies, no adverse effects were reported for silicates and talc. From the only chronic toxicity study (with calcium silicate) available, there was no indication for carcinogenicity. However, due to the limitations of this study, it was not possible to draw a reliable conclusion on the chronic toxicity and carcinogenicity of calcium silicate. Furthermore, no subchronic and reproductive toxicity studies with silicates or talc were available.

The Panel noted that the biological and toxicological studies performed with Silene EF were conducted with a hydrated calcium silicate described as having an average particle size of 30 nm (Columbia-Southern Chemical Corporation, 1953 (Documentation provided to EFSA n. 8)).

The Panel noted that the SCF established a group ADI 'not specified' for sodium silicate, silicon dioxide, calcium silicate, magnesium silicate and potassium silicate (SCF, 1991) presumably on the basis that they share a common moiety. The Panel noted that more recent evidence suggested that this assumption might not be valid. Therefore, the Panel considered that on the evidence currently available, there is no mechanistic rationale for a group ADI for silicates and silicon dioxide. Therefore the Panel considered this group ADI obsolete.

Due to the limitations in the available toxicological database for individual silicates, the Panel was unable to derive ADIs for calcium silicate (E 552), magnesium silicate (E 553a(i)), magnesium trisilicate (E 553a(ii)) and talc (E 553b).

Silicates (E 552-553) are authorised in 28 food categories, including FC 0, according to Annex II to Regulation (EC) No 1333/2008. Their use in FC 0 means that they are 'permitted in all categories of foods excluding foods for infants and young children, except where specifically provided for'. Silicates (E 552–553) are also authorised according to Annex III to Regulation (EC) No 1333/2008 (Parts 1, 2 and 5 A) in food-improving agents and nutrients, except nutrients intended for foods for infants and young children. As such, silicates (E 552–553) can be found in many foods via carry-over. The industry provided use levels for silicates (E 552–553) for their use according to Annex II. No analytical data on the concentration of these food additives in foods were made available by the Member States.

Dietary exposure to silicates (E 552–553) from their use as food additives according to Annex II was calculated for different exposure scenarios based on the provided use levels (Section 3.4). The Panel noted that 287 (98%) out of the 292 reported use levels applied in the exposure scenarios related to the use of talc (E 553b) (Appendix A). This reported use was in line with the information from the Mintel GNPD, showing that 89% of the foods labelled with silicates (E 552–553) were labelled to contain talc (E 553b). Therefore, the Panel noted that the calculated exposure reflects chiefly the exposure to talc (E 553b).

Additionally, 266 (91%) out of the 292 reported use levels were related to the use of silicates (E 552–553) in food supplements, again mainly talc (E 553b). The Panel noted that the main food category labelled with silicates (E 552–553) in the Mintel GNPD was also food supplements

(Appendix B). Therefore, the Panel considered the food supplements consumers only scenario as the most appropriate scenario for risk characterisation of silicates (E 552–553). Dietary exposure to silicates (E 552–553) via this exposure scenario was up to 31 mg/kg bw per day at the mean level in children and up to 46 mg/kg bw per day at the high (P95) level in the elderly.

The exposure assessment was hampered by several uncertainties (Table 8). Overall, it was considered that the exposure was most likely overestimated due to the use levels used and assumptions made in the exposure assessment. For a more detailed discussion on the uncertainties, see Section 3.4.5. Furthermore, the Panel noted that no foods belonging to an important contributing food category in all population groups, i.e. ripened cheese, were labelled to contain silicates (E 552-553) according to the Mintel GNPD.

The Panel noted that the exposure estimates were based on reported use levels of silicates (E 552–553). If current practice changes, these refined estimates may no longer be representative and should be updated.

Considering the possible high levels of nickel and aluminium in chlorite, an associated mineral in talc (E 553b), the Panel estimated the potential worst case exposure to these elements of concern from the use of silicates (E 552–553). Based on the mean intake for the population group with highest exposure (children) in the food supplement scenario, and the reported level of chlorite (9% w/w), exposure to nickel from the use of silicates (E 552–553) as food additives could be around 300 times its tolerable daily intake (TDI) of 2.8 μg/kg bw (EFSA CONTAM Panel, 2015). Exposure to aluminium could be around five times its tolerable weekly intake (TWI) of 1 mg/kg bw (EFSA, 2008). Therefore, the Panel considered that maximum limits for aluminium and nickel should be included in the EU specifications for talc (E 553b).

4. Conclusions

The Panel noted that:

- the absorption of silicates and talc was very low;
- there was no indication for genotoxicity or developmental toxicity for calcium and magnesium silicate and talc;
- no confirmed cases of kidney effects have been found in the EudraVigilance database despite the wide and long-term use of high doses of magnesium trisilicate up to 4 g/person/day over decades.

However, the Panel considered that accumulation of silicon from calcium silicate in kidney and liver was reported in rats and reliable data on subchronic and chronic toxicity, carcinogenicity, and that reproductive toxicity of silicates and talc were lacking. Therefore, the Panel concluded that the safety of calcium silicate (E 552), magnesium silicate (E 553a(i)), magnesium trisilicate (E 553a(ii)) and talc (E 553b) when used as food additives cannot be assessed.

The Panel also concluded that due to the uncertainties regarding a common moiety, the current group ADI for sodium silicate, silicon dioxide, calcium silicate, magnesium silicate and potassium silicate could not be mechanistically justified. The Panel concluded that on the available toxicological database for silicates it was not possible to establish ADIs for calcium silicate (E 552), magnesium silicate (E 553a(i)), magnesium trisilicate (E 553a(ii)) and talc (E 553b).

Based on the food supplement scenario considered as most representative for risk characterisation, exposure to silicates (E 552–553) for all population groups was below the maximum daily dose of magnesium trisilicate used as antacid (4 g/person per day).

The Panel noted that there were a number of approaches which could decrease the uncertainties in the current toxicological database. These approaches include but are not limited to toxicological studies as recommended for Tier 1 approach as described in the EFSA Guidance for the submission of food additives (EFSA ANS Panel, 2012) and conducted with adequately characterised material. Since the available data showed that nano particles are present in calcium silicate (E 552), the studies should be conducted with a material that contains a fraction of nano particles typical for silicates used as food additives.

5. Recommendations

The Panel recommended that:

- the European Commission considers the revision of the EU specifications for calcium silicate (E 552), magnesium silicate (E 553a(i)), magnesium trisilicate (E 553a(ii)) and talc (E 553b) in order to include better definitions, assays in line with the definitions, and characterisation of particle size distributions (using appropriate statistical descriptors (e.g. range, median, quartiles) as well as the percentages (in number and by mass) of particles in the nanoscale (with at least one dimension < 100 nm). With regard to the characterisation of the particle size distribution, the analytical methodologies applied should comply with those recommended in the EFSA Guidance on risk assessment of the application of nanoscience and nanotechnologies in the food and feed chain (EFSA Scientific Committee, 2018)).
- in first instance, toxicological studies as recommended for a Tier 1 approach as described in the EFSA Guidance for the submission of food additives (EFSA ANS Panel, 2012) should be conducted with adequately characterised material(s) in order to decrease the uncertainties in the current toxicological database.
- more data on the actual usage and use levels of silicates (E 552, E 553a(i)) and E 553a(ii)) should be provided because most of the data submitted were for talc (E 553b).
- the European Commission considers lowering the current limits for toxic elements (arsenic, lead and mercury) in the EU specifications for calcium silicate (E 552), magnesium silicate (E 553a(i)), magnesium trisilicate, (E 553a(ii)) and talc (E 553b) in order to ensure that the food additives will not be a significant source of exposure to these toxic elements in food.
- the European Commission considers inclusion of maximum limits for aluminium, nickel, fluoride and crystalline silica (alpha-quartz) in the EU specifications for talc (E 553b).

Documentation provided to EFSA

1) Association of the European Self-Medication Industry (AESGP), 2017. Data on usage levels of calcium silicate (E 552), magnesium silicate (E 553a(i)), magnesium trisilicate (E 553a (ii)) and talc (E 553b) 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 (2017). Submitted to EFSA on 31 January 2017.
2) ASASP (2012). Calcium silicate (E 552). CEFIC-ASASP 15/08/2012. Reply to EFSA: re-evaluation of food additives: call for data (15.08.2012). Submitted to EFSA by CEFIC, August 2012.
3) Bundesamt für Verbraucherschutz und Lebensmittelsicherheit, 2012. Response to EFSA's call for scientific data. Submitted to EFSA by Bundesamt für Verbraucherschutz und Lebensmittelsicherheit, August 2012.
4) CEFIC, 2017a. Re-evaluation of calcium silicate (E552). Response to EFSA's letter dated 9 June 2016- Request for additional information. Submitted to EFSA by CEFIC on behalf of the ASASP, November 2017.
5) CEFIC, 2017b. Re-evaluation of magnesium silicate (E553a). Response to EFSA's letter dated 9 June 2016- Request for additional information. Submitted to EFSA by CEFIC on behalf of the ASASP, November 2017.
6) CEFIC, 2018a. Response to EFSA request on 8 March 2018 on particle size distribution for magnesium silicate and magnesium trisilicate. Submitted to EFSA by CEFIC on behalf of the ASASP, April 2018.
7) CEFIC, 2018b. Personal communication to EFSA following an EFSA's request. April, 2018.
8) Columbia-Southern Chemical Corporation, 1953. Silene Bulletin No, 1. September 1953. Submitted to EFSA by CEFIC, April 2017.
9) European Snacks Association/SNACMA, 2017. Data on usage levels of calcium silicate (E 552), magnesium silicate (E 553a(i)), magnesium trisilicate (E 553a(ii)) and talc (E 553b) 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 (2017). Submitted to EFSA on 25 January 2017.
10) EUROTALC, 2012. Data submitted to EFSA following EFSA's call for data in 2012: Analytical method available for determination of the food additive in food and beverage; Information

on the manufacturing process the food additive E 553b (talc); Determination and burning behaviour tests; Information on particle size, Talc E 553b, Marvern; Harlan Project. Talc (asbestos free). Evaluation of the carcinogenic potential and potential target organ toxicity in humans. Expert statement, 16 April 2010; Literature search report for talc. Submitted to EFSA by EUROTALC, August 2012.

11) EUROTALC, 2018a. Data on usage levels of calcium silicate (E 552), magnesium silicate (E 553a(i)), magnesium trisilicate (E 553a(ii)) and talc (E 553b) 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 (2017). Submitted to EFSA on 25 January 2018.
12) EUROTALC, 2018b. Re-evaluation of talc (E 553b) as food additive request for additional data. Submitted to EFSA by EUROTALC, May 2018.
13) FASEB, 1979. Evaluation of the health aspects of certain silicates as food ingredients. Prepared for Bureau of Foods. Food and Drug Administration Departmenet of Health, Education and Welfare. Washington, DC. Contract No FDA 223-75-2004. Submitted to EFSA by PQ Corporation, August 2012.
14) FDE (FoodDrinkEurope), 2017. Data on usage levels of calcium silicate (E 552), magnesium silicate (E 553a(i)), magnesium trisilicate (E 553a(ii)) and talc (E 553b) 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 (2017). Submitted to EFSA on 1 February 2017.
15) FDRL (Food and Drug Research Laboratories) 1972. Teratologic evaluation of FDA 71-41 (hydrated calcium silicate). Teratological test results in three species of animals (rats, mice, hamsters). FDA contract 71-260. Report No FDABF-GRAS-068. Submitted to EFSA by the FDA, July 2017.
16) Food Supplements Europe (FSE), 2017. Data on usage levels of calcium silicate (E 552), magnesium silicate (E 553a(i)), magnesium trisilicate (E 553a(ii)) and talc (E 553b) 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 (2017). Submitted to EFSA on 1 February 2017.
17) Grupo AC MARCA, 2017. Data on usage levels of calcium silicate (E 552), magnesium silicate (E 553a(i)), magnesium trisilicate (E 553a(ii)) and talc (E 553b) 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 (2017). Submitted to EFSA on 22 November 2016.
18) Hazelton Laboratories, 1956. Chronic Toxicity Final Report on Material Silene EF, May 24, 1956. Submitted to EFSA by CEFIC, April 2017.
19) Hill Top Biolabs, Inc, 1989. Acute oral toxicity in rats- limit test of: magnesium silicate SRR#:281-60-3 fro: the Dallas Group of America, Inc. Project No 89-38338-21 (A). Submitted to EFSA by the Dallas Group of America, Inc, September 2016.
20) ICGA (International Chewing Gum Association), 2017. Data on usage levels of calcium silicate (E 552), magnesium silicate (E 553a(i)), magnesium trisilicate (E 553a(ii)) and talc (E 553b) 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 (2017). Submitted to EFSA on 19 May 2017.
21) IFREB (Institu Francais de Recherches et Essais Biologiques), 1983. Test de tolerance locale chez le lapin. IFREB- R 912337. 4 October 1983. Submitted to EFSA by EUROTALC, August 2012.
22) Jopseph Crossfield&Sons Limited, Warrinton, Englans. Acid bases and salts-proposed EEC Directive. Submission to the EEC Scientific Committee on Food concerning the use of certain synthetic siliceous materials in foo, 1982. Submitted to EFSA by PQ Corporation, August 2012.
23) LOGES (Dr Loges Naturheilkunde neu entdecken), 2017. Data on usage levels of calcium silicate (E 552), magnesium silicate (E 553a(i)), magnesium trisilicate (E 553a(ii)) and talc (E 553b) 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 (2017). Submitted to EFSA on 15 November 2016.

24) PQ Corporation, 2012. Magnesium silicate (E 553a). 15/08/2012. Reply to EFSA: re-evaluation of food additives: call for data (14.08.2012). Submitted to EFSA by PQ Corporation, August 2012.
25) Pre-evaluation document. Peter Fisk Associates finalised on 25/11/2013.
26) Rhône-Poulenc, 1986. Tixosil 53. Essary de toxicite paar voie orale chez le rat. Unpublished report 601203 by Guillot JP and Braise J, Hazlenton France, L'Arbrele. Rhône-Poulenc, Courbevoie, France. Submitted to EFSA by CEFIC, April 2017.
27) Specialised Nutrition Europe (SNE), 2017. Data on usage levels of calcium silicate (E 552), magnesium silicate (E 553a(i)), magnesium trisilicate (E 553a(ii)) and talc (E 553b) 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 (2017). Submitted to EFSA on 31 January 2017.
28) Tox Monitor Laboratories, Inc, 2000. OPPTS Acute Oral toxicity study. Study number 00-102-3. Compound: magnesol, grade: HMR-LS, SRR# 000-21-1. Submitted to EFSA by the Dallas Group of America, Inc, September 2016.
29) Unilever Research Laboratory Colworth, 1964. Toxicity of amorphous silicates and their use as food additives in the USA. 21 October 1964. Serial No CH 64888. Submitted to EFSA by PQ Corporation, August 2012.

References

Afzal M, Saleem S, Singh N, Kazmi I, Khan R, Nadeem MS, Zamzami MA, Al-Abbasi FA and Anwar F, 2018. Evaluation of diphenydramine in talc induced type 2 diabetes mellitus in Wistar rats. Biomedicine and Pharmacotherapy, 97, 652–655.

Aslam M, Fatima N and Rahman Q, 1993. Cytotoxic and genotoxic effects of calcium silicates on human lymphocytes in vitro. Mutation Reserach, 300, 45–48.

Benke GM and Osborn TW, 1979. Urinary silicon excretion by rats following oral administration of silicon compounds. Food and Cosmetics Toxicology, 17, 123–127.

CIR (Cosmetic Ingredient Review), 2013. Safety assessment of talc as used in cosmetics. Available online: http://www.cir-safety.org/sites/default/files/talc032013rep.pdf

Dobbie JW and Smith MJ, 1982. Silicate nephrotoxicity in the experimental animal: the missing factor in analgesic nephropathy. Scottish Medical Journal, 27, 10–16.

Dobbie JW and Smith MJ, 1986. Urinary and serum silicon in normal and uraemic individuals. In: Evered D and O'Connor M (eds.). *Silicon Biochemistry*. Vol 121. Ciba foundation symposium, Wiley, Chichester. pp. 194–208.

ECHA (European Chemicals Agency), online. Available at: https://echa.europa.eu/

Edwards IR and Biriell C, 1994. Harmonization in pharmacovigilance. Drug Safety, 10, 93–102.

EFSA (European Food Safety Authority), 2007. Scientific opinion of the Scientific Committee related to uncertainties in dietary exposure assessment. EFSA Journal 2007;5(1):438, 54 pp. https://doi.org/10.2903/j.efsa.2007.438

EFSA (European Food Safety Authority), 2008. Scientific Opinion of the Panel on Food Additives, Flavourings, Processing Aids and Food Contact Materials on a request from European Commission on Safety of aluminium from dietary intake. EFSA Journal 2008;6(7):754, 34 pp. https://doi.org/10.2903/j.efsa.2008.754

EFSA (European Food Safety Authority), 2011a. Use of the EFSA Comprehensive European Food Consumption Database in Exposure Assessment. EFSA Journal 2011;9(3):2097, 34 pp. https://doi.org/10.2903/j.efsa.2011.2097

EFSA (European Food Safety Authority), 2011b. Evaluation of the FoodEx, the food classification system applied to the development of the EFSA Comprehensive European Food Consumption Database. EFSA Journal 2011;9(3):1970, 27 pp. https://doi.org/10.2903/j.efsa.2011.1970

EFSA ANS Panel (EFSA Panel on Food Additives and Nutrient Sources), 2009. Calcium silicate and silicon dioxide/silicic acid gel added for nutritional purposes to food supplements. EFSA Journal 2009;7(6):1132, 24 pp. https://doi.org/10.2903/j.efsa.2009.1132

EFSA ANS Panel (EFSA Panel on Food Additives and Nutrient Sources), 2012. Guidance for submission for food additive evaluations. EFSA Journal 2012;10(7):2760, 60 pp. https://doi.org/10.2903/j.efsa.2012.2760

EFSA ANS Panel (EFSA Panel on Food Additives and Nutrient Sources added to Food), Younes M, Aggett P, Aguilar F, Crebelli R, Dusemund B, Filipič M, Frutos MJ, Galtier P, Gott D, Gundert-Remy U, Kuhnle GG, Leblanc J-C, Lillegaard IT, Moldeus P, Mortensen A, Oskarsson A, Stankovic I, Waalkens-Berendsen I, Woutersen RA, Wright M, Boon P, Chrysafidis D, Gürtler R, Mosesso P, Parent-Massin D, Tobback P, Kovalkovicova N, Rincon AM, Tard A and Lambré C, 2018. Scientific opinion on the re-evaluation of silicon dioxide (E 551) as a food additive. EFSA Journal 2018;16(1):5088, 60 pp. https://doi.org/10.2903/j.efsa.2017.5088

EFSA CONTAM Panel (EFSA Panel on Contaminants in the Food Chain), 2009a. Scientific opinion on cadmium in food. EFSA Journal 2009;7(10):980, 139 pp. https://doi.org/10.2903/j.efsa.2009.98

EFSA CONTAM Panel (EFSA Panel on Contaminants in the Food Chain), 2009b. Scientific Opinion on arsenic in food. EFSA Journal 2009;7(10):1351, 199 pp. https://doi.org/10.2903/j.efsa.2009.1351
EFSA CONTAM Panel (EFSA Panel on Contaminants in the Food Chain), 2010. Scientific Opinion on lead in food. EFSA Journal 2010;8(4):1570, 151 pp. https://doi.org/10.2903/j.efsa.2010.1570
EFSA CONTAM Panel (EFSA Panel on Contaminants in the Food Chain), 2012a. Scientific Opinion on the risk for public health related to the presence of mercury and methylmercury in food. EFSA Journal 2012;10(12):2985, 241 pp. https://doi.org/10.2903/j.efsa.2012.2985
EFSA CONTAM Panel (EFSA Panel on Contaminants in the Food Chain), 2012b. Scientific Opinion on lead dietary exposure in the European population. EFSA Journal 2012;10(7):2831, 59 pp. https://doi.org/10.2903/j.efsa.2012.2831
EFSA CONTAM Panel (EFSA Panel on Contaminants in the Food Chain), 2012c. Scientific Opinion on cadmium dietary exposure in the European population. EFSA Journal 2012;10(1):2551, 59 pp. https://doi.org/10.2903/j.efsa.2012.2831
EFSA CONTAM Panel (EFSA Panel on Contaminants in the Food Chain), 2014. Scientific Opinion on dietary exposure to inorganic arsenic in the European population. EFSA Journal 2014;12(3):3597, 68 pp. https://doi.org/10.2903/j.efsa.2014.3597
EFSA CONTAM Panel (EFSA Panel on Contaminants in the Food Chain), 2015. Scientific Opinion on the risk to public health related to the presence of nickel in food and drinking water. EFSA Journal 2015;13(2):4002, 202 pp. https://doi.org/10.2903/j.efsa.2015.4002
EFSA Scientific Committee, 2009. Guidance of the scientific committee on transparency in the scientific aspects of risk assessments carried out by EFSA. Part 2: general principles. EFSA Journal 2009;7(7):1051, 22 pp. https://doi.org/10.2903/j.efsa.2009.1051
EFSA Scientific Committee, 2011. Scientific Opinion on genotoxicity testing strategies applicable to food and feed safety assessment. EFSA Journal 2011;9(9):2379, 69 pp. https://doi.org/10.2903/j.efsa.2011.2379
EFSA Scientific Committee, 2012. Guidance on selected default values to be used by the EFSA Scientific Committee, Scientific Panels and Units in the absence of actual measured data. EFSA Journal 2012;10(3):2579, 32 pp. https://doi.org/10.2903/j.efsa.2012.2579
EFSA Scientific Committee, Hardy A, Benford D, Halldorsson T, Jeger MJ, Knutsen HK, More S, Naegeli H, Noteborn H, Ockleford C, Ricci A, Rychen G, Schlatter JR, Silano V, Solecki R, Turck D, Younes M, Chaudhry Q, Cubadda F, Gott D, Oomen A, Weigel S, Karamitrou M, Schoonjans R and Mortensen A, 2018. Guidance on risk assessment of the application of nanoscience and nanotechnologies in the food and feed chain: part 1, human and animal health. EFSA Journal 2018;16(7):5327, 95 pp. https://doi.org/10.2903/j.efsa.2018.5327
Elmore AR, 2003. Final report of the safety assessment of aluminium silicate, calcium silicate, magnesium aluminium silicate, magnesium silicate, magnesium trisilicate, sodium magnesium silicate, zirconium silicate, attapulgite, bentonite, fuller's earth, hecorite, kaolin, lithium magnesium silicate, lithium magnesium sodium silicate, montmorillonite, pyrophyllite and zeolite. International Journal of Toxicology, 22, 37–102.
Endo-Capron S, Renier A, Janson X, Kheuang L and Jaurand MC, 1993. In vitro response of rat pleural mesothelial cells to talc samples in genotoxicity assays (sister chromatid exchanges and DNA repair). Toxicology In Vitro, 7, 7–14.
EudraVigilance, online. European Database of Suspected Adverse Drug Reactions. Available online: http://www.adrreports.eu/en/index.html [Accessed: 8 May 2018]
EVM (Expert Group on Vitamins and Minerals), 2003. Safe upper levels for vitamins and minerals, Silicon. UK FoodStandards Agency. Available online: http://www.food.gov.uk/multimedia/pdfs/vitmin2003.pdf
FDRL (Food and Drug Research Laboratories), 1973a. Teratologic evaluation of FDA 71-41 (hydrated calcium silicate) in rabbits. Contract no FDA 71-260.
FDRL (Food and Drug Research Laboratories), 1973b. Teratologic evaluation of FDA 71-43 (talc) in mice, rats and hamsters. Contract no FDA 71-260.
FDRL (Food and Drug Research Laboratories), 1973c. Teratologic evaluation of FDA 71-43 (talc). Teratological test results in rabbits. FDA contract 71-260. Report No FDABF-GRAS-147.
Fiume MM, Boyer I, Bergfeld WF, Belsito DV, Hill RA, Klaassen CD, Liebler DC, Marks Jr JG, Shank RC, Slaga TJ, Snyder PW, Andersen FA, 2015. Safety assessment of talc as used in cosmetics. International Journal of Toxicology, 34, 66S–129S.
IARC (International Agency for Research on Cancer), 1987. IARC monographs on the evaluation of the carcinogenic risk of chemicals to humans - Silica and some silicates. Volume 42. World Health Organization.
IARC (International Agency for Research on Cancer), 1997. IARC monographs on the evaluation of the carcinogenic risk of chemicals to humans - Some silicates. Volume 68. World Health Organization.
IARC (International Agency for Research on Cancer), 2010. IARC monographs on the evaluation of the carcinogenic risk of chemicals to humans - Carbon black, titanium dioxide, and talc. Volume 93. World Health Organization.
JECFA (Joint FAO/WHO Expert Committee on Food Additives), 1969. Toxicological evaluation of some food colours, emulsifiers, anti-caking agents and certain other substances. FAO Nutrition Meetings Report Series, 46A.
JECFA (Joint FAO/WHO Expert Committee on Food Additives), 1974. Toxicological evaluation of some food additives including anticaking agents, antimicrobials, antioxidants, emulsifiers, and thickening agents. FAO Nutrition Meetings Report Series No. 53A. WHO Food Additives Series, 5.

JECFA (Joint FAO/WHO Expert Committee on Food Additives), 1976. Evaluation of certain food additives and contaminants. Twentieth Report of the Joint FAO/WHO Expert Committee on Food Additives. World Health Organization Technical Report Series, 599.
JECFA (Joint FAO/WHO Expert Committee on Food Additives), 1980. Evaluation of certain food additives. Twenty-fourth report of the Joint FAO/WHO Expert Committee on Food Additives. World Health Organization Technical Report Series, 653.
JECFA (Joint FAO/WHO Expert Committee on Food Additives), 1982. Evaluation of certain food additives and contaminants. Twenty-sixth Report of the Joint FAO/WHO Expert Committee on Food Additives. Who Technical Report Series, 683.
JECFA (Joint FAO/WHO Expert Committee on Food Additives), 1986. Evaluation of certain food additives and contaminants. Twenty-ninth Report of the Joint FAO/WHO Expert Committee on Food Additives. World Health Organization Technical Report Series, 733.
JECFA (Joint FAO/WHO Expert Committee on Food Additives), 1987. Evaluation of certain food additives and contaminants. Thirtieth Report of the Joint FAO/WHO Expert Committee on Food Additives. World Health Organization Technical Report Series, 751, 1–57.
JECFA (Joint FAO/WHO Expert Committee on Food Additives), 2000. Guidelines for the preparation of toxicological working papers for the Joint FAO/WHO Expert Committee on Food Additives. Geneva, Switzerland.
JECFA (Joint FAO/WHO Expert Committee on Food Additives), 2006. Monograph 1. C. Prepared at the 61st JECFA (2003) and published in FNP 52 Add 11 (2003). Online Edition "Combined compendium of food additive specifications". Available online: http://www.fao.org/food/food-safety-quality/scientific-advice/jecfa/jecfa-additives/en/
JECFA (Joint FAO/WHO Expert Committee on Food Additives), 2011. Monograph 11. Prepared at the 74th JECFA (2011) and published in FAO JECFA monographs 11 (2011). Online Edition "Combined compendium of food additive specifications". Available online: http://www.fao.org/food/food-safety-quality/scientific-advice/jecfa/jecfa-additives/en/
JECFA (Joint FAO/WHO Expert Committee on Food Additives), 2015. Monograph 17. Specifications prepared at the 80th JECFA (2015) and published in FAO JECFA monographs 17 (2015). Online Edition "Combined compendium of food additive specifications". Available online: http://www.fao.org/food/food-safety-quality/scientific-advice/jecfa/jecfa-additives/en/
JECFA (Joint FAO/WHO Expert Committee on Food Additives), 2016. Compendium of food additive specifications. 82nd meeting.
Joekes AM, Rose GA and Sutor J, 1973. Multiple renal silica calculi. British Medical Journal, 1, 146–147.
Lee MH, Lee YH, Hsu TH, Chen MT and Chang LS, 1993. 1993 Silica stone-development due to long time oral trisilicate intake. Scandinavian Journal of Urology and Nephrology, 27, 267–269.
Litton Bionetics Inc, 1974a. Summary of mutagenicity screening studies host-mediated assay cytogenetics dominant lethal assay. Contract FDA 71-268, compound FDA 71-41, Calcium Silicate. LBI Project 2446.
Litton Bionetics Inc, 1974b. Mutagenic Evaluation of Compound FDA 71-43, Talc. PB Report, 245–458.
Neiberger RE, 1992. Developmental changes in the renal capacity for sulfate reabsorption in the guinea pig. Pediatric Nephrology (Berlin, Germany), 6, 65–67.
Newberne PM and Wilson RB, 1970. Renal damage associated with silicon compounds in dogs. Proceedings of the National Academy of Sciences, 65, 872–875.
Nishizono T, Eta S, Enokida H, Nishiyama K, Kawahara M and Nakagawa M, 2004. Renal silica calculi in an infant. International Journal of Urology, 11, 119–121.
Page RC, Heffner RR and Frey A, 1941. Urinary excretion of silica in humans following oral administration of magnesium trisilicate. The American Journal of Digestive Diseases, 8, 13–15.
Pestel S, Krzykalla V and Weckesser G, 2007. Measurement of glomerular filtration rate in the conscious rat. Journal of Pharmacological and Toxicological Methods, 56, 277–289.
Phillips JC, Young PJ, Hardy K and Gangolli SD, 1978. Studies on the absorption and disposition of 3H-labelled talc in the rat, mouse, guinea-pig and rabbit. Food and Cosmetics Toxicology, 16, 161–164.
Prival MJ, Simmon VF and Mortelmans KE, 1991. Bacterial mutagenicity testing of 49 food ingredients gives very few positive results. Mutation Research, 260, 321–329.
Rashid I, Daraghmeh NH, Al Omari MM, Chowdry BZ, Leharne SA, Hodali HA and Badwan AA, 2011. Magnesium Silicate. In Brittain HG (ed). *Profiles of Drug Substances, Excipients and Related Methodology, Vol. 36*. Academic Press, Burlington. pp. 241–285.
SCF (Scientific Committee for Food), 1991. Reports from the Scientific Committee for Food (25th series). Opinion expressed 1990. Food - science and techniques.
SCF (Scientific Committee for Food), 2001. Guidance on submissions for food additive evaluations by the Scientific Committee on Food. SCF/CS/ADD/GEN/26 Final. 12 July 2001.
Singh R, Muhammad A, Kazmi I and Anwar F, 2014. Talc used in anticancer drugs is promoter for diabetes in hepatocellular carcinoma induced rats. European Journal of Cancer, 50, 247–248.
Singh R, Hemant Deepak T, Khan R and Anwar F, 2016. Histopathological analysis of talc in doxorubinin induced cardiac remodelling. International Journal of Emerging Research in Management and Technology, 5, 83–86.

Sripanyakorn S, Jugdaohsingh R, Dissayabutr W, Anderson SHC, Thompson RPH and Powell JJ, 2009. The comparative absorption of silicon from different foods and food supplements. British Journal of Nutrition, 102, 825–834.

Takizawa Y, Hirasawa F, Noritomi E, Aida M, Tsunoda H and Uesugi S, 1988. Oral ingestion of syloid to mice and rats and its chronic toxicity and carcinogenicity. Acta Medica et Biologica, 36, 27–56.

Tasdemir M, Fuçucuoğlu D, Özman O, Sever L, Önal B and Bilge I, 2017. Silicate calculi, a rare cause of kidney stones in children. Pediatric Nephrology (Berlin, Germany), 32, 271–274.

TemaNord (Nordic Council of Ministers), 2002. E 475 Polyglycerol esters of fatty acids. Food Additives in Europe 2000 - Status of safety assessments of food additives presently permitted in the EU, 668-670.

Ulinski T, Sabot JF, Bourlon I and Cochat P, 2004. Bilateral urinary calculi after treatment with a silicate-containing milk thickener. European Journal of Pediatrics, 163, 239–240.

Wehner AP, Tanner TM and Buschbom RL, 1977. Absorption of ingested talc by hamsters. Food and Cosmetics Toxicology, 15, 453–456.

Glossary and Abbreviations

AESGP	Association of the European Self-Medication Industry
ADI	acceptable daily intake
ANS	EFSA Panel on Food Additives and Nutrient Sources added to Food
ASASP	Association of Synthetic Amorphous Silica Producers
bw	body weight
CAS	Chemical Abstracts Service
EINECS	European Inventory of Existing Commercial Chemical Substances
ESA	European Snacks Association/SNACMA
EVM	Expert Group on Vitamins and Minerals
FC	food category
FCS	food categorisation system
FDA	Food and Drug Administration
FDE	Food Drink Europe
FDRL	Food and Drug Research Laboratories
FSE	Food Supplements Europe
GD	gestation day
GLP	good laboratory practice
GNPD	Global New Products Database
IARC	International Agency for Research on Cancer
ICGA	International Chewing Gum Association
ISO	International Organization for Standardization
JECFA	Joint FAO/WHO Expert Committee on Food Additives
LD	laser diffraction
LD_5	lethal dose, 5%, i.e. dose that causes death among 5% of treated animals
LD_{50}	lethal dose, median
MPL	maximum permission limit
MS	mass spectrometry
OECD	Organisation for Economic Co-operation and Development
QS	*quantum satis*
REACH	Registration, Evaluation, Authorisation and Restriction of Chemicals
SSA	specific surface area
SCF	Scientific Committee on Food
SEM	scanning electron microscopy
SNE	Specialised Nutrition Europe
TEM	transmission electron microscopy
TemaNord	is a publishing series for results of the often research-based work that working groups or projects under Nordic Council of Ministers have put in motion
TDI	tolerable daily intake
TWI	tolerable weekly intake
UDS	unscheduled DNA synthesis
WHO	World Health Organization

Appendix A – Summary of reported use levels (mg/kg or mg/L as appropriate) of silicates (E 552–553) provided by industry

Appendix B – Number and percentage of food products labelled with silicates (E 552–553) out of the total number of food products present in the Mintel GNPD per food subcategory between 2013 and 2018

Appendix C – Concentration levels of silicates (E 552–553) used in the exposure assessment scenarios (mg/kg or mL/kg as appropriate)

Appendix D – Summary of total estimated exposure of silicates (E 552–553) from their use as food additives for the regulatory 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 silicates (E 552–553) at the regulatory maximum level exposure assessment scenario and the refined exposure assessment scenarios (> 5% to the total mean exposure)

Appendix F – Summary of total estimated exposure of silicates (E 552–553) from their use as food additives for the food supplements consumers only scenario per population group and survey: mean and 95th percentile (mg/kg bw per day)

Appendix A–F can be found in the online version of this output ('Supporting information' section):