European Food Safety Authority

The EFSA Journal (2009) 1009, 1-17

Scientific opinion

Selenious acid as a source of selenium added for nutritional purposes to food supplements [1]

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

(Question No EFSA-Q-2006-278)

Adopted on 19 March 2009

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.M.C.M. Rietjens, I. Stankovic, P. Tobback, T. Verguieva, R.A. 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 selenious acid added for nutritional purposes as a source of selenium in food supplements and the bioavailability of selenium from this source.

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

Selenious acid is the acid form of sodium selenite. In assessing the bioavailability and safety of selenious acid as a source of selenium in food supplements, the Panel considers that toxicity and bioavailability data on sodium selenite, an inorganic source of selenium, are directly applicable to selenious acid, since the latter will dissociate to its component ions in the gastrointestinal tract.

The absorption of selenite following oral administration is of the order of 40-70% of an oral dose, based on studies in humans. Bioavailability of selenite is broadly similar to that of

[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 selenious acid added for nutritional purposes to food supplements. *The EFSA Journal* (2009) 1009, 1-17.

selenate, as indicated by plasma levels of selenium and levels of selenoproteins in human and animal studies, but lower than that of organic forms of selenium.

The toxicity of selenium compounds has been evaluated by various organisations including the Scientific Committee on Food (SCF), the UK Expert group on Vitamin and Minerals (EVM) and the US Agency for Toxic Substances and Disease Registry (ATSDR). The SCF has established a Tolerable Upper Intake Level (thereafter referred to as Upper Level, UL) for selenium of 300 µg/day in adults.

Based on the information provided by the petitioner, the daily intake of selenious acid from food supplements according to the proposed use levels will be 8 – 163 µg/day, equivalent to 5-100 µg selenium/day. The intended typical use level is 65 µg/day (equivalent to 40 µg selenium/day). The maximum use level of selenious acid in food supplements proposed by the petitioner of 100 µg selenium/day will be below the UL of 300 µg selenium/day in adults, established by the SCF in 2000.

Selenium is a natural component of the diet, with an average intake for the adult European population lying in the range of 24 - 89 µg/day and a high dietary exposure of 108 µg selenium/day. When dietary intakes of selenium are taken into account, additional use of selenious acid as a food supplement could result in a total anticipated daily selenium intake of between 124 and 189 µg selenium/day in an adult at the average level of dietary exposure and an anticipated high exposure of 208 µg selenium/day, based on the maximum intake of 100 µg selenium/day arising from use of the food supplement. This intake will be below the UL for selenium of 300 µg/day established by SCF for adults in 2000.

The Panel notes that the use levels of selenium as selenious acid proposed by the petitioner, of between 5 and 100 µg/day, are generally lower than the ULs defined by the SCF for selenium of 90 - 250 µg/day for children aged 4 to 17 years depending on their body weight. For children (2 to 17 years old), the Panel estimates that when dietary intakes of selenium are also taken into account, use of selenious acid in food supplements at the maximum proposed use levels of 100 µg selenium/day could result in an total anticipated exposure between 123 and 142 µg selenium/day at average dietary intakes and between 132 and 177 µg selenium/day for high percentile intakes.

The Panel noted that these intakes will exceed the UL of 90 and 130 µg selenium/day for children at the ages of 4 - 6 and 7 - 10 years respectively. The highest proposed use level of 100 µg selenium per day from selenious acid is also above the UL of 60 µg selenium per day defined by the SCF for children aged 1 - 3 years. The ULs of 200 µg selenium/day for children between 11 and 14 years old and 250 µg selenium/day for children between 15 and 17 years old will not be exceeded.

The Panel noted that these estimates include higher intake figures from selenium-rich foods or where selenium is coming from the addition of selenium to fertilisers e.g. Finland, or to animal feed.

Based on these considerations, the Panel concludes that the use of selenious acid as a source for selenium in food supplements at the proposed use levels is of no safety concern, provided that the exposure to selenium from the diet plus the use in food supplements is not above the ULs for selenium defined by the SCF for adults or for children.

The Panel noted that the petitioner did not provide specifications for mercury in selenious acid. The Panel notes that, according to Commission Regulation (EC) No 629/2008, the maximum levels of mercury in food supplements as sold should be 0.1 mg/kg.

Key words:

Selenious acid, selenium dioxide monohydrated, CAS No. 7783-00-8

Table of Contents

BACKGROUND AS PROVIDED BY THE 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 selenious acid 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 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 selenious acid 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.

The Scientific Panel on Food Additives and Nutrient Sources added to Food (ANS) would like to thank E. Konings (Seconded National Expert of the DATEX Unit) for his contribution to the preparation of this opinion.

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

ASSESSMENT

1. Introduction

The present opinion deals only with the safety of selenious acid as a source of selenium and with the bioavailability of selenium from this source, intended to be used in food supplements. The safety of selenium (Se) itself, in terms of amounts that may be consumed, is outside the remit of this Panel. The Scientific Committee on Food (SCF) has previously given an opinion on the Tolerable Upper Intake Level (UL) of selenium (SCF, 2000).

2. Technical data

2.1. Chemistry

Selenious acid (synonym: selenium dioxide, monohydrated) is a white, water-soluble, odourless crystalline powder with the molecular formula H_2SeO_3 and a relative molecular weight of 128.97 g/mol (Technical dossier, 2005). The CAS Registry Number is 7783-00-8. Selenious acid is the corresponding acid of (di)sodium selenite, Na_2SeO_3, CAS No. 10102-18-8.

2.2. Specifications

Name	Content
Selenious acid	not less than 93.0% and not more than 101.0% of H_2SeO_3 calculated on the dried basis
Carbonate	not more than 50 mg/kg
Chloride	not more than 10 mg/kg
Water-insoluble matter	not more than 100 mg/kg
Alcohol-insoluble matter	not more than 500 mg/kg
Selenate [SeO_4^{2-}] and sulphate	not more than 50 mg/kg
Residue on ignition	not more than 0,1%
Lead (Pb)	not more than 3 mg/kg
Cadmium (Cd)	not more than 1 mg/kg

These specifications are according to the US Pharmacopeia, USP. The petitioner indicated that selenious acid typically has a purity of 100%. The petitioner did not provide specifications for mercury in selenious acid, but states that the heavy metal content is in compliance with Commission Regulation (EC) No 629/2008 (EC, 2008).

The Panel notes that according to Commission Regulation (EC) No 629/2008 the maximum level of mercury in food supplements as sold should be 0.1 mg/kg.

2.3. Manufacturing process

The petitioner declared that the manufacturing process of selenious acid is confidential, and it was not provided in the technical dossier.

2.4. Methods of analysis in food

Quantitative determination of selenium in food supplements is performed by Inductively Coupled Plasma-Atomic Emission Spectrometry (ICP-AES). The petitioner stated that a specific method for the determination of selenious acid in food supplements is not available.

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

The petitioner indicated that the selenium content of the food supplement is not expected to change over extended periods, and provided data covering a two-year period that supported this claim.

2.6. Case of need and proposed uses

Selenious acid is intended to be used as a source of selenium in food supplements in the form of chewable, effervescent, film-coated, hard gelatine and uncoated tablets. According to the petitioner, selenious acid is intended to be used in food supplements to provide an intake of 5 - 100 µg selenium/day, with a typical use level of 40 µg selenium/day.

2.7. Information on existing authorisations and evaluations

A Population Reference Intake (PRI) of 55 µg selenium per day for adults was established by the SCF in 1993 (SCF, 1993). The SCF has also established a UL for selenium of 300 µg/day (SCF, 2000), while the UK Expert Committee on Vitamins and Minerals (EVM) derived a safe upper level (SUL) of 450 µg/day for total selenium (EVM, 2003). The US Food and Nutrition Board (FNB) estimated a UL of 400 µg/day (NAS, 2000). Both the SCF UL and that of the FNB also apply to pregnant and lactating women, and while the SCF commented that there were no specific data to support a derivation of a UL for children, they noted that there are no reports indicating that children are more susceptible than adults to adverse effects from selenium. Hence, they concluded that it was appropriate to extrapolate the UL from adults to children on a body weight basis (SCF, 2000). This provided ULs ranging from 60 µg/day for children aged 1-3 years, 90 µg/day for children aged 4 - 6 years, and 250 µg/day for children aged 15 - 17 years. Specific legislative provisions on nutrient sources apply to foods manufactured for infants and young children.

2.8. Exposure

Selenium is a natural component of the diet, and is present in fish (0.32 mg/kg), offal (0.42 mg/kg), brazil nuts (0.25 mg/kg), eggs (0.16 mg/kg) and cereals (0.02 mg/kg). In foods, selenium is generally present as the amino acid derivates selenomethionine and selenocysteine (EVM, 2003). The amount of selenium available in the soil for plant growth varies, and consequently the intake of selenium by humans may differ considerably among regions and countries (SCF, 2000). Table 1 summarises information on selenium intake from food in various European countries, anticipated exposure to selenium by using selenious acid food supplements as proposed by the petitioner, and ULs.

According to the petitioner, selenious acid is intended to be used in food supplements to provide an intake of 5 - 100 µg selenium/day. The latter intake is equivalent to 8 - 163 µg selenious acid/day. The petitioner indicated that the typical use level is 40 µg selenium/day.

Assuming a mean dietary selenium intake in the range of 24 – 89 µg/day and a high percentile intake of 108 µg/day in Europe, the Panel estimated that daily consumption of an additional

food supplement containing 100 µg selenium (highest proposed use level) would result in a total anticipated exposure between 124 and 189 µg selenium/day in an adult at the average level of dietary exposure and an anticipated high exposure of 208 µg selenium/day.

Table 1: Summary information on selenium intake and anticipated exposure to selenium from selenious acid

Nutrient: Selenium	**Intake (µg/day)**		**References**
Recommended Intake (range) for adults (all ages)	55 (8 - 70)		SCF, 1993
Tolerable Upper Intake Level for adults	300		SCF, 2000
Tolerable Upper Intake Level for children (1-3 y/15-17y)	60 - 250		SCF, 2000
Nutrient: Selenium	**Average intake (µg/day)**	**High intake (95th or 97.5th, µg/day)**	**References**
Intake range from food in Europe for adults	24 - 89	108	SCF, 2000 ; Paturi *et al*. 2008
Intake range from food in Europe for children (2-17y)	23 - 42	32 - 77	Lyhne *et al*, 2005; Ocké *et al*, 2008; Enghardt Barbieri *et al*, 2006; AFSSA, 2009
Typical amount (range) of selenium added to supplements by selenious acid as indicated by the petitioner	40 (5 - 100)		Technical dossier
Total anticipated exposure to selenium from supplement and food intake[1] for adults	124 - 189	208	Calculation by Panel
Total anticipated exposure to selenium from supplement and food intake[2] for children (2-17y)	123 - 142	132 - 177	Calculation by Panel

[1]calculation based on highest proposed use level of 100 µg/day plus average dietary intake of 24 - 89 µg/day and high dietary intake of 108 µg/day for adults

[2]calculation based on highest proposed use level of 100 µg/day plus average dietary intake of 23 - 42 µg/day and high dietary intake of 32 – 77 µg/day for children

Assuming a mean dietary selenium intake for children between 2 and 17 years old in the range of 23 - 42 µg/day and a high percentile intake range of 32 - 77 µg/day in Europe, the Panel estimated that daily consumption of an additional food supplement containing 100 µg selenium (highest proposed use level) would result in a total anticipated exposure between 123 and 142 µg/day at the average level of dietary exposure and an anticipated high exposure between 132 and 177 µg selenium/day.

The Panel noted that these estimates include higher intake figures from selenium-rich foods, or where selenium is coming from addition of selenium to fertilisers e.g. Finland, (SCF, 2000, Rayman, 2004) or to animal feed (EFSA, 2006a, b).

3. Biological and toxicological data

The Panel considers that data on the toxicity and bioavailability of sodium selenite, an inorganic source of selenium, which is already included in Annex II of Commission Directive 2002/46/EC (EC, 2002), are directly applicable to selenious acid, since the latter will dissociate to its component ions in the gastrointestinal tract.

3.1. Bioavailability

No data were provided by the petitioner on the bioavailability of selenious acid. However, as indicated above, the bioavailability of selenious acid can be regarded as equivalent to that of sodium selenite.

Studies in humans suggest that selenite is less readily absorbed than selenate and organic selenium compounds such as selenomethionine. For example, the absorption of an oral 10 µg dose of ^{75}Se labelled selenite ranged from 44 to 70% in three human volunteers (Thomson and Stewart, 1974). Analysis of 72 hour urine samples from a study in which 48 Norwegian women were given a 200 µg supplement of selenium in the form of selenite or selenium-rich pea flour indicated approximately 50% absorption of selenite (Meltzer *et al*., 1990).

The enzyme glutathione peroxidase (GPx) contains selenium-amino acid residues, and activity of this enzyme has been used as a biological marker to determine relative bioavailability of selenium from different sources. In a selenium-deficient population in China in which five groups of 10 men each were given 0.5 g/day DL-methionine, or 150 µg selenium/day as sodium selenite with or without methionine, or 150 µg selenium/day as L-selenomethionine with or without methionine for eight weeks, sodium selenite was reported to have a lower bioavailability than L-selenomethionine (Luo *et al.*, 1987). Plasma levels of selenium reached approximately 60 µg/L at the end of the eight-week period in the group given sodium selenite, compared with approximately 100 µg/L in the group given L-selenomethionine, although levels of GPx were comparable.

The lower bioavailability of selenite, in comparison to other selenium sources, has been confirmed more recently in a further, more extensive, supplementation trial in a selenium-deficient population in China using 120 subjects administered sodium selenite or L-selenomethionine at levels ranging from 13 to 66 µg selenium/day for 20 weeks (Xia *et al*., 2005). At a supplemental level of 66 µg selenium/day, plasma selenium levels rose to a mean of 52 µg/L in subjects (men and women combined) receiving selenite, compared with 88 µg/L in subjects (men and women combined) receiving L-selenomethionine, from base line values of 21 µg/L in women and 23.2 µg/L in men (Xia *et al*., 2005).

In a study examining the effects of selenium supplementation on plasma selenium biomarkers and urinary selenium excretion in selenium-replete subjects, supplements containing moderate (approximately 200 µg/day) to high (approximately 600 µg/day) selenium concentrations in the form of sodium selenite, high-selenium yeast or L-selenomethionine were administered (Burk *et al*., 2006). Plasma biomarkers (selenium concentration, selenoprotein P concentration, and GPx activity) were determined before supplementation and every four weeks for 16 weeks, and urinary selenium excretion was determined at 16 weeks. Supplementation with L-selenomethionine and high-selenium yeast raised the plasma selenium concentration in a dose-dependent manner, while selenite did not.

In animal studies, approximately 90% absorption of selenite by male Sprague Dawley rats was reported, with only 10% of the ingested selenium being detected in the faeces

(Janghorbani *et al.*, 1990). A similar degree of absorption was reported in mice and dogs. A study on the effects of various dietary levels of selenium as selenite or selenomethionine on tissue selenium levels and GPx activity in rats indicated that the relative bioavailability of inorganic selenium and L-selenomethionine in rats is similar to that found in humans (Whanger and Butler, 1988). In rats given drinking water supplemented with 0.5, 2, 6 or 15 ppm selenium (equivalent to 0.05, 0.2, 0.6 or 1.5 mg/kg bw/day) as selenite daily for up to six months, plasma selenium levels were elevated at intakes above 0.5 ppm selenium in drinking water (Crespo *et al.*, 1993). There was a significant correlation between plasma selenium levels and selenium intake for the first month of treatment but this declined thereafter.

3.2. Metabolic fate and biological distribution

Following oral intake and absorption, selenium from sodium selenite is found in the highest concentrations in the liver and kidneys of humans and animals (EVM, 2003). There was a significant correlation between liver selenium levels and selenium intake in rats given drinking water supplemented with 0.5, 2, 6 or 15 ppm selenium (equivalent to 0.05, 0.2, 0.6 or 1.5 mg/kg bw/day) as selenite daily for up to six months (Crespo *et al.*, 1993).

Absorbed selenium, from both inorganic sources such as selenite and organic sources such as selenomethionine, is converted to hydrogen selenide, followed by incorporation into essential selenoproteins (Berry *et al.*, 1991, 1993). Hydrogen selenide surplus to requirements is further metabolised to methylated derivatives or selenosugars and excreted in urine or oxidised to selenium dioxide, a pathway associated with toxicity (Rayman, 2004).

3.3. Toxicological data

A number of expert bodies (e.g. ATSDR, 1996; EVM, 2003; SCF, 2000) have reviewed the toxicity of selenium. Little information was provided by the petitioner on the toxicity of selenious acid itself; however summaries of toxicological studies on selenite and other selenium compounds, based on the evaluation of selenium carried out by the EVM in 2003, were submitted (EVM, 2003). The petitioner indicated that the toxicity of selenious acid will be similar to that of sodium selenite (Technical dossier, 2005), the toxicity of which primarily reflects the toxicity of selenium, and the Panel agrees with this conclusion.

3.3.1. Animal studies

As summarised by the EVM (2003), in animals, acute toxicity of selenium is characterised by central nervous system toxicity and degenerative changes in the liver. As a result of the excretion of volatile selenium compounds, garlic-smelling breath also occurs. Adverse effects on growth rates, kidneys and reproductive parameters have been reported in rats and mice dosed with selenium compounds chronically and sub-chronically. Domestic animals develop a condition known as blind staggers, involving impaired vision and eventual respiratory failure. Selenite, selenate and selenomethionine are teratogenic in birds and fish. While positive results have been reported for several selenium compounds in *in vitro* genotoxicity assays, *in vivo* genotoxicity studies in rodents are considered overall to be negative (EVM, 2003).

3.3.2. Human studies

As summarised by the SCF (2000) and by the EVM (2003), acute selenium toxicity is characterised by gastrointestinal disturbance, hair loss, numbness in the arms, fatigue and garlic-smelling breath. In China where endemic selenosis occurs primarily from selenium in food, symptoms such as brittle and pigmentless hair, skin lesions, pathological changes to the nails and neurological disturbances are observed (EVM, 2003). The available literature suggests that intakes of selenium in the range of 3200 - 6990 µg/day (mean 4990 µg/day) by humans are associated with chronic selenosis, with no selenosis observed in an intake range of 240-1510 µg/day (mean 750 µg/day) (Yang *et al*., 1983, 1989a, b).

Investigations into the health effects of high dietary intakes of selenium in populations living in the seleniferous areas of South Dakota, Venezuela and China have indicated that the highest long-term daily intake of selenium that can be tolerated without the development of toxicity in most individuals is approximately 800 µg while prolonged daily intakes of 1000 µg or greater may cause adverse reactions.

4. Discussion

Selenious acid is the acid form of sodium selenite, an inorganic source of selenium. In assessing the safety of selenious acid as a source of selenium in food supplements, the Panel considers that the toxicity and bioavailability data on sodium selenite are directly applicable to selenious acid, since the latter will dissociate to its component ions in the gastrointestinal tract. The Panel considers that the UL as defined by the SCF (2000) for selenium can be used for judging the bioavailability and safety of selenious acid as a source of selenium.

Selenite appears to be less readily absorbed than organic selenium compounds such as selenomethionine, based on studies in humans indicating an absorption of 40 - 70% of an oral dose of selenite. Bioavailability of selenite is broadly similar to that of selenate, as indicated by plasma levels of selenium and levels of selenoproteins in human and animal studies, but lower than that of organic forms of selenium. Following absorption, selenium from selenite is converted to hydrogen selenide, followed by incorporation into essential selenoproteins. Hydrogen selenide surplus to requirements is further metabolised to methylated derivatives or selenosugars and excreted in urine or oxidised to selenium dioxide, a pathway associated with toxicity.

In animal studies, selenium compounds such as selenite are acutely toxic, causing central nervous system toxicity and degenerative changes in the liver. Adverse effects on growth rates, kidneys and reproductive parameters have been reported in rats and mice dosed with selenium compounds chronically and subchronically. Selenite, selenate and selenomethionine are developmental toxicants in laboratory animals, birds and fish. While positive results have been reported for several selenium compounds in *in vitro* genotoxicity assays, *in vivo* genotoxicity studies in rodents are considered overall to be negative. The Panel considered that the toxicity profile of selenious acid is likely to be similar.

In humans, selenium intakes in the range of 3200-6990 µg/day (mean 4990 µg/day) are associated with chronic selenosis, with no selenosis being observed in the intake range of 240-1510 µg/day (mean 750 µg/day).

Based on the information provided by the petitioner, the daily intake of selenious acid from the proposed use levels in food supplements will range from 8 to 163 µg, equivalent to 5 –

100 µg selenium/day. The intended typical use level is 65 µg selenious acid/day, equivalent to 40 µg selenium/day. The maximum use level of selenious acid in food supplements proposed by the petitioner of 100 µg selenium/day will be below the UL of 300 µg selenium/day in adults, established by the SCF in 2000.

Selenium is a natural component of the diet, with a mean intake for the adult European population lying in the range of 24 – 89 µg/day (SCF, 2000; Rayman, 2004).

Based on the information provided by the petitioners, and assuming a mean dietary intake for adults in the range of 24 – 89 µg selenium/day and a high percentile dietary exposure of 108 µg selenium/day in addition to daily consumption of a food supplement containing 100 µg selenium (highest proposed use level), the Panel estimates that use of selenious acid in food supplements could result in an total anticipated exposure between 124 and 189 µg selenium/day in an adult at the average level of dietary exposure and an anticipated high exposure of 208 µg selenium/day. This intake will be below the UL of 300 µg/day for selenium in adults established by the SCF in 2000.

Assuming a mean dietary intake in the range of 23 - 42 µg selenium/day for children between 2 and 17 years old, in addition to a daily consumption of a food supplement containing 100 µg selenium (highest proposed use level), the Panel estimates that use of selenious acid in food supplements could result in an total anticipated exposure between 123 and 142 µg selenium/day at average dietary intakes and between 132 and 177 µg selenium/day for high percentile intakes. This intake will exceed the UL of 60, 90, and 130 µg selenium/day for children at the ages of 1 - 3, 4 - 6 and 7 - 10 years respectively. The ULs of 200 µg selenium/day for children between 11 and 14 years old and 250 µg selenium/day for children between 15 and 17 years old will not be exceeded.

The Panel noted that these estimates include higher intake figures from selenium-rich foods, or where selenium is coming from addition of selenium to fertilisers e.g. Finland, (SCF, 2000, Rayman, 2004) or to animal feed (EFSA, 2006a, b).

CONCLUSIONS

The present opinion deals only with the safety and bioavailability of selenious acid as a particular source of selenium intended to be used in food supplements.

The Panel considers that the bioavailability of selenium from selenious acid is likely to be similar to that from sodium selenite, and that the toxicity of the two forms will be similar.

The Panel also considers that the UL defined by the SCF in 2000 for selenium can be used for judging the bioavailability and safety of selenious acid as a source of selenium.

The Panel concludes that the use of selenious acid as a source for selenium in food supplements at the proposed use levels is of no safety concern, provided that the amount of selenium from the diet plus supplements is not above the UL defined by the SCF for selenium.

The Panel notes however, that when dietary intake is taken into consideration in addition to supplementation at the proposed use level of 100 µg selenium/day, the ULs as defined by the SCF for children aged 4 - 6 years old and 7 - 10 years old will be exceeded. The highest

proposed use level of 100 µg selenium per day from selenious acid is also above the UL of 60 µg selenium per day defined by the SCF for children aged 1 - 3 years.

The Panel notes that the petitioner did not provide specifications for mercury in selenious acid. The Panel notes that, according to Commission Regulation (EC) No 629/2008, the maximum level of mercury in food supplements as sold should be 0.1 mg/kg.

DOCUMENTATION PROVIDED TO EFSA

Dossier for Safety Evaluation of Selenious Acid for Use in the Manufacture of Food Supplements. Submitted by Béres Pharmaceuticals Co. Ltd., Hungary. April 2005

REFERENCES

AFSSA, 2009. AFSSA, report of the 2006/2007 individual and national study on food consumption 2 (INCA2, coordinator L. Lafay), February 2009. Available at: www.afssa.fr.

ATSDR (Agency for Toxic Substance and Disease Registry Toxicological), 1996. Profile for Selenium (Update). US Department of Health and Human Services.

Berry MJ, Banu L, Chen YY, Mandel SJ, Kieffer JD, Harney JW and Larsen PR, 1991. Recognition of UGA as a selenocysteine codon in type I deiodinase requires sequences in the 3´untranslated region. *Nature* 353, 273–276.

Berry MJ, Banu L, Harney JW and Larsen PR, 1993. Functional characterization of the euk aryotic SECIS elements which direct selenocysteine insertion at UGA codons. *EMBO J* 12, 3315–3322.

Burk RF, Norsworthy BK, Hill KE, Motley AK and Byrne DW, 2006. Effects of chemical form of selenium on plasma biomarkers in a high-dose human supplementation trial. *Cancer Epidemiol Biomarkers Prev* 15(4), 804-810.

Crespo A, Neve J, and Pinto R, 1993. Plasma and Liver Selenium Levels in the Rat During Supplementation with 0.5, 2, 6 and 15 ppm Selenium in Drinking Water. *Biol Trace Elem Res* 38, 139-147.

EC (European Commission), 2002. Directive No 2002/46/EC of the European Parliament and of the Council of 10 June 2002 on the approximation of the laws of the Member States relating to food supplements. OJ L 183, 12.7.2002, p. 51.

EC (European Commission), 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, p. 6.

EFSA (European Food Safety Authority), 2006a. Opinion of the Panel on additives and products or substances used in animal feed (FEEDAP) on the safety and efficacy of the product Selenium enriched yeast (Saccharomyces cerevisiae NCYC R397) as a feed additive for all species in accordance with Regulation (EC) No 1831/2003. *The EFSA Journal* 430, 1-23.

EFSA (European Food Safety Authority), 2006b. Opinion of the Panel on additives and products or substances used in animal feed (FEEDAP) on the safety and efficacy of the product Sel-Plex 2000 as a feed additive according to Regulation (EC) No 1831/2003. *The EFSA Journal* 348, 1-40.

EVM (Expert Group on Vitamins and Minerals), 2003. Safe Upper Levels for Vitamins and Minerals: 232-239 and EVM/99/17 Revised Aug 2002, 1-70. Available at: http://www.food.gov.uk/multimedia/pdfs/vitmin2003.pdf.

Enghardt Barbieri H, Pearson M and Becker W, 2006. Riksmaten barn - 2003.Livsmedels- och näringsintag bland barn i Sverige (Food and nutrient among Swedish children). Livsmedelsverket, Uppsala 2006.

Janghorbani M, Rockway S, Mooers CS, Roberts EM, Ting BT and Sitrin MD, 1990. Effect of chronic selenite supplementation on Selenium Excretion and Organ Accumulation in Rats. *J Nutr* 120, 274-279.

Luo X, Quio Ch, Liu X, Wei H, Feng Y, Guo J, Yang Ch, Liu J and Stoeker BJ, 1987. Bioavailability of selenium to residents in a low-selenium area of China.. In Selenium in Biology and Medicine, Part A, Combs GF, Spallholz JE, Levander OA and Oldfield (eds.), Avi-Van Nostrand Reinhold Company, New York, NY, 436-444.

Lyhne N, Christensen T, Velsing Groth M, Fagt S, Biltoft-Jensen A, Hartkopp H, Hinsch H-J, Matthiessen J, Møller A, Saxholt E, Trolle E, 2005. Danskernes kostvaner 2000-2002 Hovedresultater. Danmarks Fødevareforskning. Afdeling for Ernæring. ISBN: 87-91587-09-3. Available at: www.dfvf.dk.

Meltzer HM, Norheim G, Bibow K, Myhre K, and Holm H, 1990. The Form of Selenium Determines the Response to Supplementation in a Selenium Replete Population. *Eur J Clin Nutr.* 44, 435-446.

NAS, 2000. National Academy of Science Dietary Reference Intakes for Vitamin C, Vitamin E, Selenium and Carotenoids, National Academy Press, Washington, D.C.

Ocké MC, van Rossum CTM, Fransen HP, Buurma EJM, de Boer EJ, Brants HAM, Niekerk EM, van der Laan JD, Drijvers JJMM, and Ghameshlou Z, 2008. Dutch National Food Consumption Survey-Young Children 2005/2006. RIVM Report 350070001/2008. Available at: http://www.rivm.nl/bibliotheek/rapporten/350070001.pdf .

Paturi M, Tapanainen H, Reinivuo H and Pietinen P, 2008. The National FINDIET 2007 Survey (Finravinto 2007 –tutkimus).. Kansanterveyslaitoksen julkaisuja B 23 / 2008. KTL-National Public Health Institute, Department of Health Promotion and Chronic Disease Prevention Nutrition Unit, Helsinki 2008. ISBN 978-951-740-847-9. Available at: http://www.ktl.fi/attachments/suomi/julkaisut/julkaisusarja_b/2008/2008b23.pdf.

Rayman MP, 2004. The use of high-selenium yeast to raise selenium status: how does it measure up? *Br J Nutr* 92, 557–573.

SCF (Scientific Committee on Food), 1993. Nutrient and energy intakes for the European Community. Reports of the Scientific Committee for Food, Thirty First Series. European Commission, Luxembourg. Available at: http://ec.europa.eu/food/fs/sc/scf/out89.pdf .

SCF (Scientific Committee on Food), 2000. Opinion of the Scientific Committee on Food on the Tolerable Upper Intake Level of Selenium. Available at: http://ec.europa.eu/food/fs/sc/scf/out80g_en.pdf .

Thomson CD and Stewart RDH, 1976. Metabolism of [^{75} Se] selenite in young women. *British J Nutr* 32, 47-57.

Whanger PD, and Butler JA,1988. Effects of various dietary levels of selenium as selenite or selenomethionine on tissue selenium levels and glutathione peroxidase activity in rats. *J Nutr* 118, 846-852.

Xia Y, Hill KE, Byrne DW, Xu J and Burk RF, 2005. Effectiveness of selenium supplements in a low-selenium area of China. *Am J Clin Nutr* 81, 829 – 834.

Yang G, Wang S, Zhou R and Sun S, 1983. Endemic selenium intoxication of humans in China. *Am J Clin Nutr* 37, 872-81.

Yang G, Zhou R, Yin S, Gu L, Yan B, Liu Y, Liu Y and Li X, 1989a. Studies of safe maximal daily dietary Se-intake in a seleniferous area in China. Part I: Selenium intake and tissue selenium levels of the inhabitants. *J Trace Elem Electrolytes Health Dis* 3, 77–87.

Yang G, Yin S, Zhou R, Gu L, Yan B, Liu Y and Liu Y, 1989b. Studies of safe maximal daily dietary Se-intake in a seleniferous area in China. Part II: Relation between Se-intake and the manifestation of clinical signs and certain biochemical alterations in blood and urine. *J Trace Elem Electrolytes Health Dis* 3 123–130.

GLOSSARY / ABBREVIATIONS

ANS Panel	Scientific Panel on Food Additives and Nutrient Sources added to Food
ATSDR	Agency for Toxic Substances and Disease Registry
CAS	Chemical Abstract Service
EC	European Commission
EFSA	European Food Safety Authority
EVM	UK Expert Group on Vitamins and Minerals
FEEDAP	Additives and Products or Substances use in Animal Feed
FNB	Food and Nutrition Board
ICP-AES	Inductively Coupled Plasma Atomic Emission Spectrometry
GPx	Glutathione Peroxidase
PRI	Population Reference Intake
SCF	Scientific Committee on Food
SUL	Safe upper level
UL	Tolerable Upper Intake Level
USP	US Pharmacopeia