European Food Safety Authority

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Calcium silicate and silicon dioxide/silicic acid gel added for nutritional purposes to food supplements [1]

Scientific Opinion of the Panel on Food Additives and Nutrient Sources added to Food

(Questions No EFSA-Q-2005-140, EFSA-Q-2006-220, EFSA-Q-2005-098, EFSA-Q-2005-099)

Adopted on 5 June 2009

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SUMMARY

Following a request from the European Commission to the European Food Safety Authority, the Scientific Panel on Food Additives and Nutrient Sources added to Food has been asked to deliver a scientific opinion on calcium silicate, silicon dioxide and silicic acid gel added for nutritional purposes to food supplements.

The present opinion deals only with the safety of calcium silicate, silicon dioxide, silicic acid gel as sources of silicon, and with the bioavailability of silicon from these sources. The Panel notes that one petitioner also applied for the use of calcium silicate as a source of calcium. The safety of silicon and calcium itself, in terms of amounts that may be consumed, and the consideration of silicon as a nutrient, are outside the remit of this Panel.

Silicon occurs naturally in foods as silicon dioxide (SiO_2, silica) and silicates. High levels of silicon are found in foods derived from plants, and particularly cereals, whereas silicon levels are lower in foods from animal sources.

Orthosilicic acid [$Si(OH)_4$] is the major silicon species present in drinking water and other liquids, including beer, and is the most readily available source of silicon to man. After oral consumption, the main chemical species by which silicon is absorbed is orthosilicic acid.

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Silicates (i.e. E551, silicon dioxide, amorphous; E552, calcium silicate, hydrous/anhydrous; E553a(i), magnesium silicate; E553a(ii), magnesium trisilicate; E553b talc; E554 sodium aluminosilicate) are approved food additives within the EU.

The petitioner indicated that silicon dioxide will be added to food supplements to supply up to 700 mg silicon/day. Silicic acid gel under the form of a colloidal dispersion will be added to supply 196 mg silicon/day.

The Panel however notes that the essentiality of silicon for man has not been established and that a functional role for silicon has not been identified. A recommended intake for silicon has not been set.

No specific data on the bioavailability of either silicon or calcium from calcium silicate have been provided. The Panel notes the low solubility of calcium silicate in hydrochloric acid and its practical insolubility in water, but in the absence of specific data, cannot reach a conclusion on the bioavailability of either calcium or silicon from the source.

No data have been submitted on the bioavailability of silicon from either silicon dioxide or silicic acid gel. However, several studies have shown that silicon present under similar form was readily available from foods and in many cases showed absorption similar to that of silicon from liquids. Furthermore, given the conversion of silicon dioxide/silicic acid to orthosilicic acid upon hydration, and the bioavailability of silicon from orthosilicic acid, the Panel considers that silicon from silicon dioxide/ silicic acid gel is bioavailable.

The Expert group on Vitamins and Minerals (EVM) set a Safe Upper Level for daily consumption of silicon at 700 mg silicon/day for adults over a lifetime (equivalent to 12 mg silicon/kg body weight/day for a 60 kg adult). The Tolerable Upper Intake Level (UL) for calcium is 2500 mg/day for adults (equivalent to 41.3 mg calcium/kg body weight/day).

The EFSA Panel on Dietetic products, Nutrition and Allergies (NDA) was unable to set a UL for silicon, but estimated that the typical dietary intake of 20-50 mg silicon/day (equivalent to 0.3-0.8 mg/kg body weight/day in a 60 kg person) is unlikely to cause adverse effects.

For calcium, the mean and 97.5th percentile anticipated total exposure from food and food supplements would vary from 823 to 1084 mg/person/day and 1560 to 2110 mg/person/day, respectively.

The Panel concludes that, in view of the Safe Upper Level for silicon of 700 mg silicon/day established by the EVM for supplemental use and of 2500 mg calcium/day for adults established by the SCF, the exposure to calcium and to silicon resulting from the proposed uses of calcium silicate as a source of respectively silicon and calcium in food supplements, the use of calcium silicate in food supplements at the proposed use levels is of no safety concern, provided that it complies with the specifications for its use as a food additive.

The Panel also concludes that the use of silicon dioxide up to 1500 mg SiO_2/day (equal to 700 mg/day) and of silicic acid gel to supply up to 200 mg silicon/day, added to food supplements, is of no safety concern.

Key words:

Calcium silicate, [silicic acid (H_2SiO_3), calcium salt (1:1)], CAS No. 10101-39-0, [orthosilicic acid (H_4SiO_4), calcium salt (1:2)], CAS No. 1344-95-2, Silicic acid calcium salt; Calcium hydrosilicate; Tobermorite.

Silicon dioxide/Silicic acid gel, CAS No. 7631-86-9, precipitated silicon dioxide, silica gel, hydrous silica, hydrated silicic acid, polysilicic acid gel, phytolithic silicon, E551.

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BACKGROUND AS PROVIDED BY THE EUROPEAN COMMISSION

The European Community legislation lists nutritional substances that may be used for nutritional purposes in certain categories of foods as sources of certain nutrients.

The Commission has received a request for the evaluation of calcium silicate, silicon dioxide and silicic acid gel added for nutritional purposes to food supplements. The relevant Community legislative measure is:

- Directive 2002/46/EC of the European Parliament and of the Council on the approximation of the laws of the Member States relating to food supplements[2].

TERMS OF REFERENCE AS PROVIDED BY THE EUROPEAN COMMISSION

In accordance with Article 29 (1) (a) of Regulation (EC) No 178/2002, the European Commission asks the European Food Safety Authority to provide a scientific opinion, based on its consideration of the safety and bioavailability of calcium silicate, silicon dioxide and silicic acid gel added for nutritional purposes to food supplements.

ACKNOWLEDGEMENTS

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[2] OJ L 183, 12.7.2002, p.51.

ASSESSMENT

1. Introduction

The present opinion deals only with the safety of calcium silicate as a source of calcium and silicon, and of silicon dioxide/silicic acid gel as sources of silicon, and with the bioavailability of silicon from these sources.

2. Technical data

2.1. Calcium silicate

2.1.1. Chemistry

Calcium silicate, is an inorganic substance that can exist in different forms: [silicic acid (H_2SiO_3), calcium salt (1:1)], CAS Registry Number 10101-39-0, molecular formula: $CaSiO_3$, molecular weight: 116.17 g/mol or [orthosilicic acid (H_4SiO_4), calcium salt (1:2)], CAS Registry Number 1344-95-2, molecular formula Ca_2SiO_4, molecular weight 172.24 g/mol. Calcium silicates usually occur in an hydrated form containing various percentages of water of crystallisation.

Synonyms: silicic acid, calcium salt; calcium hydrosilicate; calcium metasilicate, calcium silicon oxide, Tobermorite.

2.1.2. Specifications

Calcium silicate is described as a very fine, white or off-white powder with low bulk density and high physical water absorption. The substance is practically insoluble in ethanol and water but it forms a gel with mineral acids. It is slightly soluble in hydrochloric acid. The SiO_2 content on the anhydrous basis is not less than 50 % and not more than 95 % and the CaO content is not less than 3 % and not more than 35 %. The particle size is in the range of 0.02 – 0.07 µm (Merck Index, 2006).

Purity

Not less than 98.0% on a dry basis. The Panel calculated the calcium content in the source to be not less than 352 mg/g.

Tests for silicate and calcium were satisfactorily described by the petitioner in the application dossier.

Impurities

The petitioner indicates the following levels of impurities: arsenic not more than 3 mg/kg; lead not more than 5 mg/kg; fluoride not more than 10 mg/kg; asbestos absent (by electron microscopy); heavy metals not more than 10 mg/kg (expressed as lead). The petitioner indicates that magnesium (as silicate) might also be present at <1%.

The Panel notes that these specifications comply with the specifications set for calcium silicate (E552) as food additive (Commission Directive 2008/84/EC).

The Panel also notes that according to Commission Regulation (EC) No 629/2008, the maximum levels of lead, mercury and cadmium in food supplements as sold, should be 3.0 mg/kg, 0.1 mg/kg and 3.0 mg/kg, respectively.

2.1.3. Manufacturing process

No details were provided. The petitioner states that calcium silicate is prepared by various reactions between siliceous material (e.g. diatomaceous earth) and calcium compounds such as calcium hydroxide.

2.1.4. Methods of analysis in food

The petitioner indicates that silicon can be determined by Electrothermal Atomic Absorption Spectrometry (ETAAS) with inverse longitudinal Zeeman background correction. He further indicates that, following appropriate extraction and preparation, calcium may be measured by Atomic Absorption spectroscopy or by plasma emission spectrometry.

2.1.5. Reaction and fate in foods to which the source is added

The petitioner stated that calcium silicate is stable in foods, but no data were provided.

2.2. Silicon dioxide/Silicic acid gel

2.2.1. Chemistry

Silicon dioxide/Silicic acid gel are inorganic substances, CAS Registry Number 7631-86-9. Silicon occurs in nature as silicon dioxide (SiO_2) or the corresponding silicic acids formed by the hydration of the oxide.

According to the petitioner, a precise sum formula is not defined, because there are many different possible states of condensation of orthosilicic acid [(HO-Si(OH)$_2$-OH); (H_4SiO_4)] CAS Registry Number 10193-36-9.

Orthosilicic acid (HO-Si(OH)$_2$-OH) condensates with additional molecules of orthosilicic acid to disilicic acid (HO-Si (OH)$_2$-O-Si (OH)$_2$-OH; $H_6Si_2O_7$, trisilicic acid (HO-Si(OH) $_2$-O-Si (OH)$_2$-O-Si (OH)$_2$-OH) and oligo silicic acid and poly silicic acid (HO-Si(OH)$_2$-[O-Si (OH)$_2$]$_x$-O-Si (OH)$_2$-OH; $H_{2n+2}Si_nO_{3n+1}$) (Holleman-Wiberg, 2007).

The petitioner proposed as global molecular formula $H_{2n+2}Si_nO_{3n+1}$ and mH_2O.

Orthosilicic acid [Si(OH)$_4$] is the simplest acid and the chemical form of silicon occurring when silicon dioxide is dissolved in water. Supersaturation (at concentrations >2 mmol/L) causes it to dehydrate and polymerise into less soluble polymeric forms. In plant materials the deposited forms are called ‘phytolithic silicon’ (Carlisle, 1997).

Synonyms: precipitated silicon dioxide, silica gel, hydrous silica, hydrated silicic acid, polysilicic acid gel, E551.

2.2.2. Specifications

Silicon dioxide is described as a white fluffy powder or granules; hygroscopic, slightly soluble in water (up to 120 mg/L, corresponding to 2 mmol/L) and ethanol; soluble in hydrofluoric acid and alkali (80 - 100 °C).

Silicic acid gel (silica gel) is a granular, vitreous, highly porous form of silicon dioxide. Despite its name, silicic acid gel is a solid. It can be suspended in water resulting in a turbid dispersion. Silicic acid gel is practically insoluble in water and ethanol; it is soluble in hydrofluoric acid and alkali (80 - 100 °C).

According to one petitioner, the particle size of a colloidal dispersion of silicic acid gel varies from approximately 5 nm, to approximately 1000 µm (depending on the manufacturing process).

The petitioners indicate that the chemical specifications of the two sources comply with the specifications for the food additive E551, under Directive 96/77/EC (EC, 2008a).

Microbiological characteristics have been provided by the petitioners for silicic acid gel only.

2.2.3. Manufacturing process

One petitioner provided a detailed description of the production of both silicon dioxide and silicic acid gel.

Silicon dioxide is produced by mixing diluted sodium silicate with diluted sulphuric acid under defined conditions. After reaction, the resulting mixture solidifies forming a jelly substance (a so-called hydro gel), which is homogenised, washed, dried and micronised.

Silicic acid gel is produced by stirring a mixture of hydrochloric acid, water and sodium silicate. A gel is obtained. The gel is broken by stirring and allowed to sediment. The clear supernatant obtained after sedimentation is decanted and the dry residue is homogenised and filled into bottles under continuous stirring.

2.2.4. Methods of analysis in food

The petitioner stated that silicon is determined according to the method for the assay of silicon dioxide, amorphous, as described by the Joint FAO/WHO Expert Committee on Food Additives (JECFA) (JECFA, 2001).

2.2.5. Reaction and fate in foods to which the source is added

One petitioner stated that silicon dioxide is a rather inert substance. No degradation products under normal conditions are known (Holleman-Wiberg, 2007).

3. Case of need and proposed uses of the different silicon sources

3.1. Calcium silicate

The petitioner indicated that calcium silicate is used as a source of silicon and calcium in food supplements. The petitioner stated that calcium silicate is used by food supplement manufacturers as an ingredient in tablets, caplets, capsules, chewable tablets, effervescent powders and liquids that are food supplements. The method of incorporation is determined by the individual manufacturers as appropriate for the particular type of the final products.

According to the petitioner, the quantity of silicon to be added to food supplements will be determined by individual formulators, but is normally the quantity necessary to supply not more than 100 mg silicon/day and up to 140 mg calcium/day.

3.2. Silicon dioxide/Silicic acid gel

The petitioner indicates that for silicon dioxide the recommended dose will be 1500 mg silicon dioxide/day (equivalent to 700 mg silicon/day).

For silicic acid gel a daily intake of 15 mL silicic acid gel suspension containing 420 mg silicon dioxide is recommended. 15 mL colloidal dispersed silicic acid corresponds to 196 mg silicon/day.

4. Information on existing authorisations and evaluations

Calcium silicate and silicon dioxide

In 1990 the Scientific Committee on Food (SCF) established a group Acceptable Daily Intake (ADI) 'not specified' for silicon dioxide: E551, calcium silicate: E552, magnesium silicate: E553a (i) and magnesium trisilicate: E553a (ii).

Silicon dioxide (E551) and calcium silicate (E552) are permitted food additives in the EU. They are permitted for use in dried powdered foods, salt and its substitutes, food supplements, rice, processed cheese and processed cheese analogues and seasonings, as well as for surface treatment of sausages and certain confectionery. Silicon dioxide and calcium silicate are also permitted as carriers in emulsifiers and colours at a maximum level of 5 %. Silicon dioxide is permitted as a carrier for flavourings at a maximum level of 50 g/kg. The availability of silicon from these additives varies, but is generally low.

JECFA evaluated the use of amorphous silica, calcium silicate and sodium alumino-silicate in food and concluded to an acceptance "not limited except for good manufacturing practice" (WHO, 1969).

JECFA re-evaluated silicon dioxide and a number of silicates in 1974, and concluded to a not limited ADI for man for silicon dioxide and certain silicates, except for magnesium silicate and talc (WHO, 1974).

Calcium silicate is Generally Recognized As Safe (GRAS) under United States FDA regulations (21CFR 182.2227).

The petitioner indicates that silicon dioxide is Generally Recognized as Safe (GRAS) under United States FDA regulations (21 CFR 182.90) and in New Zealand.

Silicon

The Panel notes that the essentiality of silicon for man has not been established, and a functional role for silicon has not been identified (EFSA, 2004). A recommended intake for silicon has not been set (SCF, 1993; IOM, 2000).

In 2004, EFSA concluded that there were no suitable dose-response data to establish an Upper Level for silicon and also the Institute of Medicine (IOM) reported that due to lack of data indicating adverse effects of silicon it was not possible to establish a UL (IOM, 2000). EFSA estimated that the typical dietary intake of 20-50 mg silicon/day, corresponding to 0.3-0.8 mg/kg body weight/day in a 60 kg person, is unlikely to cause adverse effects (EFSA, 2004).

The Expert group on Vitamins and Minerals (EVM) carried out a risk assessment and set a Safe Upper Level for supplemental daily exposure to silicon at 700 mg silicon/day for adults over a lifetime. In terms of elemental silicon, this is equivalent to a Safe Upper Level of 12 mg silicon/kg bw/day for a 60 kg adult for supplemental silicon (EVM, 2003).

Calcium

For calcium, in 1993 the SCF established Population Reference Intakes (PRI) for adults of 700 mg/day. A Tolerable Upper Intake Level (UL) for calcium of 2500 mg/day for adults (equivalent to 41.3 mg calcium/kg bw/day for a 60 kg person) has been established (SCF, 2003).

5. Exposure

Silicon

Silicon occurs naturally in foods as silicon dioxide (SiO_2, silica) and orthosilicic acid. High levels of silicon are found in foods derived from plants, particularly cereals such as oats (3910 – 4310 mg/kg dry weight), barley (2610 - 2720 mg/kg dry weight), white wheat flour (81 - 103 mg/kg dry weight) or polished rice (55 - 57 mg/kg dry weight). Silicon levels are lower in foods from animal sources like meat or dairy products (milk, 25 - 27 mg/kg dry weight) (Bowen and Peggs, 1984). Beer is also a source rich in of silica (9 - 39 mg silicon/L) (Sripanyakorn *et al.,* 2004). In drinking and mineral water, silicon is found as orthosilicic acid in the range of 2 to 5 mg silicon/L (Barnett *et al.,* 1969; EVM, 2003).

Dietary silicon mean intake has been estimated to be 20 - 50 mg silicon/day (Varo *et al.,* 1980; Bellia *et al.,* 1994; Bowen *et al.,* 1984; Pennington, 1991), corresponding to 0.3 - 0.8 mg/silicon/kg bw/day for a 60 kg person.

Calcium silicate

Foods particularly rich in this mineral are milk (1200 mg/kg), cheese (730-12000 mg/kg) and other dairy products (except butter), green leafy vegetables (except spinach), soybean products, bread and other baked goods made from calcium-fortified flour (variable levels), almonds (2400 mg/kg), brazil nuts (1700 mg/kg) and hazelnuts (1400 mg/kg).

According to the SCF (2003), the mean and 97.5th percentile calcium intakes from food in European countries vary from 683 to 944 mg/person/day and from 1421 to 1970 mg/person/day, respectively.

The petitioner indicated that the quantity of silicon in the form of calcium silicate, to be added to food supplements will be the quantity necessary to supply up to 100 mg silicon/day (equivalent to 1.7 mg silicon/kg bw/day for a 60 kg person) and up to 140 mg calcium/day (equivalent to 2.3 mg calcium/kg bw/day). For calcium, the mean and 97.5th percentile anticipated total exposure from food and food supplements would vary from 823 to 1084 mg/person/day and from 1560 to 2110 mg/person/day, respectively.

Silicon dioxide/Silicic acid

The petitioner indicated that silicon dioxide will be added to food supplements to supply up to 700 mg silicon/day. The Panel notes that this is about 14 to 35 times higher compared to the estimated dietary intake of silicon.

Silicic acid gel under the form of a colloidal dispersion will supply 196 mg silicon/day.

In the case calcium would simultaneously be supplemented in the form of calcium silicate at the highest proposed levels, there would be an additional amount of 0.1 g silicon/day.

6. Biological and toxicological data

6.1. Bioavailability

Introduction

The bioavailability of silicon depends on the solubility or speciation of the compound concerned. Orthosilicic acid ([$Si(OH)_4$] monomeric silicic acid) is present in saps of plants, body fluids of animals and water in low concentrations (Holleman-Wiberg, 2007; Casey *et al.*, 2003, Carlisle, 1975). The major silicon species in plants is amorphous silicon dioxide ('phytolithic silicon') (Holleman-Wiberg, 2007; Prychid *et al.,* 2004).

Popplewell *et al.* (1998) used ^{32}Si-labelled ammonium silicate to determine silicon in urine in one healthy male volunteer. Thirty-six percent of the ingested dose was absorbed and nearly completely excreted in the urine within 48 hours. Two first-order phases of elimination with half-lives of 2.7 and 11.3 hours were found.

Reffitt *et al*. (1999) studied silicon kinetics following intake of orthosilicic acid in water (27-55 mg silicon/L) in healthy individuals (6 men, 2 women). Based on urinary excretion, the average uptake of orthosilicic acid was about 50 % (range: 21-74%). The authors reported that after food consumption, there is a 4-hour delay before peak silicon absorption appears in the serum, compared to 1-hour after orthosilicic acid intake.

Jugdaohsingh *et al*. (2000) compared the bioavailability of orthosilicic acid and polymeric silicic acid. Following administration of orthosilicic acid, 53 % was excreted in the urine, whereas the ingestion of polymeric silicic acid only caused a marginal increase of silicon in the urine.

Sripanyakorn *et al*. (2004) studied the orthosilicic acid content of beer and its bioavailability from beer. The orthosilicic acid content of beer was found to be 80 % of the total silicon

content. The absorption of silicon from beer was 55 %, which was comparable with that of a solution of orthosilicic acid, suggesting that silicon in beer is present predominantly as orthosilicic acid and is bioavailable. This study is consistent with the findings of Bellia *et al*. (1994), who found that 42 - 72 % of silicon in beer is excreted in urine.

These studies illustrate that orthosilicic acid is absorbed from the gastrointestinal tract in humans and then readily excreted in urine, whereas polymeric silicic acid is not detectably absorbed nor excreted.

Bioavailability of silicon from the sources

Calcium silicate

The petitioner did not provide data on bioavailability of neither calcium nor silicon from the source. The Panel notes the low solubility of calcium silicate in hydrochloric acid and its practical insolubility in water, but in the absence of specific data, cannot reach a conclusion on bioavailability of either calcium or silicon from the source.

Silicon dioxide/Silicic acid gel

The petitioners did not provide specific data on the bioavailability of silicon from silicon dioxide in food supplements.

Silicon is abundant in certain plant foods as phytolithic silicon (amorphous silicon dioxide), a form that is poorly absorbed by the body. However, studies have shown that silicon from plant foods can be hydrolyzed to orthosilicic acid in the gastrointestinal tract (Reffitt *et al.*, 1999; Carlisle, 1984). In liquids, silicon dioxide is hydrated to form orthosilicic acid, which is much more easily absorbed by the body (Reffitt *et al*., 1999).

In a study by Jugdaohsingh *et al.* (2002) with humans consuming diets providing about 30 mg of silicon per day, it was shown that a substantial amount of the silicon as present in plant foods ('phytolithic silicon') is absorbed. The authors used the urinary excretion of silicon as an indicator for silicon absorption (silicon bioavailability) from the diet. Data show that overall, a mean of 40.9 ± 36.3% of ingested silicon was excreted over a 6-hour period in the urine, confirming that food-based, 'phytolithic silica' is digested and absorbed from the gastrointestinal tract. Silicon in grains and grain products (rice, breakfast cereals, bread and pasta) was readily absorbed, as indicated by the mean urinary excretion of 49 ± 34% of intake (range: 10 – 100%). Silicon in vegetables and fruit was less readily absorbed, as indicated by the mean urinary excretion of 21 ± 29% of intake (range: 0 – 40 %), with the exception however of green beans and raisins. Silicon uptake from bananas was low (2.1 ± 1.2% of intake), although bananas have a high silicon content (5.4 mg Si/100 g edible portion). According to the authors, this suggests either that silicon is mainly present in an unavailable form in bananas, or that this silicon is absorbed late from the gastrointestinal tract (beyond the 6-hour period).

In general however, silicon was available from foods and in many cases showed absorption similar to that of silicon from liquids. For instance, urinary silicon excretion was 41 – 86 % from corn flakes, white rice and brown rice, and 50 – 86 % from mineral waters.

Data reported by Kelsay *et al.* (1979) suggest that some forms of dietary fibre may affect silicon bioavailability, because in humans a diet high in fibre from fruits and vegetables significantly lowered the silicon balance.

6.2. Subsequent metabolic fate of the source and biological distribution

General information on the metabolic fate of silicon

Silicon is not protein-bound in plasma where it is believed to exist almost entirely as undissociated monomeric silicic acid (Berlyne *et al*., 1986). The silicon concentration in blood remains relatively constant, implying rapid distribution to tissues or excretion into the urine. While early analyses showed that serum contains 50 – 60 µg silicon/dL (Dobbie and Smith, 1982; Carlisle, 1984), more recent analyses indicate that human serum contains 11 – 25 µg silicon/dL (Van Dyck *et al.,* 2000; Calomme *et al*., 1998). Exceptions were pregnant women who had very low serum silicon concentrations (3.3 – 4.3 µg/dL) and infants who had higher concentrations (34 – 69 µg/dL).

Jugdaohsingh *et al*. (2000) and Reffitt *et al*. (1999) reported that fasting concentrations of silicon in plasma are 5.6 – 28 µg/dL. After meals, plasma concentrations increase to 56 – 84 µg/dL.

The human body contains approximately 1 g of silicon, which is present in various tissues and body fluids (Schmidt, 1998). Connective tissues, including aorta, bone, skin (and its appendages), tendon and trachea contain much of the silicon that is retained in the body (Adler *et al*., 1986; Carlisle, 1997), where it is thought to be present as a silanolate (an ether- or ester-like derivative of silicic acid), cross-linking the structural carbohydrates of connective tissue (Schwarz, 1973 and 1978). However, the silicon content in aorta, other arterial vessels and skin declines with age (Carlisle, 1984).

Loeper *et al*. (1978) reported that the concentration of silicon in the arterial wall of humans decreases with the development of atherosclerosis. Leslie *et al*. (1962) found that, although silicon levels decreased in skin, the silicon concentrations of most organs (e.g., kidney, brain, liver, spleen, and lung) increased with aging.

Absorbed silicon is mainly eliminated via the urine, where it probably exists as orthosilicic acid and/or magnesium othosilicate (Berlyne *et al.*, 1986; Carlisle, 1997). Kelsay *et al.* (1979) found that men excreted between 12 and 16 mg silicon/day. Berlyne *et al*. (1986) found slightly higher urinary silicon excretion in 23 normal individuals (about 33 mg of silicon per day). Jugdaohsingh *et al*. (2002) reported urinary excretion of silicon around 20 mg/day in young adults.

Apparently, the upper limits of urinary excretion of silicon are set by the rate and extent of silicon absorption and not by the excretory ability of the kidney, because peritoneal injection of silicon can elevate urinary excretion above the upper limit achieved by dietary intake (Sauer *et al*., 1959). This suggests that silicon homeostasis is controlled more by absorption mechanisms than by excretory mechanisms. This view is supported by the finding that in rats, guinea pigs, cattle and sheep, the urinary excretion of silicon initially increases with an increasing intake of siliceous substances, but reaches a maximum that is not exceeded by increasing the intake (Bailey, 1981). In sheep, the amount of silicon increased in urine, as dietary silica increased from 0.10 to 0.94 %. A further increase of dietary silica up to 2.84 % did not markedly affect the amount of silicon excreted with the urine (Jones and Handreck,

1965). The importance of renal elimination of silicon is highlighted by the finding of higher serum or plasma concentrations of silicon in patients with chronic renal failure compared to healthy controls (Dobbie and Smith, 1986; Gitelman *et al.,* 1992).

In the study by Popplewell *et al*. (1998), following ingestion of a tracer dose of ^{32}Si-labelled ammonium silicate by a healthy male volunteer, uptake was complete within 2 hours. Thirty-six percent of the ingested dose was absorbed and nearly completely excreted in the urine within 48 hours. Elimination occurred by two simultaneous first-order processes with half-lives of 2.7 and 11.3 hours, representing about 90 % and 10 %, respectively, of the total output. The authors suggested that the rapidly eliminated silicon was probably retained in the extracellular fluid volume, while the slower component may have represented intracellular uptake and release. In a study of silicon kinetics by Reffitt *et al.* (1999) in 8 healthy subjects, silicon peaked in blood after about one hour following intake of 27 – 55 mg silicon as orthosilicic acid in water. Renal clearance was 82 – 90 mL/min, which is similar to that found by Berlyne *et al.* (1986), suggesting high renal filtration. A significant correlation was found between creatinine clearance and silicon in urine or serum. Overall, absorbed silicon is excreted by the kidneys without accumulation in the body.

Specific information on the fate of silicon from the sources

The petitioner provided no data on calcium silicate. The petitioner referred to a publication by Bellia *et al*. (1994) which states that silicon exists most commonly as the mineral silicon dioxide (SiO_2), and that silicates in general, when exposed to water, liberate orthosilicic acid at a concentration of 1 – 15 mg orthosilicic acid/L. However, no data were provided by the petitioner to prove that this is also valid for calcium silicate.

6.3. Toxicological data

6.3.1. Calcium silicate

No specific data on acute toxicity and subchronic toxicity on the source have been provided by the petitioner.

6.3.1.1. Chronic toxicity

No specific data on oral chronic toxicity of the source were provided. The petitioner only provided information on chronic inhalation studies. The Panel is however of the opinion that these inhalation data are not relevant for the safety evaluation of oral intake of silicon from the source.

6.3.1.2. Genotoxicity

In vitro genotoxicity evaluations (Ames test, *Salmonella typhimurium*) were negative for calcium metasilicate (CCRIS, 1993; Elmore, 2003).

Aslam and Rahman (1993) evaluated chromosomal aberrations and sister chromatid exchanges (SCEs) in human peripheral blood lymphocytes cultured in the presence of calcium silicates (particle size < 30 µm) *in vitro,* at concentrations of 0.0, 0.1, 1, 10 and 100 µg/mL. The silicates significantly increased the frequencies of SCEs and chromosomal

aberrations (including gaps). The Panel notes however, that increased frequencies of gaps are not considered relevant and that no statistically significant increase in the frequency of chromosomal aberrations was observed when gaps were excluded from the evaluation. Furthermore, the study did not meet all the criteria of the current guidelines, and the SCE results described are considered as borderline. Therefore, the Panel considers that the study has limited validity and does not indicate a genotoxic potential of calcium silicate.

6.3.1.3. Reproduction and developmental toxicology

According to Elmore (2003), calcium silicate had no discernible effect on nidation or on maternal or fetal survival in rabbits. No other information was provided by the petitioner.

6.3.2. Silicon dioxide/Silicic acid gel

6.3.2.1. Acute toxicity

No toxicity or mortality has been reported in animals given silicon dioxide in doses of up to 3000 mg/kg bw/day (EVM, 2003).

6.3.2.2. Sub-chronic toxicity

In a 18-week study carried out by Najda *et al.* (1994), Wistar rats (100 male rats, of which 40 in control group), were given doses of sodium metasilicate in drinking water at levels that were increased every 6 weeks (0.05, 0.1 and 0.2%, equivalent to 100, 200 and 400 mg SiO_2/kg bw/day). It was found that the anti-oxidant enzyme activity was reduced, but no adverse effects were mentioned.

6.3.2.3. Chronic toxicity

Animal data

In a long-term oral feeding study, food grade micronised silica (an anti-caking agent) (silica gel) was administered to B6C3F1 mice (4 groups, 40 animals/group/sex, 5-week old animals) and to Fisher rats (4 groups, 40 animals/group/sex, 5-week old animals) at dose levels of 0, 12.5, 25 or 50 g SiO_2/kg of food (equivalent to 0, 1.9, 3.8 and 7.5 g SiO_2/kg bw for mice and 0, 1.25, 2.5 and 5 g SiO_2/kg bw for rats) for 21 and 24 consecutive months, respectively. The authors state that no biological or any other significant alterations in body weight, food consumption or physical features were observed. No significant effects were seen at any dose. Dietary administration of micronised silica to animals for up to 24 months, did not cause treatment-related gross or microscopic changes in the tissues examined. The occasional presence of some neoplasms did not reveal any consistent, dose-related trends in any group. The authors concluded that dietary administration of hydrated silicon dioxide had no long-term toxic effects (Takizawa *et al*., 1988).

Human data

Absorbed silicate is excreted by the kidneys without evidence of toxic accumulation in the body (WHO, 1974).

Cases of urinary calculi related to the use of magnesium trisilicate ($Mg_2Si_3O_8.nH_2O$) as an over-the-counter antacid have been described. Daudon (1999) estimated the incidence of silicon containing urinary calculi to be 0.07% of all kidney stones. The Recommended Daily Intake of magnesium trisilicate-containing medicines corresponds to about 980 to 2600 mg silicon dioxide.

WHO (1974) indicated that the probable lethal dose of oral ingested silica or magnesium trisilicate for humans is over 15 g/kg bw and for sodium silicate is between 0.5 and 5 g/kg bw. Therefore, WHO set no limit for the Acceptable Daily Intake of silicon dioxide, certain silicates and magnesium silicate (temporarily) for man.

In light of the available data, the Food and Nutrition Board in the United States has not established a maximum tolerable level for silicon in humans, nor did the EFSA (2004).

6.3.2.4. Genotoxicity

Silicon dioxide is not considered to be genotoxic in either *in vitro* or *in vivo* test systems (IARC, 1997).

6.3.2.5. Reproductive and developmental toxicity

Amorphous silica was fed respectively, to pregnant Wistar rats (up to 1350 mg/kg bw for 10 consecutive days), to pregnant CD-1 mice (up to 1340 mg/kg bw for 10 consecutive days), to pregnant Dutch rabbits (up to 1600 mg/kg bw for 13 consecutive days) and to pregnant Syrian hamsters (up to 1600 mg/kg bw for 5 consecutive days). No clearly discernible effect on nidation or on maternal or fetal survival was observed. The number of abnormalities seen in either soft or skeletal tissues of the test groups did not differ from the number of abnormalities occurring spontaneously in the controls (US EPA, 2003).

7. Discussion

Silicon occurs naturally in foods as silicon dioxide (SiO_2, silica) and orthosilicic acid. High levels of silicon are found in foods derived from plants, and particularly cereals, whereas silicon levels are lower in foods from animal sources.

Orthosilicic acid [$Si(OH)_4$], is the major silicon species present in drinking water and other liquids, including beer, and is the most readily available source of silicon to man. After oral consumption, the main chemical species by which silicon is absorbed is orthosilicic acid.

No specific data on the bioavailability of either silicon or calcium from calcium silicate have been provided. The Panel notes the low solubility of calcium silicate in hydrochloric acid and its practical insolubility in water, but in the absence of specific data, cannot reach a conclusion on the bioavailability of either calcium or silicon from the source.

No data have been submitted on the bioavailability of silicon from either silicon dioxide or silicic acid gel. However, several studies have shown that silicon present under a similar form was readily available from foods and in many cases showed absorption similar to that of silicon from liquids. Furthermore, given the conversion of silicon dioxide to orthosilicic acid upon hydration, and the bioavailability of silicon from orthosilicic acid, the Panel considers that silicon from silicon dioxide/silicic acid gel is bioavailable. However, the Panel also notes that the chemical form and matrix of silicon dioxide/silicic acid gel may influence the bioavailability of silicon.

The Panel notes that the essentiality of silicon for man has not been established and that a functional role for silicon has not been identified. A recommended intake for silicon has not been set.

The EFSA Panel on Dietetic products, Nutrition and Allergies (NDA) was unable to set a UL for silicon, but estimated that the typical dietary intake of 20 - 50 mg silicon/day (equivalent to 0.3-0.8 mg/kg body weight/day in a 60 kg person) is unlikely to cause adverse effects.

The EVM set a Safe Upper Level for silicon of 700 mg silicon/day for adults over a lifetime (equivalent to 12 mg silicon/kg bw/day for a 60 kg adult). The Tolerable Upper Intake Level (UL) for calcium is 2 500 mg/day for adults (equivalent to 41.3 mg calcium/kg bw/day).

The Panel noted that the toxicity data available for the silicon species in question do not give reasons for concern regarding oral exposure.

Silicates (i.e. E551, silicon dioxide, amorphous; E552, calcium silicate, hydrous/anhydrous; E553a(i), magnesium silicate; E553a(ii), magnesium trisilicate; E 553b talc; E554 sodium aluminosilicate) are approved food additives in the EU.

The quantity of silicon, in the form of calcium silicate, proposed to be added to food supplements will be the quantity necessary to supply up to 100 mg silicon/day (equivalent to 1.7 mg silicon/kg bw/day for a 60 kg person) and up to 140 mg calcium/day (equivalent to 2.3 mg calcium/kg bw/day), as indicated by the petitioner. For calcium, assuming a mean and 97.5th percentile intake from food of 683 to 944 mg/person/day and of 1421 to 1970 mg/person/day, respectively, consumption of this supplement would result in an anticipated total exposure of 823 to 1084 mg/person/day and to 1560 to 2110 mg/person/day, respectively.

The Panel notes that these intakes are below the UL set for calcium and that the proposed supplementation of silicon from calcium silicate is well below the Safe Upper Level of 700 mg silicon/day from supplement use, established by the EVM.

Silicon dioxide is proposed for addition to food supplements to supply up to 700 mg silicon/day. Silicic acid gel under the form of a colloidal dispersion will be added to food supplements to supply 196 mg silicon/day. The Panel noted that the proposed levels of supplementation of silicon from both sources are within the Safe Upper Level of 700 mg silicon/day from supplement use, established by the EVM. The Panel however noted that the highest proposed use level for silicon dioxide would lead to an exposure to silicon covering the entity of this Safe Upper Level.

CONCLUSIONS

The present opinion deals only with the safety of calcium silicate, silicon dioxide/silicic acid gel, as sources of silicon (Si) and with the bioavailability of silicon from these sources. The Panel notes that one petitioner also applied for the use of calcium silicate as source of

calcium. The safety of silicon and calcium itself, in terms of amounts that may be consumed and the consideration of silicon as a nutrient, are outside the remit of this Panel.

The Panel notes the low solubility of calcium silicate in hydrochloric acid and its practical insolubility in water, but in the absence of specific data, the Panel cannot conclude on the bioavailability of either calcium or silicon from the source.

No data have been submitted on the bioavailability of silicon from either silicon dioxide or silicic acid gel. However, several studies have shown that silicon present in a similar form was readily available from foods and in many cases showed absorption similar to that of silicon from liquids. Furthermore, given the conversion of silicon dioxide/silicic acid to orthosilicic acid upon hydration and the bioavailability of silicon from orthosilicic acid, the Panel considers that silicon from silicon dioxide/ silicic acid gel is bioavailable.

The Panel concludes that, in view of the Safe Upper Level for silicon of 700 mg silicon/day established by the EVM for supplemental use and of 2500 mg calcium/day for adults established by the SCF, and given the exposure to calcium and to silicon resulting from the proposed uses of calcium silicate as a source of respectively silicon and calcium in food supplements, the use of calcium silicate in food supplements at the proposed use levels is of no safety concern, provided that it complies with the specifications for its use as a food additive.

The Panel also concludes that the use of silicon dioxide up to 1500 mg SiO_2/day (equal to 700 mg of silicon/day) and of silicic acid gel to supply up to 200 mg silicon/day added to food supplements is of no safety concern.

DOCUMENTATION PROVIDED TO EFSA

1. Dossier on Calcium silicate Proposed for Addition to Annex II of Directive 2002/46/EC of the European Parliament and of the Council Relating to Food Supplements. May, 2005. Submitted by Health Food Manufacturers Association UK.
2. Dossier on Silicon Dioxide/Silicic Acid Gel Proposed for Addition to Annex II of Directive 2002/46/EC of the European Parliament and of the Council Relating to Food Supplements. April 2005. Submitted by Health Food Manufacturers Association UK on behalf of Bundesverband der Arzneimittel-Hersteller e.V. (BAH – Germany).
3. Dossier on Silicon Dioxide Proposed for Addition to Annex II of Directive 2002/46/EC of the European Parliament and of the Council Relating to Food Supplements. Submitted by Kabco Pharmaceutical, Inc., Amityville, New York. (No date of submission indicated).

REFERENCES

Aslam M, Rahman Q, 1993. Cytotoxic and genotoxic effects of Calcium Silicate on human lymphocytes *in vitro*. Mutat Res 300 (1), 45-8.

Adler AJ, Etzion Z and Berlyne GM, 1986. Uptake, distribution, and excretion of ^{31}silicon in normal rats. Am. J. Physiol. 251, E670-E673.

Bailey CB, 1981. Silica metabolism and silica urolithiasis in ruminants: a review. Can. J. Anim. Sci. 61, 219-235.

Barnett PR, Skougstad MW and Miller KJ, 1969. Chemical characterization of a public water supply. J. Am. Water Works Assoc. 61, 61-68.

Bellia JP, Birchall JD and Roberts NB, 1994. Beer: a dietary source of silicon. Lancet 343, 235 (Letter).

Berlyne GM, Adler AJ, Ferran N, Bennett S and Holt J, 1986. Silicon metabolism. I. Some aspects of renal silicon handling in normal man. Nephron 43, 5-9.

Bowen HJM and Peggs A, 1984. Determination of the silicon content of food. J. Sci. Food Agric. 35, 1225-1229.

Calomme R, Cos P, D'Haese PC, Vingerhoets R, Lamberts LV, De Broe ME, Van Hoorebeke C and Vanden Berghe DA, 1998. Absorption of silicon in healthy subjects. Pp. 228-232 in Metal Ions in Biology and Medicine, Vol. 5, Ph. Collery, P Brätter, V Negretti de Brätter, L Khassanova, JC Etienne, eds. Paris: John Libbey Eurotext.

Carlisle EM, 1975. Silicon. Nutrition reviews 33(9), 257-61.

Carlisle EM, 1984. Silicon. In Biochemistry of the Essential Ultratrace Elements, Pp. 257-291, E. Frieden, ed. New York: Plenum Press.

Carlisle EM, 1997. Silicon. In Handbook of Nutritionally Essential Mineral Elements, Pp. 603-618, B.L. O'Dell, and R.A. Sunde, eds. New York: Marcel Dekker.

Casey WH, Kinrade SD, Knight CTG, Rains DW and Epstein E, 2003. Aqueous silicate complexes in wheat, *Triticum aestivum* L. Plant Cell Environ. 27, 51-54.

CCRIS Chemical Carcinogenesis Research Information System (CCRIS) Number 4763 Calcium Silicate.

Daudon M, 1999. Les lithiases urinaires médicamenteuses en 1999. Prog Urol. 9, 1023-33.

Dobbie JW and Smith MJB, 1982. The silicon content of body fluids. Scot. Med. J. 27, 17-19.

Dobbie JW, Smith MJB, 1986. Urinary and serum silicon in normal and uraemic individuals. Pp. 194-213 in Silicon Biochemistry, Ciba Foundation Symposium 121. Chichester: John Wiley & Sons.

EC, 2008a. Commission Directive 2008/84/EC of 27 August 2008 laying down specific purity criteria on food additives other than colours and sweeteners. Journal of the European Communities, L 253/1 from 20.09.2008. Available at: http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2008:253:0001:0175:EN:PDF

EC, 2008b. Commission Regulation (EC) No 629/2008 of 2 July 2008 amending Regulation (EC) No 1881/2006 setting maximum levels for certain contaminants in foodstuffs.

EFSA, 2004. Opinion of the Scientific Panel on Dietetic Products, Nutrition and Allergies on a request from the Commission related to the Tolerable Upper Intake Level of Silicon. The EFSA Journal 60, 1-11. Available at: http://www.efsa.europa.eu/cs/BlobServer/Scientific_Opinion/opinion_nda_07_ej60_silicon_en1.pdf?ssbinary=true

Elmore AR, 2003. Final report on the safety assessment of aluminum silicate, calcium silicate, magnesium aluminum silicate, magnesium silicate, magnesium trisilicate, sodium magnesium silicate, zirconium silicate, attapulgite, bentonite, Fuller's earth, hectorite, kaolin, lithium magnesium silicate, lithium magnesium sodium silicate, montmorillonite, pyrophyllite, and zeolite. Int J Toxicol. 22 Suppl 1, 37-102.

EVM, 2003. Expert Group on Vitamins and Minerals. Safe upper levels for vitamins and minerals, Silicon & Calcium, UK Food Standards Agency. http://www.food.gov.uk/multimedia/pdfs/vitmin2003.pdf

Gitelman HJ, Alderman F and Perry SJ, 1992. Renal handling of silicon in normals and patients with renal insufficiency. Kidney Int. 42, 957-959.

Holleman AF, Wiberg E, Wiberg N, 2007. “Lehrbuch der anorganischen Chemie” 102 Auflage, Walter de Gruyter, Berlin-NewYork, seite 995.

IARC, 1997. Monographs on the Evaluation of Carcinogenic Risks to Humans and their Supplements. Vol 68. Silica, Some Silicates, Coal Dust and para-Aramid Fibrils. http://www-cie.iarc.fr/htdocs/monographs/vol68/silica.htm

IOM (Institute of Medicine), 2000. Food and Nutrition Board, 2000. Dietary Reference Intakes for Vitamin A, Vitamin K, Arsenic, Boron, Chromium, Copper, Iodine, Iron, Manganese, Molybdenum, Nickel, Silicon, Vanadium, and Zinc. National Academy Press, Washington, DC.

JECFA, 2001. Silicon dioxide, amorphous. Prepared at the 17th JECFA (1973), published in FNP 4 (1978) and in FNP 52 (1992). Metals and arsenic specifications revised at the 57th JECFA (2001). http://www.fao.org/ag/agn/jecfa-additives/specs/Monograph1/Additive-385.pdf

Jones LHP and Handreck KA, 1965. The relation between the silica content of the diet and the excretion of silica by sheep. J. Agric. Sci. 65, 129-134.

Jugdaohsingh R, Reffitt DM, Oldham C, Day JP, Fifield LK, Thompson RPH, Powell JJ, 2000. Oligomeric but not monomeric silica prevents aluminum absorption in humans. Am. J. Clin. Nutr. 71, 944-949.

Jugdaohsingh R, Anderson SHC, Tucker KL, Elliott H, Kiel DP, Thompson RPH, Powell JJ, 2002. Dietary silicon intake and absorption. Am. J. Clin. Nutr. 75, 887-893.

Kelsay JL, Behall KM and Prather ES, 1979. Effect of fiber from fruits and vegetables on metabolic responses of human subjects. II. Calcium, magnesium, iron and silicon balances. Am J Clin Nutr 32, 1876-1880.

Leslie JG, Kao K-YT, McGavack TH, 1962. Silicon in biological material. II. Variations in silicon contents in tissues of rat at different ages. Proc. Soc. Exp. Biol. Med. 110, 218-220.

Loeper J, Loeper J and Fragny M, 1978. The physiological role of the silicon and its antiatheromatous action. In Biochemistry of Silicon and Related Problems, Pp. 281-296, G. Bendz and I Lindquist, eds. New York: Plenum Press.

Merck Index, 2006. Calcium silicate, page 274.

Najda J, Goss M, Gmiński J, Węglarz L, Siemianowicz K and Olszowy Z, 1994. The antioxidant enzymes activity in the conditions of systemic hypersilicemia. Biol. Trace Elem. Res. 42, 63-70.

Pennington JAT, 1991. Silicon in foods and diets. Food Add. Contam. 8, 97-118.

Popplewell JF, King SJ, Day JP, Ackrill P, Fifield LK, Cresswell RG, di Tada ML, Liu K, 1998. Kinetics of uptake and elimination of silicic acid by a human subject: a novel application of ^{32}Si and accelerator mass spectrometry. J. Inorg. Biochem. 69, 177-180.

Prychid CJ, Rudall PJ, GregoryM, 2004. Systematics and biology of silica bodies in monocotyledons. Botanical Review 69, 377–440.

Reffitt DM, Jugdaohsingh R, Thompson RPH, Powell JJ, 1999. Silicic acid: its gastrointestinal uptake and urinary excretion in man and effects on aluminum excretion. J. Inorg. Biochem. 76, 141-147.

Sauer F, Laughland DH, Davidson WM, 1959. Silica metabolism in guinea pigs. Can. J. Biochem. Physiol. 37, 183-191.

SCF, 1990. Reports from the Scientific Committee for Food (25th series). Opinion expressed 1990. *Food science and techniques,* 1991.

SCF (Scientific Committee for Food), 1993. Nutrient and energy intakes for the European Community. Reports of the Scientific Committee for Food (Thirty-first series). European Commission, Luxembourg.

SCF (EC, Scientific Committee for Food), 2003. Opinion of the Scientific Committee on Food on the Tolerable Upper Intake Level of Calcium (Expressed on 4 April 2003). European Commission, Health & Consumer Protection Directorate-General, Directorate C – Scientific Opinions, C3 - Management of Scientific Committees II, Scientific Co-operation and Networks, Scientific Committee on Food, Brussels, Belgium.

Schmidt K, 1998. Silicium als essentielles Spurenelement. Aktueller wissenschaftlicher Erkenntnisstand. VitaMinSpur 13, 20-27.

Schwarz K, 1973. A bound form of silicon in glycosaminoglycans and polyuronides. Proc. Nat. Acad. Sci. USA 70, 1608-1612.

Schwarz K, 1978. Significance and functions of silicon in warm-blooded animals. Review and outlook. In Biochemistry of Silicon and Related Problems, Pp. 207-230, G Bendz, and I Lindquist, eds. New York: Plenum Press.

Sripanyakorn S, Jugdaohsingh R, Elliott H, Walker C, Mehta P, Shoukru S, Thompson, RPH, and Powell JJ, 2004. The silicon content of beer and its bioavailability in healthy volunteers. Brit. J. Nutr. 91, 403-409.

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 Med. Biol. 36:27-56.

US EPA (Environmental Protection Agency), 2003. Additional Discussion on Reproductive/Developmental Toxicity for Silane, dichlorodimethyl-, reaction products with Silicia (CAS No. 68611-44-9). http://www.epa.gov/chemrtk/slndichl/c14020rt.pdf

Van Dyck K, Robberecht H, Van Cauwenbergh R, Van Vlaslaer V, Deelstra H, 2000. Indication of silicon essentiality in humans. Serum concentrations in Belgian children and adults, including pregnant women. Biol. Trace Elem. Res. 77, 25-32.

Varo P and Koivistoinen P, 1980. Mineral element composition of Finnish foods. Acta Agricult. Scand. Suppl., 22: 165-171

WHO, 1969. Silicon Dioxide Amorphous, Calcium, Magnesium, and Sodium Alumino Silicates. Thirteenth report of the Joint FAO/WHO Expert Committee on Food Additives, FAO Nutrition Meetings Report Series; Wld. Hlth. Org. techn. Rep. Ser. http://www.inchem.org/documents/jecfa/jecmono/v46aje60.htm

WHO, 1974. Silicon Dioxide and Certain Silicates. Seventeenth Report of the Joint FAO/WHO Expert Committee on Food Additives, Wld. Hlth. Org. techn. Rep. Ser. No. 539. http://www.inchem.org/documents/jecfa/jecmono/v05je04.htm

GLOSSARY / ABBREVIATIONS

ADI	Acceptable Daily Intake
ANS	Panel on Food Additives and Nutrient Sources added to Foods
bw	body weight
CAS	Chemical Abstracts Service
EC	European Commission
EFSA	European Food Safety Authority
ETAAS	Electrothermal Atomic Absorption Spectrometry
EVM	Expert group on Vitamins and Minerals
FDA	U.S. Food and Drug Administration
GRAS	Generally Recognised As Safe
IOM	Institute of Medicine
JECFA	Joint FAO/WHO Expert Committee on Food Additives
NDA	Panel on Dietetic products, Nutrition and Allergies
SCEs	Sister Chromatid Exchanges
SCF	Scientific Committee on Food
UL	Tolerable Upper Intake Level
WHO	World Health Organization