

SCIENTIFIC OPINION

Calcium fluoride as a source of fluoride added for nutritional purposes to food supplements¹

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

(Question No EFSA-Q-2005-088)

Adopted on 27 November 2008

PANEL MEMBERS

F. Aguilar, U.R. Charrondiere, B. Dusemund, P. Galtier, J. Gilbert, D.M. Gott, S. Grilli, R. Guertler, G.E.N. Kass, J. Koenig, C. Lambré, J-C. Larsen, J-C. Leblanc, A. Mortensen, D. Parent-Massin, I. Pratt, I. Rietjens, I. Stankovic, P. Tobback, T. Verguieva, R. Woutersen.

SUMMARY

Following a request from the European Commission to the European Food Safety Authority (EFSA), the Scientific Panel on Food Additives and Nutrient Sources added to Food (ANS) was asked to provide a scientific opinion on the safety of calcium fluoride added for nutritional purposes as a source of fluoride in food supplements and on the bioavailability of fluoride from this source.

The present opinion deals only with the safety of calcium fluoride as a source of fluoride and the bioavailability of the fluoride from this source. The safety of fluoride itself, in terms of amounts that may be consumed, is outside the remit of this Panel.

Most of the available toxicity data examined in this opinion comes from exposure to freely soluble forms of fluoride, such as sodium fluoride, and the results of comprehensive evaluations carried out on these substances concluded that the most sensitive effect of chronic fluoride exposure in humans is dental fluorosis. The conclusions of these evaluations also indicated that genotoxicity and carcinogenicity are not of concern for fluoride exposure in humans. Upper tolerable intake levels for fluoride have been established in Europe amounting to 1.5 mg/day for 1–3 year old children, 2.5 mg/day for 4–8 year old children, 5 mg/day for

¹ For citation purposes: Scientific Opinion of the Panel on Food Additives and Nutrient Sources added to Food on a request from the Commission on Calcium fluoride as a source of fluoride added for nutritional purposes to food supplements. *The EFSA Journal* (2008) 882, 1-15.

9–15 year old children and 7 mg/day for adults (≥ 15 year old). The scarce literature available on the toxicity of calcium fluoride suggests that calcium fluoride shows less toxicity than soluble forms of fluoride at equivalent dosages.

Proposed supplementation foresees that calcium fluoride will be added to food supplements to supply approximately 1 mg calcium fluoride, corresponding to approximately 0.5 mg fluoride/day. However, due to its reported low solubility and bioavailability actual fluoride exposure from calcium fluoride supplementation should be at best about half the anticipated daily amounts (0.25 mg fluoride/day). Daily calcium exposure from this source will be very small and of no safety concern.

The Panel noticed that the foreseen supplementation with calcium fluoride will not exceed fluoride upper tolerable intake levels established in Europe for different populations. Furthermore, the potential added contribution of this supplementation for adults to the available total fluoride daily exposures' estimates will not exceed the specific upper tolerable intake level for the adult population and for children above the age of 8 year old. The Panel concludes that the use of calcium fluoride as food supplement at the proposed use levels would be of no safety concern for these populations.

However, the Panel noted that one available exposure scenario, which considers drinking water fluoride supplementation of 1 mg/l, suggests that the potential added contribution of calcium fluoride supplementation to the total estimated dietary exposure from food and drinking water could reach or exceed most upper tolerable intake level values established in Europe for children in age ranges of 1 to 3 and 4 to 8 year old.

The Panel concludes that the use of calcium fluoride as food supplement would be of no safety concern provided that fluoride upper tolerable intake level values established in Europe are not exceeded by the combined exposure from food supplements and the diet.

The Panel 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 mg/kg, 0.1 mg/kg and 1 mg/kg, respectively.

Key words:

Calcium fluoride, CAS 7789-75-5, food supplements

TABLE OF CONTENTS

Panel Members	1
Summary	1
Table of Contents	3
Background as provided by Commission.....	4
Terms of reference as provided by Commission.....	4
Acknowledgements	4
Assessment	5
1. Introduction	5
2. Technical data.....	5
2.1. Chemistry.....	5
2.2. Specifications.....	5
2.3. Manufacturing process.....	5
2.4. Methods of analysis in food.....	6
2.5. Reaction and fate in foods to which the source is added	6
2.6. Case of need and proposes uses	6
2.7. Exposure	6
2.8. Information on existing authorisations and evaluations	7
3. Biological and toxicological data	8
3.1. Bioavailability.....	8
3.2. Toxicological data.....	9
4. Discussion.....	11
Documentation provided to EFSA	13
References	13

BACKGROUND AS PROVIDED BY COMMISSION

The European Community legislation lists 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 fluoride 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 supplements².

TERMS OF REFERENCE AS PROVIDED BY 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 fluoride added for nutritional purposes in food supplements.

ACKNOWLEDGEMENTS

The European Food Safety Authority wishes to thank the members of the Working Group A on Food Additives and Nutrient Sources of the ANS Panel for the preparation of this opinion: F. Aguilar, N. Bemrah, P. Galtier, J. Gilbert, S. Grilli, R. Guertler, G.E.N. Kass, C. Lambré, J.C. Larsen, J-C. Leblanc, A. Mortensen, I. Pratt, I. Stankovic.

² OJ L 183, 12.7.2002, p.51.

ASSESSMENT

1. Introduction

Fluoride supplementation has been used for years essentially to prevent dental caries, especially if the fluoride concentration from drinking water is low. The widespread use of fluoridated toothpaste in the western world has been associated with an effective decline in caries prevalence. Fluoride compounds have also been used in intervention clinical studies to prevent and treat age-dependent osteoporosis. The Scientific Panel on Dietetics Products, Nutrition and Allergies (NDA) established tolerable upper intake levels of fluoride that include intake from water, beverages, foodstuffs, including fluoridated salt, dental health products and fluoride tablets for caries prevention (EFSA, 2005a). Similarly, the Food and Nutrition Board (FNB) of the National Academies in the US established tolerable upper intake levels of fluoride representing total intake from food, water, and food supplements (FNB, 2002). The Scientific Committee on Cosmetic Product and Non-Food Products intended for consumers (SCCNFP) has also evaluated the safety of fluoride compounds in oral hygiene products for children (SCCNFP, 2003).

The present opinion deals only with the safety of calcium fluoride as a source of fluoride and the bioavailability of the fluoride from this source. The safety of fluoride itself, in terms of amounts that may be consumed, is outside the remit of this Panel.

2. Technical data

2.1. Chemistry

Calcium fluoride is described as an inorganic compound with a molecular formula CaF_2 and a relative molecular mass of 78.08 g/mol (Technical dossier, 2005). Its CAS Registry number is 7789-75-5. Synonyms: calcium difluoride.

2.2. Specifications

The petitioner provided the following specifications for calcium fluoride: purity 99%, white crystalline and hygroscopic powder, solubility in water 17 mg/l (18 °C). The loss on drying is not more than 0.5% (at 105°C for 2 h). The pH of a saturated aqueous solution is in the range from 5 to 7. The impurities are sulphates (not more than 100 mg/kg), iron (not more than 100 mg/kg), chloride (not more than 500 mg/kg), arsenic (not more than 5 mg/kg) and lead (not more than 10 mg/kg) (Technical dossier, 2005).

The Panel notes that according to Commission Regulation (EC) No 629/2008 (EC, 2008) the maximum levels of lead, mercury and cadmium in food supplements as sold should be 3 mg/kg, 0.1 mg/kg and 1 mg/kg, respectively.

2.3. Manufacturing process

The manufacturing process of calcium fluoride is briefly described and is based on its precipitation from solution during the reaction of sodium fluoride and calcium chloride.

2.4. Methods of analysis in food

The petitioner presents a method to assay fluoride in foods, beverages, and diets (Lopez and Navia, 1988), as well as four alternative methods referenced by the Food Chemicals Codex (FCC, 1981). The calcium assay was done by inductively coupled plasma atomic emission spectroscopy (ICP-AES).

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

The petitioner indicated that calcium fluoride is stable in food. However, no supporting data have been provided.

2.6. Case of need and proposes uses

Calcium fluoride is intended to be used in food supplements in the form of tablets, caplets, capsules, chewable tablets, effervescent powders and liquids.

2.7. Exposure

According to the petitioner, the use of calcium fluoride in supplements is intended to supply approximately 1 mg calcium fluoride, equivalent to 0.5 mg fluoride/day (Technical dossier, 2005).

The most recent available exposure estimates to fluoride from all sources in Europe show total intakes from 0.5 to 1.2 mg/day, when no fluoridated salt or fluoride containing tooth paste are used, and no supplements are taken (EFSA, 2005a). In the case where fluoridated salt is used and fluoridated water is drunk and used for the preparation of food and tea, the sum of fluoride intake could reach 6 mg/day, without taking into consideration toothpaste use. For children, given that only very few reliable data were available on fluoride content from different sources, it was not possible to estimate total exposure to fluoride in the European children population in the NDA opinion (EFSA, 2005a).

The Scientific Panel on Contaminants in the Food Chain (CONTAM) mentions in its opinion on fluoride in mineral waters that exposure values to fluoride from sources other than mineral waters are 1 mg fluoride/day for the age group 9–14 year old and 3 mg fluoride/day for the population older than 15 years (EFSA, 2005b).

In the UK, total dietary exposure in children to fluoride from food and fluoridated water was calculated assuming two different water fluoride concentrations scenarios (Table 1). In the same report it was mentioned that breast milk contains only trace amounts of fluoride, providing less than 0.01 mg fluoride/day to infants.

Table 1 **Total exposure estimates to fluoride from the diet and drinking water in UK children (adapted from COT, 2003)**

Population group (age)	Fluoride concentration of drinking water			
	0.7 mg/l		1 mg/l	
	Mean intake (mg/kg bw/day) ~ (mg/day)	97.5 th percentile intake (mg/kg bw/day) ~ (mg/day)	Mean intake (mg/kg bw/day) ~ (mg/day)	97.5 th percentile intake (mg/kg bw/day) ~ (mg/day)
1.5 to 4.5	0.066 ~ 0.86 ^a	0.096 ~ 1.25 ^a	0.085 ~ 1.10 ^a	0.115 ~ 1.49 ^a
4 to 6	0.054 ~ 1.46 ^b	0.083 ~ 2.24 ^b	0.064 ~ 1.73 ^b	0.093 ~ 2.51 ^b
7 to 10	0.047 ~ 1.29 ^b	0.070 ~ 1.89 ^b	0.057 ~ 1.54 ^b	0.080 ~ 2.16 ^b

Assuming an average of: **a** = 13 kg bw, **b** = 27 kg bw

For infants and children in the USA, it has been estimated that the total daily intakes of fluoride from all sources can amount to 0.08 and 0.11 mg/kg bw/day in non-fluoridated areas, and 0.06 and 0.23 mg/kg bw/day in fluoridated areas.

2.8. Information on existing authorisations and evaluations

The NDA Panel established upper tolerable intake levels for fluoride of 1.5 mg/day for 1–3 year old children, 2.5 mg/day for 4–8 year old children, 5 mg/day for 9–15 year old children and 7 mg/day for adults (≥ 15 year old) (EFSA, 2005a). These upper tolerable intake levels apply to fluoride intake from water, beverages and foodstuffs including fluoridated salt, dental health products and fluoride tablets for caries prevention. The NDA Panel considered that an intake of 0.1 mg fluoride/kg bw/day in children up to 8 year old was a dose at which no significant occurrence of moderate forms of fluorosis in permanent teeth would occur.

The CONTAM Panel issued an opinion on concentration limits for fluoride in natural mineral waters (EFSA, 2005b). The Panel applied different scenarios for setting maximum limits for fluoride in mineral waters and concluded that at a concentration of 1 mg/l exposure to fluoride in the whole population, including young children, from all sources would be unlikely to reach the upper tolerable intake level values. A second scenario using higher fluoride concentration value exposure (5 mg/l) to fluoride would exceed upper tolerable intake level values for the populations under 15 year old.

The FNB of the National Academies in the US established upper tolerable intake levels of fluoride of 0.7 mg/day for infants 0 to 6 months old, 0.9 mg/day for infants 7 to 12 months old, 1.3 mg/day for children 1 to 3 year old, 2.2 mg/day for children 4 to 8 year old, and 10 mg/day for infants older than 9 year old and for the rest of the adult population including pregnant and lactating women (FNB, 2002). These upper tolerable intake levels apply to fluoride intake from food, water and food supplements.

The SCCNFP evaluated the safety of fluoride compounds (mainly sodium fluoride) in oral hygiene products for children under the age of 6 years (SCCNFP, 2003). The SCCNFP concluded that the *threshold that could cause serious symptoms and need immediate emergency treatment was 5 mg fluoride/kg bw for these children*. Additionally, it was concluded that toothpaste containing up to 0.15 % fluoride does not pose a safety concern for children under this age.

The Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment (COT) in the UK considered an intake of 0.05 mg/kg bw/day to be a no observable adverse effect level (NOAEL) for moderate dental fluorosis (COT, 2003), even though the Committee pointed out that the threshold dose at which fluoride causes moderate dental fluorosis was 0.1 mg/kg bw/day.

Sodium and potassium fluorides are authorised substances in Europe that may be added for specific nutritional purposes in foods for particular nutritional uses (EC, 2001).

The World Health Organisation (WHO) established a guideline value for naturally occurring fluoride in drinking-water of 1.5 mg/l (WHO, 2006). According to the WHO, recommended artificial fluoridation of water supplies is usually 0.5 – 1 mg/l.

The Scientific Committee on Food (SCF) established a tolerable upper intake level for calcium of 2500 mg/day from all sources for adults, pregnant and lactating women (SCF, 2003).

3. Biological and toxicological data

3.1. Bioavailability

Calcium fluoride is reported to be 3000 times less soluble in water than sodium fluoride as well as in dilute acids and bases (EHC, 2002). Water solutions of calcium fluoride needed up to 15 weeks to reach saturation state in which no further dissolution occurred (Bruun *et al.*, 1983). In 0.1 M HCl solutions (simulated gastric juice) one hour was needed to release 50% of fluoride from calcium fluoride tablets whereas no release was detected after a 5 h incubation in 0.2 M PO₄-buffer solution at pH 6.8 (simulated intestinal fluid) (Afseth *et al.*, 1987).

Calcium fluoride was also the less soluble fluoride salt in salivary body fluid and less well absorbed from the mouth *in vivo*. In a human study, parotid saliva samples were collected from five volunteers, who received oral doses of 10 mg/day of either a placebo, sodium fluoride (NaF), sodium monofluorophosphate (Na₂FPO₃), calcium fluoride (CaF₂), tin fluoride (SnF₂) or aluminium fluoride (AlF₃) for one week over a 6-week experimental period (Shannon and Edmonds, 1977). The 10 mg dose was divided into five 2 mg portions taken with 5 ml flavoured water.

The samples were collected over the first hour after dosage and then at 2, 3, and 4 h time-points. Urine excreted during the saliva collection periods was also collected. Results showed that parotid saliva fluoride levels increased within one hour after dosage for all fluoride sources except for calcium fluoride. Peak fluoride mean concentrations found in saliva were Na₂FPO₃ > SnF₂ > NaF > AlF₃ > CaF₂. Fluoride concentrations after calcium fluoride intake remained 2 to 4 fold lower than the other more soluble fluoride sources. Urinary fluoride excretion followed a similar pattern, calcium fluoride intake showing the lowest urinary concentration. After four hours of treatment, parotid saliva fluoride concentrations had decreased significantly though remaining higher than the placebo in the same sequence as before.

In humans, the dominating route of fluoride absorption is via the gastrointestinal tract. Fluoride ions are readily released from soluble fluoride compounds such as sodium fluoride, hydrogen fluoride, fluorosilicic acid and sodium monofluorophosphate (EHC, 2002). Fluoride originating from sodium fluoride tablets or solutions is rapidly absorbed showing an increase in plasma fluoride concentration a few minutes after intake and a plasma peak within 30 min (EHC, 2002). The height of the plasma peak is proportional to the fluoride dose ingested. Soluble forms of fluoride salts have reported absorption efficiencies of between 80–100 % (ATSDR, 2003). Conversely, insoluble sources of fluoride such as calcium fluoride, are much less well

absorbed. Supplementation of four overnight-fasting healthy volunteers (19-25 years of age) with 4 mg of calcium fluoride showed very small fluoride bioavailability (< 10 %) based on plasma fluoride concentration curves measured during a 6-hour period (Afset *et al.*, 1987). Similar results were found in another study with calcium fluoride supplemented as tablets to six overnight-fasting volunteers (16-18 years of age) by measuring plasma and urinary fluoride concentrations and calculating area under the curve (AUC) profiles (Trautner and Einwag, 1987). In this study fluoride bioavailability from calcium fluoride was estimated to vary widely between 0-47%. However supplementation of calcium fluoride as a powder showed higher fluoride availability compared to the solid tablet forms. Ingested fluoride can be retained in bones and teeth, being incorporated in their crystal lattice.

The degree of fluoride absorption may be altered by interactions with food components (EHC, 2002). It has been shown that ingestion of fluoride with a meal can increase the absorption of fluoride (Trautner and Einwag, 1987) but concomitant supplementation of sodium fluoride with milk or dairy products reduced its availability by 13–50% in humans and animals (Pratz, 1977; ATSDR, 2003). It was suggested that formation of sparingly soluble calcium fluoride, in the presence of high concentration of calcium from milk and dairy products, reduces the absorption of more soluble forms of fluoride (EHC, 2002). In laboratory animals, the presence of food and fluoride-binding ions (i.e., aluminium, calcium, magnesium) in the gastrointestinal tract significantly reduced the amount of fluoride absorbed (EHC, 2002). The absorption of ingested fluoride by female Wistar rats was reduced from 76 to 47% when the level of calcium in their diet was increased from 0.5 to 2%, and in male albino rabbits, the levels of fluoride in the serum (and femoral bone) were approximately 2-fold higher in animals administered a diet low in calcium than in controls administered a diet containing 4-fold more calcium (EHC, 2002).

3.2. Toxicological data

Most of the available data on fluoride toxicity comes from exposure to sodium fluoride. The toxicity of fluoride is dependent upon the type or species of the compound ingested, and therefore, the more soluble salts of inorganic fluorides (e.g. sodium fluoride and sodium monofluorophosphate) are the most toxic (EHC, 2002; ATSDR, 2003). Only scarce toxicity literature is available specifically on calcium fluoride. It is generally considered that calcium fluoride, being much less soluble and less bioavailable than other chemical fluoride forms tested, is much less toxic than the soluble forms of fluoride.

A number of expert bodies (IARC, 1982; EHC, 2002; COT, 2003; ATSDR, 2003; EFSA, 2005a) have reviewed the toxicity of fluorides in general. The following text summarises the major toxicological findings on fluorides reported in these evaluations.

Overall, acute exposure to soluble fluoride can induce vomiting, diarrhoea, respiratory arrest, cardiac depression and gastric mucosal changes. The latter have been reported following exposure to 18 mg fluoride/kg bw administered as sodium fluoride. Haematological changes (reduced numbers of blood cellular constituents), reduced collagen synthesis, signs of trabecular bone mineralisation and increased bone matrix formation have been reported on short-term studies in animals exposed to sodium fluoride. Body weight reduction, dental fluorosis, histological changes in the kidney, liver, testes and myocardium have been reported in medium-term studies in animals exposed to high-doses of fluoride (up to 270 mg/l of water). In long-term toxicity studies, signs of hyperkeratosis of the stomach mucosa, changes in blood chemistry and bone composition disturbances have been reported in animals exposed to high doses of sodium fluoride. Chronic exposure to fluoride has not been related to reproductive or teratogenic effects in animals. Some studies have found behavioural or brain abnormalities in mice exposed to fluoride, however these findings could not be fully assessed and results on

well conducted long-term studies in rodents at high doses did not show neurotoxicity effects. In general it is considered that exposure to fluoride by the oral route has no effect upon the frequency of chromosomal aberrations, micronuclei, sister chromatid exchange, DNA strand breaks or sperm morphology. On animal carcinogenicity, there was a reported occurrence of small numbers of osteosarcomas in a long-term study on male F344/N rats at doses of approximately 5 and 8 mg sodium fluoride/kg bw/day. However, there was no evidence of carcinogenicity in females F344/N rats and male or female B6C3F₁ mice at any of the same doses. The EFSA opinion on fluoride concluded that *there is equivocal evidence of carcinogenicity in male rats and no evidence of carcinogenicity in mice* (EFSA, 2005a).

Fluoride salts have been classified by the International Agency for Research on Cancer (IARC) as Group 3 (the agent is not classifiable as to its carcinogenicity to humans). In humans, many epidemiological studies on drinking-water consumption containing naturally or artificially added fluoride have not related fluoride exposure to an increased risk of developing cancer. The main effect reported in this type of studies was dental or enamel fluorosis and in some populations skeletal fluorosis. The most sensitive population to dental fluorosis is children under the age of eight particularly during the pre-eruptive formation and maturation of enamel in teeth. It has been considered that exposure to up 0.1 mg/kg bw/day in children less than eight years old does not result in dental fluorosis in permanent teeth. Very mild forms of dental fluorosis are of aesthetic concern only. No epidemiological association was found between fluorides in drinking-water and the incidence of Down's syndrome. There was no evidence of increased incidence of true allergic reactions after fluorides exposure.

In a study, briefly described by the authors, in pregnant female Swiss-ICR mice (5 to 9 animals/group), single intraperitoneally injections of increasing amounts of calcium fluoride showed some evidence of embryotoxicity (resorptions) at doses of 1600, 3200 and 6400 mg/kg bw, with the last two showing however high maternal mortality (> 70%) (Stratmann, 1979). Compared to other soluble fluoride sources tested in the same study (SnF₂, BaF₂, KF), calcium fluoride embryo toxicity appeared only at dosage levels at least 10 times higher than those tested with the other sources. No firm conclusions can be drawn from this study on chronic oral exposure given the fact that the test substances were administered intraperitoneally at a single dose. However, comparatively it can be concluded that calcium fluoride shows much less effect at equivalent doses of more soluble fluoride forms.

In another briefly described oral chronic toxicity study exposure of pregnant female Swiss-ICR mice (8–12 per group) to calcium fluoride at doses from 0.04 to 20.48 g/100 g of feed (approximately equivalent to 60–30720 mg/kg bw/day) showed increased signs of embryotoxicity (resorptions) but not dose-related at dosages approximately equivalent to 960 mg/kg bw/day (9.5% resorptions), 1920 mg/kg bw/day (7% resorptions), 15360 mg/kg bw/day (8.7% resorptions) and 30720 mg/kg bw/day (20.4% resorptions) (Stratmann *et al.*, 1979). Controls showed a resorption rate of 5.2 %. No data on both maternal toxicity and the duration of the assay were given. In this publication, some results were also reported from an one-generation reproductive toxicity study carried out with pregnant female Swiss-ICR mice (2–7 per group) at the three dosage levels of 2.56, 10.24 and 20.48 % (approximately equivalent to 3840, 15360 and 30720 mg/kg bw/day, respectively), which showed increased signs of embryotoxicity (resorption) and modest decreases in weight of surviving foetus at the two highest doses tested (39.2 and 41.2 % resorptions). No data on maternal toxicity and the duration of the assay were given. No effects were reported in foetus of two F1-generation groups exposed to 2.56 and 10.24 % calcium fluoride.

4. Discussion

Most of the available toxicity data comes from exposure to freely soluble forms of fluoride such as sodium fluoride. Conclusions of comprehensive evaluations carried out on these substances are the following:

- the most sensitive effect of fluoride exposure in humans is dental fluorosis
- genotoxicity and carcinogenicity are not of concern for fluoride exposure in humans.

The scarce toxicity literature available on calcium fluoride suggests that calcium fluoride shows less toxicity than soluble forms of fluoride at equivalent dosages. Embryotoxicity in mice has been reported in two studies for calcium fluoride but only at doses ten times higher of those showing overt embryotoxicity from soluble forms of fluoride. Overall, calcium fluoride, being much less soluble and less bioavailable than other soluble forms of fluoride, can be considered less toxic.

The upper tolerable intake levels of fluoride established in Europe amount to 1.5 mg/day for 1–3 year old children, 2.5 mg/day for 4–8 year old children, 5 mg/day for 9–15 year old children and 7 mg/day for adults (≥ 15 year old).

Proposed supplementation data foresees that calcium fluoride will be added to food supplements to supply approximately 0.5 mg fluoride/day. This level of supplementation is below all upper tolerable intake levels established for different populations in Europe. Assuming that fluoride from calcium fluoride is less available than from other sources of fluoride, the actual fluoride supplementation level from this source would be at best approximately 0.25 mg/day. Under these conditions the potential contribution of calcium fluoride supplementation to the total fluoride daily exposures estimates in Europe (~ 6 mg/day for adults) should not exceed fluoride upper tolerable intake levels established for adults in Europe (7 mg/day).

For children, total exposure estimates from food and drinking water in the UK, assuming a fluoride water concentration of 1 mg/l, shows that the 97.5th percentile population of the 1.5 to 4.5 year old and 4 to 6 year old children could exceed upper tolerable intake levels established by the NDA panel to equivalent age ranges (1 to 3 and 4 to 8 year old), if calcium fluoride supplementation was to be added to these intakes. For the 7 to 10 year old children, addition of calcium fluoride supplementation (at the proposed use levels) to the total exposure estimates from food and drinking water at the 97.5th percentile would be within the upper tolerable intake level value for the equivalent age range (9–15 year old children). Daily calcium exposure from this source (0.5 mg) will be very small compared to the upper tolerable intake level value of 2500 mg/day (SCF, 2003).

CONCLUSIONS

The present opinion deals only with the safety of calcium fluoride as a source of fluoride and the bioavailability of the fluoride from this source. The safety of fluoride itself, in terms of amounts that may be consumed, is outside the remit of this Panel.

Proposed supplementation data foresees that calcium fluoride will be added to food supplements to supply approximately 0.5 mg fluoride/day, corresponding to approximately 1 mg calcium fluoride. However, due to its reported low solubility and bioavailability, the actual fluoride exposure from calcium fluoride supplementation would be at best about half the anticipated daily amounts (0.25 mg fluoride/day). Daily calcium exposure from this source will be very small and of no safety concern.

However, the Panel noted that one available exposure scenario in the UK (1 mg/l fluoride supplementation of drinking water) suggested that the potential added contribution of calcium fluoride supplementation to the total estimated dietary exposure from food and drinking water could reach or exceed upper tolerable intake level values established in Europe for 1 to 3 and 4 to 8 year old children.

The ANS Panel concludes that the use of calcium fluoride as food supplement would be of no safety concern provided that fluoride upper tolerable intake level values established in Europe are not exceeded by the combined exposure from food supplements and the diet.

Most of the available toxicity data from freely soluble and much more bioavailable sources of fluoride (e.g. sodium fluoride) shows that the most sensitive effect of fluoride exposure in humans is dental fluorosis. Based on toxicity data from readily bioavailable fluoride upper tolerable intake levels for fluoride have been established. The Panel noticed that the foreseen supplementation with calcium fluoride will not exceed fluoride upper tolerable intake levels established in Europe for different populations. Furthermore, the potential added contribution of this supplementation, at the proposed use levels, to the total fluoride daily exposures estimates available for adults should not exceed the established upper tolerable intake level for this population. The Panel concludes that the use of calcium fluoride as food supplement at the proposed use levels would be of no safety concern for adults and children above the age of 8.

The Panel 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 mg/kg, 0.1 mg/kg and 1 mg/kg, respectively.

DOCUMENTATION PROVIDED TO EFSA

1. Technical dossier, 2005. Dossier on Calcium Fluoride Proposed for Addition to Annex II of Directive 2002/46/EC of the European Parliament and of the Council Relating to Food Supplements. March, 2005. Submitted by Blackmores Ltd, Australia.

REFERENCES

- Afseth J, Ekstrand J, Hagelid P, 1987. Dissolution of calcium fluoride tablets *in vitro* and bioavailability in man. *Scand. J. Dent. Res.* 95, 191-192.
- ATSDR, 2003. Toxicological profile for fluorides, hydrogen fluoride, and fluorine. U.S. Department of Health and Human Services. Public Health Service. Agency for Toxic Substances and Disease Registry. Division of Toxicology/Toxicology Information Branch. September 2003. Atlanta, Georgie.
- Bruun C, Moe D, Lundager Madsen H.E. 1983. Study on the dissolution behaviour of calcium fluoride. *Eur. J. Oral Sci.* 91, 247-250.
- COT, 2003. Committee on toxicity of chemical in food, consumer products and the environment. COT Statement on fluorine in the 1997 total diet study. September 2003.
- EC, 2001. Commission directive 2001/15/EC of 15 February 2001 on substances that may be added for specific nutritional purposes in foods for particular nutritional uses. *OJ L* 52/19, 22.2.2001.
- EC, 2008. Commission Regulation (EC) No 629/2008 of 2 July 2008 amending Regulation (EC) No 1881/2006 setting maximum levels for certain contaminants in foodstuff. *OJ L* 173, 3.07.2008.
- EFSA, 2005a. 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 Fluoride. *The EFSA Journal* 192, 1-65.
- EFSA, 2005b. Opinion of the Scientific Panel on Contaminants in the Food Chain on a request of the Commission related to concentration limits for boron and fluoride in natural mineral waters. *The EFSA Journal* 237, 1-8.
- EHC, 2002. Environmental Health Criteria 227. Fluorides. World Health Organization, Geneva.
- FCC, 1981. Food Chemicals Codex 3rd Edition, National Academy Press, 1981.

- FNB, 2002. Dietary reference intakes for energy, carbohydrate, fiber, fat, fatty acids, cholesterol, protein and aminoacids (macronutrients). Institute of Medicine. Year of publication 2005.
- IARC, 1982. Some aromatic amines, anthroquinones and nitroso compounds, and inorganic fluorides used in drinking water and dental preparations. IARC Monographs on the Evaluation of Carcinogenic Risks of Chemicals in Humans. Vol 27, pages 237-303. Lyon, France.
- Lopez H and Navia JM, 1988. A method to assay fluoride in foods, beverages, and diets. Caries Res. 22, 210-216.
- Pratz, VJ, Henschler, D, Fickenscher, H, 1977. Bioverfügbarkeit von Fluorid aus verschiedenen Salzen und unter dem Einfluß verschiedener Nahrungsbestandteile. Dtsch. Zahnärztl. Z. 32, 482-486.
- SCCNFP, 2003. Opinion of The Scientific Committee on Cosmetic Products and Non-Food Products intended for Consumers, concerning The safety of fluorine compounds in oral hygiene products for children under the age of 6 years. Adopted by the SCCNFP on 24-25 June 2003.
- SCF, 2003. Opinion of the Scientific Committee on Food on tolerable upper intake level of calcium. Expressed on 4 April 2003. European Commission, Bruxelles, Belgium.
- Shannon IL, Edmonds EJ, 1977. Fluoride levels in human parotid saliva following ingestion of fluoride compounds of varying solubility. J. Dent. Res. 56, 1521-1525.
- Stratmann von R, Eifinger FF, Köhler F, 1979. Teratologische Aspekte einer CaF₂-Medikation. Dtsch. Zahnärztl. Z. 34, 124-126.
- Stratmann Von KR, 1979. Vergleich des embriotoxischen Wirkungen anorganischer Fluoride. Dtsch. Zahnärztl. Z. 34, 484-486.
- Trautner K, Einwag J, 1987. Factors influencing the bioavailability of fluoride from calcium-rich, health-food products and CaF₂ in man. Archs. Oral Biol. 32, 401-406.
- WHO, 2006. Guidelines for drinking-water quality. First addendum to third edition. Volume 1 – Recommendations. World Health Organisation, Geneva, Switzerland.

GLOSSARY / ABBREVIATIONS

ANS	Scientific Panel on Food Additives and Nutrient Sources added to Food
bw	Body weight
CAS	Chemical Abstract Service
CONTAN	Scientific Panel on Contaminants in the Food Chain
COT	Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment
EFSA	European Food Safety Authority
FCC	Food Chemicals Codex
FNB	Food and Nutrition Board
IARC	International Agency for Research on Cancer
ICP-ES	Inductively coupled plasma atomic emission spectroscopy
NDA	Scientific Panel on Dietetics Products, Nutrition and Allergies
SCCNFP	Scientific Committee on Cosmetic Product and Non-Food Products
SCF	Scientific Committee on Food
WHO	World Health Organisation