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SCIENTIFIC OPINION

Scientific Opinion on the safety and efficacy of selenium compounds (E8) as feed additives for all animal species: sodium selenite (coated granulated preparation), based on a dossier submitted by Doxal Italia S.p.A.[1]

EFSA Panel on Additives and Products or Substances used in Animal Feed (FEEDAP)[2,3]

European Food Safety Authority (EFSA), Parma, Italy

ABSTRACT

Selenium is a trace element that is essential for vertebrates and involved in a series of vital metabolic functions. The additive, a coated granulated preparation of sodium selenite, consists of carrier granules to which the active compound, sodium selenite, is fixed using filming agents; it is manufactured with different selenium contents. Sodium selenite is considered to be a safe source of selenium for all animal species/categories, also when applied in coated granulated preparations. Based on extensive published literature data, the use of sodium selenite as a source of selenium in animal nutrition is considered to be safe for the consumer, provided that the total maximum authorised content of selenium in complete feed is respected. No concerns would arise from inhalation of selenium during the handling of the coated granulated preparation of sodium selenite owing to the very low estimated exposure. The coated granulated preparation of sodium selenite is considered to be an irritant to the skin, eyes and the respiratory system, and a skin sensitizer. Systemic exposure to selenium could result from dermal contact, particularly when cutaneous absorption of sodium selenite might be facilitated by skin damage; any dermal contact with the additive should be avoided. The use of sodium selenite in animal nutrition up to the maximum authorised content in feed would not raise concerns regarding the soil compartment, the ground or surface water. Concerning the marine sediments, given standard aquaculture practices and the low potential maximum concentration of selenium from fish feeds, any impact on the environment is unlikely. The coated granulated preparation of sodium selenite is an efficacious source of the essential trace element selenium for all animal species.

KEY WORDS

nutritional additive, compounds of trace elements, selenium, sodium selenite, coated granulated preparation, safety, efficacy

[1] On request from the European Commission, Question No EFSA-Q-2014-00508, adopted on 20 October 2015.

[2] Panel members: Gabriele Aquilina, Vasileios Bampidis, Maria de Lourdes Bastos, Georges Bories, Andrew Chesson, Pier Sandro Cocconcelli, Gerhard Flachowsky, Jürgen Gropp, Boris Kolar, Maryline Kouba, Secundino López Puente, Marta López-Alonso, Alberto Mantovani, Baltasar Mayo, Fernando Ramos, Guido Rychen, Maria Saarela, Roberto Edoardo Villa, Robert John Wallace and Pieter Wester. Correspondence: FEEDAP@efsa.europa.eu

[3] Acknowledgement: The Panel wishes to thank the members of the Working Group on Trace Elements, including Noël Dierick, Mikolaj Antoni Gralak, Christer Hogstrand, Lubomir Leng and Johannes Westendorf, for the preparatory work on this scientific opinion.

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SUMMARY

Following a request from the European Commission, the Panel on Additives and Products or Substances used in Animal Feed (FEEDAP) was asked to deliver a scientific opinion on the safety and efficacy of selenium compounds as feed additive for all animal species: sodium selenite (coated granulated preparation), based on a dossier submitted by Doxal Italia S.p.A.

Selenium is a trace element that is essential for vertebrates and is involved in a series of vital metabolic functions (e.g. prevention of oxidative stress, proper thyroid function, maintenance of cellular redox status, immunocompetence, detoxification of heavy metals and xenobiotics).

Sodium selenite is considered to be a safe source of selenium for all animal species/categories, also when applied in coated granulated preparations.

Based on extensive published literature data, the use of sodium selenite as a source of selenium in animal nutrition is considered to be safe for the consumer, provided that the total maximum authorised content of selenium in complete feed is respected.

No concerns would arise from inhalation of selenium during the handling of the coated granulated preparation of sodium selenite owing to the very low estimated exposure. In the absence of specific studies, the coated granulated preparation of sodium selenite is considered to be an irritant to the skin, eyes and the respiratory system, and a skin sensitiser. Systemic exposure to selenium could result from dermal contact, particularly when cutaneous absorption of sodium selenite might be facilitated by skin damage; any dermal contact with the additive should be avoided.

The FEEDAP Panel concludes that the use of sodium selenite in animal nutrition up to the maximum authorised content in feed would not raise concerns regarding the soil compartment, the ground or surface water. Concerning the marine sediments, given standard aquaculture practices and the low potential maximum concentration of selenium from fish feeds, any impact on the environment is unlikely.

The FEEDAP Panel concludes that the coated granulated preparation of sodium selenite is an efficacious source of the essential trace element selenium for all animal species.

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BACKGROUND

Regulation (EC) No 1831/2003[4] establishes the rules governing the Community authorisation of additives for use in animal nutrition. Article 10(2) of that Regulation also specifies that for existing products within the meaning of Article 10(1), an application shall be submitted in accordance with Article 7, at the latest one year before the expiry date of the authorisation given pursuant to Directive 70/524/EEC for additives with a limited authorisation period, and within a maximum of seven years after the entry into force of this Regulation for additives authorised without time limit or pursuant to Directive 82/471/EEC.

The European Commission received a request from Doxal Italia S.p.A.[5] for re-evaluation of authorisation of the selenium-containing additive *sodium selenite (coated granulated preparation)*, when used as feed additive for all animal species (category: Nutritional additives; functional group: compounds of trace elements).

According to Article 7(1) of Regulation (EC) No 1831/2003, the Commission forwarded the application to the European Food Safety Authority (EFSA) under Article 10(2) (re-evaluation of an authorised feed additive). EFSA received directly from the applicant the technical dossier in support of this application.[6] According to Article 8 of that Regulation, EFSA, after verifying the particulars and documents submitted by the applicant, shall undertake an assessment in order to determine whether the feed additive complies with the conditions laid down in Article 5. The particulars and documents in support of the application were considered valid by EFSA as of 18 November 2014.

The additive 'Sodium selenite' had been authorised in the EU under the element Selenium-Se (E8) for all animal species 'Without a time limit' (Council Directive 70/524/EEC concerning additives in feedingstuffs – List of authorised additives in feedingstuffs (2004/C 50/01)).[7] Following the provisions of Article 10(1) of Regulation (EC) No 1831/2003 the compound was included in the EU Register of Feed Additives under the category 'Nutritional additives' and the functional group 'Compounds of trace elements'.[8]

A compilation of risk assessments carried out on selenium and its compounds, including opinions from EFSA Panels other than the FEEDAP Panel, is in Appendix A. A list of authorisations of selenium compounds in the EU, other than as feed additive, is reported in Appendix B.

TERMS OF REFERENCE

According to Article 8 of Regulation (EC) No 1831/2003, EFSA shall determine whether the feed additive complies with the conditions laid down in Article 5. EFSA shall deliver an opinion on the safety for the target animals, consumer, user and the environment and the efficacy of sodium selenite (coated granulated preparation), when used under the conditions described in Table 1.

[4] Regulation (EC) No 1831/2003 of the European Parliament and of the Council of 22 September 2003 on additives for use in animal nutrition. OJ L 268, 18.10.2003, p. 29.
[5] Doxal Italia S.p.A. Via Mascagni 6. I-20050 Sulbiate (MI). Italy.
[6] EFSA Dossier reference: FAD-2010-0369.
[7] Commission list of the authorised additives in feedingstuffs published in application of Article 9t (b) of Council Directive 70/524/EEC concerning additives in feedingstuffs (2004/C 50/01). OJ C 50, 25.2.2004, p. 1.
[8] European Union Register of Feed Additives pursuant to Regulation (EC) No 1831/2003. http://ec.europa.eu/food/food/animalnutrition/feedadditives/docs/comm_register_feed_additives_1831-03.pdf

Table 1: Description and conditions of use of the additive as proposed by the applicant

Additive	Film granulated preparation of sodium selenite
Registration number/EC No/No (if appropriate)	E8
Category(-ies) of additive	3. Nutritional additive
Functional group(s) of additive	b. Compounds of trace elements

Description			
Composition, description	Chemical formula	Purity criteria (if appropriate)	Method of analysis (if appropriate)
Selenium, sodium selenite (CAS 10102-18-8)	Na_2SeO_3	Selenium: Min. 45%	Iodometric titration against 0.1 N sodium thiosulphate

Trade name (if appropriate)	-
Name of the holder of authorisation (if appropriate)	-

Conditions of use				
Species or category of animal	Maximum Age	Minimum content	Maximum content	Withdrawal period (if appropriate)
		mg/kg of complete feedingstuffs		
All animal species and categories	-	-	0.5 mg/kg selenium (total)	-

Other provisions and additional requirements for the labeling	
Specific conditions or restrictions for use (if appropriate)	- For use in animal nutrition only. - For use in premixtures and in feedingstuffs. - The additive shall contain selenium in the form of sodium selenite prepared in order to limit dust emissions to a maximum of 2 mg (total dust) per filter (Stauber-Heubach test).
Specific conditions or restrictions for handling (if appropriate)	-
Post-market monitoring (if appropriate)	No specific requirements other than the traceability and complaint system implemented in compliance with the requirements of Regulation No 183/2005.
Specific conditions for use in complementary feedingstuffs (if appropriate)	-

Maximum Residue Limit (MRL) (if appropriate)			
Marker residue	Species or category of animal	Target tissue(s) or food products	Maximum content in tissues
-	-	-	-

ASSESSMENT

1. Introduction

The additive under assessment is sodium selenite for use in feed for all animal species/categories. This inorganic compound has been used in animal nutrition as a source of the essential trace element selenium for decades.

The selenium content of grain and forages is generally low in most European countries; therefore, livestock is routinely supplied with extra dietary selenium in order to avoid the consequences of selenium deficiency.

The biological role of selenium and its deficiency and toxicity symptoms in farm animals were described in a previous opinion of the Panel on Additives and Products or Substances used in Animal Feed (FEEDAP Panel) (EFSA, 2006). Selenium is a trace element, which is essential for vertebrates and is involved in a series of vital metabolic functions (e.g. prevention of oxidative stress, proper thyroid function, maintenance of cellular redox status, immunocompetence, detoxification of heavy metals and xenobiotics). To the knowledge of the FEEDAP Panel, there is no additional relevant information that may lead it to reconsider its previous opinion.

Sodium selenite is already authorised in the European Union (EU) as a nutritional feed additive; the current application is sought for re-evaluation. The additive is intended to be marketed as a coated granulated preparation.

The European Food Safety Authority (EFSA) commissioned the University of Gent (Belgium) and the University Rovira i Virgili (Spain) to carry out studies of selected trace and ultratrace elements, and on the bioavailability interactions and incompatibilities of trace elements, respectively. The findings were submitted to the EFSA in the form of technical reports (Van Paemel et al., 2010; Cano-Sancho et al., 2014); both reports included selenium. Information from these reports has been used in this opinion.

2. Characterisation

For compounds of trace elements, the activity of the element itself is considered.

The final formulation contains a precisely defined carrier granule to which the active agent, sodium selenite, is fixed using filming agents (dispersants and non-ionic surfactants). The additive can be produced with different selenium contents. Products containing 1 % and 4.5 % selenium are exemplarily introduced in the dossier; however, the product is typically produced to contain 4.5 % selenium.

2.1. Characterisation of the formulated additive

The coated granulated preparation of the additive is based on sodium selenite (International Union of Pure and Applied Chemistry (IUPAC) name disodium, selenite; other names: selenious acid disodium salt, sodium selenium oxide, disodium selenium trioxide, hydrogen sodium selenite, sodium hydrogen trioxoselenite and sodium hydroselenite; Chemical Abstracts Service (CAS) number 10102-18-8 and the European Inventory of Existing Commercial chemical Substances (EINECS) number 233-267-9). Sodium selenite has the chemical formula Na_2SeO_3 (molecular weight 172.94 Da, theoretical maximum selenium content 45.7%). The structural form of the sodium selenite is given in Figure 1.

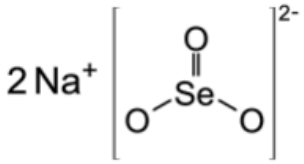

Figure 1: Molecular structure of sodium selenite.

The final additive contains up to 10% sodium selenite (preparation of 4.5% selenium (Se)). The product contains coating agents and dispersants (polyoxyethylene (20) sorbitan monolaurate (E 432), glycerol polyethyleneglycol ricinoleate (E 484), polyethyleneglycol 300, sorbitol (E 420ii) and maltodextrin) up to 5% w/w, and feed materials (calcium magnesium carbonate, calcium carbonate, corn cobs) as granulating agents made up to 100% w/w of the final preparation. The coat-granulating agents comply with the EU requirements for food additives and/or the European Pharmacopoeia and/or the Joint Food and Agriculture Organization of the United Nations (FAO)/World Health Organization (WHO) Expert Committee on Food Additives (JECFA) specifications (see Appendix C).

The company provided analytical data for two production series of the 1 % (ten batches analysed per series)[9] and 4.5% (nine batches analysed per series)[10] selenium-containing preparations. The results revealed selenium contents of 1.02 to 1.09 % and 4.33 to 4.78 %, respectively.

Levels of heavy metals (lead (Pb), cadmium (Cd) and mercury (Hg)), arsenic (As) and fluorine (F), measured in three batches for each 1% and 4.5% Se formulations, were as follows: Pb < 2 mg/kg product; Cd < 1 mg/kg product; Hg ≤ 0.08 and ≤ 0.11 mg/kg product, respectively; As < 10 mg/kg product; F < 200 and < 500 mg/kg product, respectively.[11,12] These levels comply with the applicable thresholds set in Directive 2002/32/EC[13] and do not represent a concern.

Levels of dioxins and the sum of dioxin and dioxin-like polychlorinated biphenyls (PCBs) measured in each one batch for 1% and 4.5% Se formulations were as follows: 0.32 and 0.46 ng WHO-PCDD/F-TEQ/kg, respectively and 0.34 and 0.47 ng World Health Organization-polychlorinated dibenzodioxin/dibenzofuran (PCDD/F)-PCB-toxic equivalents (TEQ)/kg, respectively.[14] These levels are compliant with EU legislation. Control methods are in place.

2.2. Physical state of the final formulation

The product appears as white-grey coloured free-flowing granules. It has bulk density of 1.36 kg/L and 1.26 kg/L for the 1% and 4.5% Se preparations, respectively.[15]

Particle size distribution was determined by laser diffraction on three batches of each of the 1% and the 4.5% Se preparations. No particles with a diameter less than 100 µm were found in the 1% selenium preparation, whereas in the 4.5% preparation, up to 0.4%, 4.5% and 7.1% (v/v) of particles were found below 10, 50 and 100 µm diameter, respectively.[16]

The dusting potential of two times ten batches of each of the 1 and 4.5% Se preparations (as such and after compaction (5 t/cm²) was measured according to Stauber-Heubach test. The highest mass on the filter out of the 20 batches was 0.4 and 0.5 mg for the 1 and 4.5% Se preparations, respectively. Compressing the additives increased the dust on the filter by about two-fold. However, all values were

[9] Technical Dossier/Section II/Annex 2.1.3.a.
[10] Technical Dossier/Section II/Annex 2.1.3.b.
[11] Technical Dossier/Section II/Annex 2.1.4.f.
[12] Technical Dossier/Supplementary Information/Annex 2.1.
[13] Directive 2002/32/EC of the European Parliament and of the Council of 7 May 2002 on undesirable substances in animal feed. OJ L 140, 30.5.2002, p. 10.
[14] Technical Dossier/Section II/Annex 2.1.4.g.
[15] Technical Dossier/Section II/Annex 2.1.5.c.
[16] Technical Dossier/Section II/Annex 2.1.5.a.

considerably below the specification (2 mg/filter). Comparing the dusting potential of the compressed additives with the untreated sodium selenite (mean of three batches: 19.5 mg/filter) it can be stated that the mechanical stability of the granules under compression was principally demonstrated.

The dusting potential, expressed in mg^3/m (a dimension required for the assessment of user safety), was calculated to be 12.5 mg/m^3 for both preparations, the compacted 1 and 4.5% preparations showing higher values (33.5 mg/m^3 and 42.0 mg/m^3, respectively).[17] Since the selenium content in the dust was analysed,[18] the mean selenium content in the air could be calculated to be 0.0062 and 0.0095 mg Se/m^3 for the 1% and the 4.5% Se preparations, respectively; the highest values being 0.0105 and 0.013 mg Se/m^3.

2.3. Characterisation of the sodium selenite

The sodium selenite used for production of the formulated additive is a white/cream crystalline powder containing by specification a minimum of 45% selenium; its solubility in water is 780 g/L at 20 °C and the pH varies between 9 and 10 in a 1% aqueous solution. Analysis of three batches showed selenium contents in the range of 45.2 to 45.7%.[19]

The applicant stated that the specification set for the undesirable substances in the sodium selenite would ensure that the material used for the production of the preparations complies with the thresholds set by Directive 2002/32/EEC. No specific analytical data were submitted.

Particle size distribution was characterised in two batches of sodium selenite (one for each normal grade-dried and milled material and spray dried).[20] In the normal-grade batch, up to 21.6, 67.2 and 90.1% of particles were found to have a diameter of less than 10, 50 and 100 µm, respectively. For the spray-dried batch, up to 43.8, 93.0 and 99.8% of particles were found to have a diameter of less than 10, 50 and 100 µm, respectively. Dust emissions of three batches of sodium selenite ranged from 665 to 1445 mg/m^3 in the Stauber-Heubach test.[21]

2.4. Manufacturing process

Sodium selenite is manufactured by reacting high-purity selenium with oxygen to produce selenium dioxide, which is then dissolved in water and neutralised with sodium hydroxide to produce sodium selenite in solution; this solution is decolourised, sodium selenite crystallised and recovered by evaporation and centrifugation. The product is then dried and milled. The formulated additive is prepared by binding the active agent onto the surface of the carrier granule using coat-forming agents and dispersants; the coating agents create a 'net' across the granule surface and thus capture the selenium compound. On completion of the addition of the excipients the mass is blended until a dry free-flowing granule has formed.

Material safety data sheets for the process ingredients and the final product were submitted.[22]

2.5. Stability and homogeneity

Stability data are not required for inorganic compounds of trace elements.

The capacity of the two preparations (i.e. 1% and 4.5% selenium) containing the additive to distribute homogeneously in feed was studied in pig feed (based on cereals) in comparison with uncoated powdered sodium selenite.[23] The test items were added to a vitamin/trace element premixture which was incorporated in the complete feed to provide a total selenium level of 0.5 mg/kg. Ten subsamples

[17] Technical Dossier/Section II/Annex 2.1.5.i.
[18] Technical Dossier/Supplementary Information/Annex 3.1.
[19] Technical Dossier/Section II/Annex 2.4.3.a.
[20] Technical Dossier/Section II/Annex 2.1.5.b.
[21] Technical Dossier/Section II/Annex 2.2.2.b.
[22] Technical Dossier/Section II/Annex 2.3.2.a.
[23] Technical Dossier/Section II/Annex 2.4.2.a.

of the three feeds were analysed for total selenium (recovery: 88–89 %). Mean selenium concentrations (coefficients of variation are given in brackets) were 0.44 mg/kg (8.6 %) for the 1 % Se preparation, 0.45 (10.0 %) for the 4.5 % Se preparation and 0.44 mg/kg (5.4 %) for the powdery sodium selenite.

2.6. Physico-chemical incompatibilities in feed

Based on current knowledge, under practical use conditions, no incompatibilities resulting from the use of sodium selenite in compound feed are expected with other feed materials, carriers, other approved additives or medicinal products.

2.7. Conditions of use

The coated granulated preparation of sodium selenite is intended to be used as a source of the trace element selenium for all animal species and categories up to a maximum total content of 0.5 mg/kg complete feed.

2.8. Evaluation of the analytical methods by the European Union Reference Laboratory (EURL)

EFSA has verified the EURL report as it relates to the methods used for the control of sodium selenite in animal feed. The Executive Summary of the EURL report can be found in Annex A.

3. Safety

3.1. Safety for the target species

Symptoms of deficiency and toxicosis of selenium in farm animals are described in detail in a previous opinion of the FEEDAP Panel (EFSA, 2006) and scientific reviews (e.g. McDowell, 2003; Suttle, 2010).

Tolerance studies are not required for compounds of trace elements already authorised. Consequently, the applicant did not submit any of these studies, but provided a literature review on the effects of feed supplementation with sodium selenite for three major animal species covering the years from 2000 to present (databases searched: CAB Abstracts and PubMed).[24] The results are summarised in brief below.

3.1.1. Safety of selenium from sodium selenite

The maximum tolerable level (MTL) of selenium for cattle and sheep set by the US National Research Council (NRC) is 5 mg Se/kg dry matter (DM) feed (NRC, 2005). Up to 10 mg Se/kg complete feed from sodium selenite is tolerated by ruminants; this conclusion is based on the absence of clinical signs of selenium toxicosis (abnormal hoof growth or loss of hair/wool) and histopathological evaluation of liver, kidney, diaphragm, heart and the muscles, and has been supported by further studies (Davis et al., 2006).

The MTL of selenium for poultry set by the NRC is 3 mg Se/kg DM feed (NRC, 2005). No adverse morphological or histological changes in liver or kidneys were noticed in chickens for fattening fed 2 or 5 mg Se/kg feed, but concentrations of 10 mg Se/kg and higher caused certain alterations in liver and kidney (see also Todorović et al., 2004).

The MTL of selenium for pigs set by the NRC is 4 mg Se/kg DM feed (NRC, 2005). A level of 3 mg Se/kg diet was well tolerated in gilts from 25 kg body weight (bw) through a complete reproductive cycle. Adverse effects were reported in pigs for fattening (general body weakness and/or staggering gait within 3 to 6 weeks after the start of the study) at 5 mg Se/kg feed.

[24] Technical Dossier/Supplementary Information/Annex 4.1.

The MTLs for horses and fish were derived from interspecies extrapolation and amount to 5 and 2 mg Se/kg DM feed, respectively (NRC, 2005).

Information on the tolerance of pet animals to selenium is scarce. No MTLs for cats and dogs are set by the NRC (2005). Todd et al. (2012) carried out two consecutive sodium selenite studies in 18 adult cats and 18 adult dogs. The animals were fed a control diet (0.6 µg Se/g DM) or the control diet supplemented with selenium to 8 to 10 µg Se/g DM for three weeks. No clinical signs of selenosis were observed in either cats or dogs. At the end of the study (day 21) the plasma selenium concentration was significantly higher in all animals that received the selenium-supplemented diet than in control animals, and levels were similar in both species. No differences in plasma glutathione peroxidase activity were observed between the control and treated groups of either cats or dogs. Selenium clearance from plasma in cats was about double that in dogs, and hepatic selenium concentrations in dogs were about double those observed in cats. Based on these findings, Todd et al. (2012) conclude that cats would probably tolerate greater dietary selenium concentrations as they are more efficient at excreting excess selenium in the urine and storing less selenium in the liver.

The literature review confirms the scenario as already described in a former FEEDAP Panel opinion on selenium (EFSA, 2006), that the tolerated dietary concentrations of selenium (independent from the source of selenium) for the different target species are markedly above the currently authorised maximum content for total selenium in complete feed (0.5 mg Se/kg).

3.1.2. Conclusions on the safety for the target species

Sodium selenite is considered to be a safe source of selenium for all animal species/categories, also when applied in coat granulated preparations.

3.2. Safety for the consumer

Absorption, distribution, metabolism and excretion of selenium have been already described in the opinions of the FEEDAP Panel (EFSA, 2006) and the NDA Panel (EFSA NDA Panel, 2014).

3.2.1. Metabolic and residue studies

The deposition of selenium and speciation of its compounds in edible tissues and products of animal origin is related to different metabolism of inorganic and organic selenium sources used as feed additives. When sodium selenite is given as supplement to feed animals, the selenite anion is, after being absorbed, taken up rapidly by erythrocytes and reduced by glutathione into dihydrogen selenide (H_2Se) within a very short time. After efflux into plasma, H_2Se is bound to albumin and transported to the liver for the synthesis of selenoprotein P and subsequently of further specific selenoproteins (Kobayashi et al., 2001). Selenium in the structural centre of specific selenoproteins occurs in the form of selenocystein (SeCys), which is synthetised from H_2Se via selenophosphate and activated serine (Ser) residue on ^{SeCys}tRNA (Ser ^{SeCys}tRNA) to SeCys ^{SeCys}tRNA, but not directly from free SeCys (Suzuki, 2005). Consequently the predominant selenium species in edible tissue and products of animals fed diets supplemented with inorganic selenium sources is SeCys incorporated into specific selenoproteins. On the other hand, in animals fed diets enriched with organic selenium sources based on selenomethionine (SeMet), also a significant non-specific incorporation of SeMet, particularly into general proteins of milk and muscle, occurs (Phipps et al., 2008; Juniper et al., 2008, 2009, 2011). It is well known that SeMet cannot be synthesised in the body by mammals, birds and fish. The scientific literature provides a huge amount of experimental evidence that animals fed diets supplemented with inorganic selenium sources show a considerably smaller selenium deposition in edible tissue/products than animals given organic selenium based on SeMet.

No data on tissue/product deposition of selenium specific to the feed additive under assessment were submitted by the applicant. However, based on available published literature, the FEEDAP Panel identified a total selenium concentration and/or its range in muscle, liver, kidney, eggs and milk when sodium selenite (as such, not formulated) was supplemented to animal feed providing levels between 0.3 and 0.5 mg Se/kg feed (Table 2). When original data were available on a dry matter basis only, the

selenium concentration on fresh weight basis was calculated using foodstuff tables published by Souci et al. (2008).

Table 2: Selenium concentration in edible tissues, eggs and milk (on fresh weight basis) from animals fed diets supplemented with sodium selenite providing levels between 0.3 and 0.5 mg Se/kg

Tissues and products	Animal species and/or categories					
	Pigs for fattening [(a)]	Chickens for fattening [(b)]	Turkeys [(c)]	Ruminants	Laying hens	Fish [(d)]
Muscle (mg/kg)	0.10–0.20	0.04–0.17	0.26	0.09–0.14 [(e)]	–	0.15–0.82
Liver (mg/kg)	0.42–0.68	0.30–0.70	0.49	0.45– 0.50 [(e)]	–	
Kidney (mg/kg)	1.23–3.74	0.30–1.95	0.92	1.43–3.70 [(e)]	–	
Milk (µg/L)	–	–	–	11.80–19.70 [(f)]	–	
Egg (mg/kg)	–	–	–	–	0.15–0.30 [(g)]	

(a): Based on: Mahan and Parrett, 1996; Mahan et al., 1999; Mateo et al., 2007; Svoboda et al., 2009; Kawecka et al., 2013; Jlali et al., 2014.
(b): Based on: Payne and Southern, 2005; Skřivan et al., 2008; Petrovic et al., 2010; Hu et al., 2012; Ryzner et al., 2013; Chen et al., 2013; Briens et al., 2014.
(c): Based on: Juniper et al., 2011.
(d): Based on: Souci et al., 2008; Kouba et al., 2014.
(e): Based on: Juniper et al., 2008 (cattle for fattening), 2009; Gresakova et al., 2013 (lambs).
(f): Based on: Aspila, 1991; Syrjala and Aspila, 1993; Ortman and Pehrson, 1999; Knowles et al., 1999; Gierus et al., 2002; Brzoska, 2004; Slavik et al., 2008; Ceballos et al., 2009; Meyer et al., 2014.
(g): Based on: Paton et al., 2002; Payne et al., 2005; Utterback et al., 2005; Skřivan et al., 2006; Pan et al., 2007; Pavlovic et al., 2009; Cobanová et al., 2011; Surai and Fisinin, 2014.

3.2.2. Toxicological studies

The toxicology of selenium salts, including sodium selenite, has been extensively reviewed, for example by the European Medicines Agency (EMA, 2015), the EU Scientific Committee on Food (SCF) (EC, 2000), the Agency for Toxic Substances and Disease Registry (ATSDR, 2003), the WHO (2011), and particularly for genotoxic effects by Cemeli et al. (2006) and Valdiglesias et al. (2010). A Cochrane review of prospective observational studies and randomised controlled trials with selenium has been reported by EFSA NDA Panel (2014).

In summary, the following conclusions can be drawn from the cited papers:

- Selenosis is a well-known human disease resulting from acute (e.g. 250 mg selenium as a single dose) or chronic selenium toxicity (NOAEL of 850 µg Se/day) (EC, 2000). Other related toxic effects in humans are disruption of endocrine function, synthesis of thyroid and growth hormones and an insulin-like growth factor metabolism (Valdiglesias et al., 2010). Nevertheless, these effects were reversible and disappeared in adult individuals as soon as the intake of toxic selenium tested doses was stopped.
- The genotoxic and antigenotoxic properties of sodium selenite, sodium selenate and selenous acid are highly dependent on the conditions under which they are evaluated (Cemeli et al., 2006), and could be related to changes in the equilibrium between pro-oxidant to antioxidant conditions.
- *In vitro* studies indicate that the genotoxic effects of selenium salts are associated with production of reactive oxygen species and that glutathione promotes these reactions. However, these effects could be shown *in vivo* only when toxic doses were applied (EC, 2000).

- The only selenium compound shown to be carcinogenic in animals is selenium sulphide. However, this compound is chemically different (insoluble in water) from the organic and inorganic forms for use in food, feed and the environment (ATSDR, 2003).
- Selenium at doses higher than 15 ppm in the diet of birds (Spallholz and Hoffman, 2002) and higher than 3 ppm in the diet of fish (Lemly, 2002) is teratogenic; findings on developmental toxicity in mammals are controversial (EC, 2000; ATSDR, 2003; WHO, 2011).

3.2.3. Assessment of consumer exposure

The EU SCF (EC, 2000) established 300 µg Se/day as Tolerable Upper Intake Level (UL) for adults (including pregnant and lactating women). This figure was based on the No Observed Adverse Effect Level (NOAEL) of 850 µg Se/day for clinical selenosis in the study on 349 subjects carried out by Yang et al. (1989), and followed up in the study by Yang and Zhou (1994) on five individuals who recovered from selenosis (when their intake had been reduced to a mean of 819 µg Se/day), and applying an uncertainty factor of 3. As there were no data to support a derivation of a UL for children, the SCF (EC, 2000) extrapolated the UL from adults to children on the basis of reference body weights. The proposed UL values range from 60 µg/day (1–3 years) to 250 µg selenium/day (15–17 years).

In a recent opinion on Dietary References Values (DRV) for selenium (EFSA NDA Panel, 2014), the estimated average selenium intakes in the EU for children aged 1 to < 3 years and adults (≥ 18 years) ranged from 17 to 36 µg Se/day and from 31 to 66 µg Se/day, respectively. These figures include also selenium intake from food of animal origin.

Based on selenium deposition data in animal tissues/products obtained by reviewing available published literature (see section 3.2.1), the FEEDAP Panel made an assessment of consumer exposure to selenium when sodium selenite was used as feed additive up to the maximum authorised selenium level in feed. For total selenium concentrations in tissue/products of animal origin the higher values found in various edible tissues and products were used. The food basket and its application, as described in the FEEDAP Guidance on consumer safety (EFSA, 2012), were used to make a conservative estimate of the intake of selenium by adults and toddlers from animal tissues/products following supplementation of the feed with sodium selenite (Table 2). The results (Tables 3 and 4) show that daily intake of selenium from two food items of animal origin would be below the ULs for both adults and toddlers. Even with the addition of the selenium intake from the consumption of food items, without considering food of farmed animal origin—values being estimated as 60 and 10 µg/day for adults (EFSA, 2006) and toddlers (EFSA, 2011), respectively—the ULs for adults and toddlers will not be exceeded.

Table 3: Selenium exposure in adults (mg/day) consuming tissues/products from animals fed diets supplemented with 0.3–0.5 mg Se/kg feed from sodium selenite

Food	Amount consumed (kg/day)	Se content in food (mg/kg)	Se intake (mg/day)
Meat	0.290	0.260	0.075
Kidney	0.015	3.740	0.056
Total (mg/day)			0.131

Table 4: Selenium exposure in toddlers (mg/day) consuming tissues/products from animals fed diets supplemented with 0.3–0.5 mg Se/kg feed from sodium selenite

Food	Amount consumed (kg/day)	Se content in food (mg/kg)	Se intake (mg/day)
Meat	0.090	0.260	0.023
Milk	1.050	0.020	0.021
Total (mg/day)			0.044

3.2.4. Conclusions on the safety for the consumer

Based on extensive published literature data, the use of sodium selenite as a source of selenium in animal nutrition is considered to be safe for the consumer, provided that the total maximum authorised content of selenium in complete feed is respected.

3.3. Safety for the user

The occupational safety related to selenium compounds has been comprehensively reviewed, for example, by the International Programme on Safety (IPCS, 1987) and by the ATSDR (2003). Selenium compounds are recognised as highly toxic by inhalation, ingestion and skin contact.

3.3.1. Effects on the respiratory system

Concerning threshold limit values (TLV) for selenium compounds, calculated as selenium, values between 0.02 and 0.2 mg/m^3 have been set by different committees (e.g. German Maximale Arbeitsplatz Konzentration (MAK) List, Occupational Safety and Health Administration (OSHA), National European Authorities). The lowest value of 0.02 mg/m^3 (MAK) was taken for further considerations.

The highest selenium content measured in the dust of a 4.5% Se-containing preparation was 0.013 mg/m^3; this concentration of selenium in dust would result in 65% of the MAK. In practice, the exposure of users handling the additive to selenium would be lower than indicated by the relation of the MAK to dusting potential. The MAK describes a tolerable 8-hr exposure, whereas handling the feed additive preparation is limited to < 30 minutes per working day (see Guidance on user safety; EFSA, 2012).

3.3.2. Effects on the eyes and skin

No specific data have been provided regarding the toxicity of the film-coated additive under assessment to skin and eyes. Inorganic selenium is able to cause severe irritation of skin, eyes and mucous membranes after contact. Selenium compounds are also known to be skin sensitisers (US EPA 2000; ATSDR, 2003). Moreover, cutaneous absorption of selenium may occur after skin contact causing systemic exposure. In the absence of specific data for the additive under assessment, the findings described above are considered applicable to sodium selenite and its preparation.

3.3.3. Conclusions on the safety for users

No concerns would arise from inhalation of selenium during the handling of the coated granulated preparation of sodium selenite owing to the very low estimated exposure. Owing to the lack of specific data, the additive is considered to be an irritant to the skin, eyes and the respiratory system, and a skin sensitiser. Systemic exposure to selenium could result from dermal contact, particularly when cutaneous absorption of sodium selenite might be facilitated by skin damage; any dermal contact with the additive should be avoided.

3.4. Safety for the environment

Based on the conservative calculation method provided in the technical guidance for assessing the safety of feed additives for the environment (EFSA, 2008), addition of sodium selenite to animal feed at a concentration of 0.5 mg Se/kg complete feed would maximally result in addition of 10.7 µg Se/kg soil after a 1-year application of manure, assuming that 100% of the dose will be excreted. This addition is small compared with the background concentration of selenium in soil which is, on a global average, of 330 µg Se/kg. There are currently no EU Environmental Quality Standards (EQSs) for selenium in soil, but the Netherlands has a long-term target value of 700 µg Se/kg dry weight (dw) (Warmer and van Dokkum, 2002) and the Canadian Council of Ministers of the Environment (CCME) has derived a Soil Quality Guideline for agricultural and residential/parkland use of 1 000 µg/kg (CCME, 2009). As the addition of selenium to soils from feed additives is small compared with background concentrations and regulatory limits (where in place), sodium selenite in feeds for

terrestrial farm animals is considered safe to the soil compartment. Using the same reasoning, there would also be no concern for the ground or surface water compartments resulting from this application.

Using its technical guidance for assessing the safety of feed additives for the environment (EFSA, 2008), the FEEDAP Panel calculated the worst-case concentrations in the environment resulting from the supplementation of fish feeds with sodium selenite at a total level of 0.5 mg Se/kg. In applications for land-based aquaculture operations, the surface water effluent from the fish farm is considered to be the most vulnerable compartment (EFSA, 2008). The Predicted Environmental Concentration in surface water (PEC_{sw}) was calculated to be at maximum 0.01 µg/L, which is an order of magnitude below the trigger value and therefore no further assessment is required for this particular aspect. When fed to fish in sea cages, the sediment under the cage is considered the compartment of concern (EFSA, 2008). The PEC_{sed} was calculated to be 106 µg/kg wet weight, which exceeds the threshold for Phase I assessment (10 µg/kg). The conservative estimate of 106 µg Se/kg wet weight which could result from the use of sodium selenite in marine fish feed is lower than the lowest published sediment quality criterion (700 µg/kg; Warmer and van Dokkum, 2002). Since the location of fish cages rotates on a regular basis, build-up of selenium in the sediment from sodium selenite added to fish feed is unlikely. Given the low theoretical maximum concentration of selenium in marine sediments resulting from selenium in fish feeds, it is unlikely that the use of sodium selenite as a feed additive would have any impact on the marine environment.

The FEEDAP Panel concludes that the use of sodium selenite in animal nutrition up to the maximum authorised content in feed would not raise concerns to the soil compartment, the ground or surface water. Concerning the marine sediments, given the standard aquaculture practices and the low potential maximum concentration of selenium from fish feeds, any impact on the environment is unlikely.

4. Efficacy

Sodium selenite has been used in animal nutrition as source of the essential trace element selenium for decades. Its efficacy (based on response in blood/serum and liver selenium levels, and in glutathione peroxidase activity in blood/plasma) is well documented in the scientific literature for swine (Mahan and Parrett, 1996), poultry (Kuricova et al., 2003) and bovine (Ortman and Pehrson, 1999).

The applicant provided an *in vitro* study to demonstrate the availability of selenium from the coated granulated additive.[25] The dissolution of the active compound from the coated granulated form was compared to that from pure sodium selenite after 1, 2, 5 and 10 minutes in buffer solutions at pH values of 3.0, 6.0 and 7.4. No differences in water selenium concentrations were observed between the formulated additive and pure sodium selenite. It can therefore be concluded that the coated granulated additive effectively releases the sodium selenium salt under the various pH conditions occurring in the gastrointestinal tract.

4.1. Conclusions on the efficacy for the target species

The FEEDAP Panel concludes that the coated granulated preparation of sodium selenite is an efficacious source of the essential trace element selenium for all animal species.

5. Post-market monitoring

The FEEDAP Panel considers that there is no need for specific requirements for a post-market monitoring plan other than those established in the Feed Hygiene Regulation[26] and Good Manufacturing Practice.

[25] Technical Dossier/Section IV/Annex 4.1.2.a

[26] Regulation (EC) No 183/2005 of the European Parliament and of the Council of 12 January 2005 laying down requirements for feed hygiene. OJ L 35, 8.2.2005, p. 1.

CONCLUSIONS

Sodium selenite is considered to be a safe source of selenium for all animal species/categories, also when applied in coat granulated preparations.

Based on extensive published literature data, the use of sodium selenite as a source of selenium in animal nutrition is considered to be safe for the consumer, provided that the total maximum authorised content of selenium in complete feed is respected.

No concerns would arise from inhalation of selenium during the handling of the coated granulated preparation of sodium selenite owing to the very low estimated exposure. The coated granulated preparation of sodium selenite is considered to be an irritant to the skin, eyes and the respiratory system, and a skin sensitiser. Systemic exposure to selenium could result from dermal contact, particularly when cutaneous absorption of sodium selenite might be facilitated by skin damage; any dermal contact with the additive should be avoided.

The FEEDAP Panel concludes that the use of sodium selenite in animal nutrition up to the maximum authorised content in feed would not raise concerns to the soil compartment, the ground or surface water. Concerning the marine sediments, given the standard aquaculture practices and the low potential maximum concentration of selenium from fish feeds, any impact on the environment is unlikely.

The FEEDAP Panel concludes that the coated granulated preparation of sodium selenite is an efficacious source of the essential trace element selenium for all animal species.

DOCUMENTATION PROVIDED TO EFSA

1. Dossier sodium selenite (E8), film granulated preparations. October 2010. Submitted by Doxal Italia S.p.A.

2. Dossier sodium selenite (E8), film granulated preparations. Supplementary information. April 2015. Submitted by Doxal Italia S.p.A.

3. Evaluation report of the European Union Reference Laboratory for Feed Additives on the Methods(s) of Analysis for Sodium selenite.

4. Comments from Member States.

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ABBREVIATIONS

ATSDR	Agency for Toxic Substances and Disease Registry
As	arsenic
bw	body weight
CAS	Chemical Abstracts Service
Cd	cadmium
DM	dry matter
dw	dry weight
EC	European Commission
EEC	European Economic Community
EFSA	European Food Safety Authority
EPA	Environmental Protection Agency
EINECS	European Inventory of Existing Commercial chemical Substances
EQS	Environmental Quality Standard
EU	European Union
EURL	European Union Reference Laboratory
F	fluorine
FAO	Food and Agriculture Organization of the United Nations
FEEDAP	Panel on Additives and Products or Substances used in Animal Feed
H_2Se	dihydrogen selenide
Hg	mercury
IPCS	International Programme on Safety
IUPAC	International Union of Pure and Applied Chemistry
JECFA	Joint FAO/WHO Expert Committee on Food Additives
MAK	Maximale Arbeitsplatz Konzentration
MTL	Maximum Tolerable Level
MRL	Maximum Residue Limit
NDA	EFSA Panel on Dietetic Products, Nutrition and Allergies
NOAEL	No Observed Adverse Effect Level
No	number
NRC	National Research Council
OSHA	Occupational Safety and Health Administration
Pb	lead
PCBs	polychlorinated biphenyls
PCDD	polychlorinated dibenzodioxin
PCDF	polychlorinated dibenzofuran
PEC	Predicted Environmental Concentration
PNEC	Predicted No Effect Concentrations
SCF	Scientific Committee on Food
Se	selenium
SeCys	selenocystein
SeMet	selenomethionine
Ser	serine
TEQ	Toxic Equivalent Factor
TLV	Threshold Limit Value
tRNA	transfer ribonucleic acid
UL	Tolerable Upper Intake Level
US	United States
WHO	World Health Organization

APPENDICES

Appendix A. List of Risk Assessment Reports on selenium and selenium compounds

In addition to the reports cited in the this Opinion, other risk assessments have been carried out by EU bodies, institutions and industry (see list below).

1. EC Committees Opinions

Report of the Scientific Committee on Food on the revision of essential requirements of infant formulae and follow-on formulae. Available online: http://www.ec.europa.eu/food/fs/sc/scf/out199_en.pdf

2. EU Member States Risk Assessment Reports

The Environmental Agency, UK. Contaminants in soil: updated collation of toxicological data and intake values for humans Selenium Better Regulation Science Programme Science report: SC050021. March 2009. Available online: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/291235/scho0309bpqo-e-e.pdf

Scientific Advisory Committee on Nutrition (SACN). SACN Position Statement on Selenium and Health. UK. May 2013. Available online: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/339431/SACN_Selenium_and_Health_2013.pdf

3. EFSA FEEDAP Panel Opinions

Safety and efficacy of the product SelPlex® 2000 as a feed additive according to Regulation (EC) No 1831/2003. Scientific Panel on Additives and Products or Substances used in Animal Feed. Available online: http://www.efsa.europa.eu/en/efsajournal/pub/348

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. Scientific Panel on Additives and Products or Substances used in Animal Feed. Available online: http://www.efsa.europa.eu/en/efsajournal/pub/430

Safety and efficacy of SELSAF (Selenium enriched yeast from *Saccharomyces cerevisiae* CNCM I-3399) as feed additive for all species. Scientific Panel on Additives and Products or Substances used in Animal Feed. http://www.efsa.europa.eu/en/efsajournal/pub/992

Safety and efficacy of selenium in the form of organic compounds produced by the selenium-enriched yeast *Saccharomyces cerevisiae* NCYC R645 (SelenoSource AF 2000) for all species. Scientific Panel on Additives and Products or Substances used in Animal Feed. Available online: http://www.efsa.europa.eu/en/efsajournal/doc/3797.pdf

Safety and efficacy of Sel-Plex® (organic form of selenium produced by *Saccharomyces cerevisiae* CNCM I-3060) for all species. Scientific Panel on Additives and Products or Substances used in Animal Feed. Available online: http://www.efsa.europa.eu/en/efsajournal/doc/2110.pdf

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Selenium-enriched yeast as source for selenium added for nutritional purposes in foods for particular nutritional uses and foods (including food supplements) for the general population. Scientific Opinion of the Panel on Food Additives, Flavourings, Processing Aids and Materials in Contact with Food. Available online: http://www.efsa.europa.eu/en/efsajournal/pub/766

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Scientific Opinion on the substantiation of health claims related to selenium and maintenance of normal hair (ID 281), maintenance of normal nails (ID 281), protection against heavy metals (ID 383), maintenance of normal joints (ID 409), maintenance of normal thyroid function (ID 410, 1292), protection of DNA, proteins and lipids from oxidative damage (ID 410, 1292), and maintenance of the normal function of the immune system (ID 1750) pursuant to Article 13(1) of Regulation (EC) No 1924/2006. EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA). Available online: http://www.efsa.europa.eu/en/efsajournal/doc/1727.pdf

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to Article 13(1) of Regulation (EC) No 1924/2006. EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA). Available online: http://www.efsa.europa.eu/en/efsajournal/doc/2239.pdf

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Scientific Opinion on Dietary Reference Values for selenium. EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA). Available online: http://www.efsa.europa.eu/en/efsajournal/doc/3846.pdf

Scientific Opinion on the substantiation of a health claim related to selenium and protection of DNA, proteins and lipids from oxidative damage pursuant to Article 14 of Regulation (EC) No 1924/2006. EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA). Available online: http://www.efsa.europa.eu/en/efsajournal/doc/3890.pdf

Appendix B. List of authorisations of selenium other than as a feed additive

Sodium selenite is authorised for use in food as a food supplement (Regulation (EC) No 1170/2009)[28] and a substance which may be added to foods as a mineral (Regulation (EC) No 1925/2006).[29] Sodium selenite is also authorised as a substance that may be added for specific nutritional purposes in foods (Commission Regulation (EC) No 953/2009).[30]

Regarding pharmacologically active substances and their classification regarding Maximum Residue Limits (MRLs) in foodstuffs of animal origin, sodium selenite listed in Table 1 of the Annex of Regulation 37/2010[31] as 'Allowed substances, no MRL required'.

Sodium selenite can be used for cosmetic purposes (Regulation (EC) No 1223/2009 of the European Parliament and of the Council).[32]

According to the Annex to Regulation (EC) No 432/2012[33] the following health claims can be made only for food which is at least a source of copper as referred to in the claim SOURCE OF [NAME OF VITAMIN/S] AND/OR [NAME OF MINERAL/S] as listed in the Annex to Regulation (EC) No 1924/2006: 'Selenium contributes to normal spermatogenesis', 'Selenium contributes to the maintenance of normal hair', 'Selenium contributes to the maintenance of normal nails', 'Selenium contributes to the normal function of the immune system', 'Selenium contributes to the normal thyroid function', 'Selenium contributes to the protection of cells from oxidative stress'.

[28] Commission Regulation (EC) No 1170/2009 of 30 November 2009 amending Directive 2002/46/EC of the European Parliament and of Council and Regulation (EC) No 1925/2006 of the European Parliament and of the Council as regards the lists of vitamin and minerals and their forms that can be added to foods, including food supplements. OJ L 314, 1.12.2009, p. 36.

[29] Regulation (EC) No 1925/2006 of the European Parliament and of the Council of 20 December 2006 on the addition of vitamins and minerals and of certain other substances to foods . OJ L 404, 31.12.2006, p. 26

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

[31] Commission Regulation (EU) No 37/2010 of 22 December 2009 on pharmacologically active substances and their classification regarding maximum residue limits in foodstuffs of animal origin. OJ L 15, 20.1.2010, p. 1.

[32] Regulation (EC) No 1223/2009 of the European Parliament and of the Council of 30 November 2009 on cosmetic products. OJ L 342, 22.12.2009, p. 59.

[33] Commission Regulation (EC) No 432/2012 of 16 May 2012 establishing a list of permitted health claims made on foods, other than those referring to the reduction of disease risk and to children's development and health. OJ L 136, 25.05.2012, p. 1.

Appendix C. Specific purity criteria for the coat-granulating agents

Polyoxolethylene (20) sorbitan monolaureate (E 432) meets the purity criteria defined in Commission directive 98/86/EC of 11 November 1998 amending Commission Directive 96/77/EC laying down specific purity criteria on food additives other than colours and sweeteners. Glycerol polyethyleneglycol ricinoleate (E 484) meets the purity criteria specified in the United States Pharmacopeia entry for Polyoxyl 35 castor oil and the European Pharmacopoeia entry for macrogolglyceryl ricinoleate (monograph 01/2005:1082). Polyethylene glycol 300 comprises 100% polyethylene glycol in accordance with European Pharmacopoeia monograph 1444 and JECFA Monograph 316. Sorbitol meets the purity criteria specified for sorbitol liquid in Commission Directive 95/31/EC of 5 July 1995 laying down specific criteria of purity concerning sweeteners for use in foodstuffs. Maltodextrin (food grade) has the specific purity criteria SO_2 maximum 10 mg/kg and heavy metals maximum 0.5 mg/kg.

ANNEX

Annex A. Executive Summary of the Evaluation Report of the European Union Reference Laboratory for Feed Additives on the Method(s) of Analysis for Sodium selenite[34]

In the current applications authorisation is sought under article 10(2) for *sodium selenite* under the category/functional group (3b) 'nutritional additives'/'compounds of trace elements', according to the classification system of Annex I of Regulation (EC) No 1831/2003. Specifically, authorisation is sought for the use of the *feed additive* for all categories and species. According to two of the Applicants (FAD-2010-0104 and FAD-2010-0362) the *feed additive* is a white powder containing at least of 98% of *sodium selenite* (based on anhydrous weight), which corresponds to a minimum content of 45% *selenium* and 13% *sodium*. Applicant FAD-2010-0369 intends to market a film granulated preparation of *sodium selenite* containing a minimum of 1% of *total selenium*. All feed additives are intended to be incorporated into *feedingstuffs* through *premixtures* with a maximum level of 0.5 mg *total selenium*/kg feedingstuffs.

For the characterisation of *sodium selenite* in the *feed additive* containing at least 98% of *sodium selenite* Applicant FAD-2010-0362 submitted the European Pharmacopoeia Monograph 1677, where identification is based on specific reactions involving ascorbic acid, barium chloride and sodium ions; while quantification is based on redox titration with potassium iodide, sodium thiosulfate and iodine solutions.

For the quantification of *total selenium* in the feed additive containing at least 98% of *sodium selenite* Applicant FAD-2010-0104 submitted a single-laboratory validated method based on conversion of sodium selenite to selenium and its further quantification by gravimetry; while Applicant FAD-2010-0369 applied a quantification assay derived from the European Pharmacopoeia method – based on redox titration with potassium iodide and sodium thiosulfate.

Additionally, two alternative single-laboratory validated and further verified methods based on (1) inductively coupled plasma atomic emission spectrometry (ICP-AES) and (2) inductively coupled plasma mass spectrometry (ICP-MS) – submitted in the frame of the dossiers FAD-2009-0010 and FAD-2012-0042 – were previously evaluated and recommended by the EURL – in the frame of other selenium dossiers – for the quantification of *total selenium* in *feed additives*.

Based on the information available, the EURL recommends for official control the titrimetric method described in the European Pharmacopoeia and/or the equivalent gravimetric method submitted by the Applicant for the characterisation of the *feed additive* containing at least 98% of *sodium selenite*; while ICP-MS or ICP-AES methods are recommended to quantify *total selenium* in the film granulated preparation (*feed additive*).

For the quantification of *total sodium* in the *feed additive*, containing at least 98% of *sodium selenite*, the EURL recommends for the official control two internationally recognised ring-trial validated methods: (i) EN ISO 6869:2000, based on Atomic Absorption Spectrometry (AAS) after dissolving in hydrochloric acid; and (ii) EN 15510:2007, based on Inductively Coupled Plasma Atomic Emission Spectrometry (ICP-AES) after dissolving in hydrochloric acid, for which relative precisions ranging 4–27% were reported.

For the quantification of *total selenium* in *premixtures* and *feedingstuffs* two Applicants (FAD-2010-0362 and FAD-2010-0369) suggested several CEN and AOAC methods, while the Applicant FAD-2010-0104 submitted the EN 16159:2012 method based on Hydride Generation Atomic Absorption Spectrometry (HGAAS) after microwave digestion with HNO3/H2O2. This method was already evaluated and recommended by the EURL in the frame of previous selenium dossiers.

[34] The full report is available on the EURL website: https://ec.europa.eu/jrc/sites/default/files/finrep-fad-sodium_selenite_group.pdf

Further testing or validation of the methods to be performed through the consortium of National Reference Laboratories as specified by article 10 (Commission Regulation (EC) No 378/2005) is not considered necessary.