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SCIENTIFIC OPINION

Scientific Opinion on the safety and efficacy of iodine compounds (E2) as feed additives for all animal species: calcium iodate anhydrous, based on a dossier submitted by Calibre Europe SPRL/BVBA[1]

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

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This scientific output, published on 19 May 2014, replaces the earlier version published on 19 February 2013.[4]

ABSTRACT

Calcium iodate anhydrous is considered a safe source of iodine for all animal species/categories when used up to the currently authorised maximum content of total iodine in complete feed, with the exception of horses and dogs, for which maximum tolerated levels are 3 and 4 mg I/kg complete feed, respectively. The limited data available on iodine tolerance in cats support a provisional tolerated level of 5 mg I/kg complete feed. Exposure of consumers was calculated in two scenarios applying the currently authorised maximum iodine contents in feed and reduced contents. The iodine content of food of animal origin, if produced taking account of the currently authorised maximum content of iodine in feed, would represent a substantial risk to high consumers. The risk would originate primarily from the consumption of milk and to a minor extent from eggs. The UL for adults (600 µg/day) and for toddlers (200 µg/day) would be exceeded by a factor of 2 and 4, respectively. If the authorised maximum iodine concentrations in feed for dairy cows and laying hens were reduced to 2 and 3 mg I/kg feed, respectively, the exposure of adult consumers would be below the UL. However, iodine intake in high-consuming toddlers would remain above the UL (1.6-fold). Calcium iodate is considered as irritant to the eye, skin and respiratory tract, and a dermal sensitiser. The exposure by inhalation should be avoided. The use of calcium iodate in animal nutrition is not expected to pose a risk to the environment. Calcium iodate is efficacious to meet animal iodine requirements. The FEEDAP Panel recommends that the maximum iodine contents in complete feed be reduced as follows: dairy cows and minor dairy ruminants, 2 mg I/kg; laying hens, 3 mg I/kg; horses, 3 mg I/kg; dogs, 4 mg I/kg; cats, 5 mg I/kg.

KEY WORDS

nutritional additive, compounds of trace elements, iodine, calcium iodate anhydrous, safety, efficacy

[1] On request from the European Commission, Question No EFSA-Q-2011-00745, adopted on 29 January 2013.

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[4] Revision 1: erratum. The assessment of the tolerance of iodine to cats has been revised. The following sections have been amended accordingly: Abstract, Summary, Sections 3.1.1 and 3.1.2, Conclusions and Recommendations.

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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 safety and efficacy of calcium iodate anhydrous as feed additive for all animal species.

The only known role of iodine in the metabolism is its incorporation into the thyroid hormones, thyroxine and triiodothyronine as well as the precursor iodothyrosines. Both hormones have multiple functions as regulators of cell activity (energy metabolism) and growth and as transmitters of nervous stimuli and play an important role in brain development.

The use of calcium iodate anhydrous and potassium iodide as sources of iodine is considered safe for all animal species/categories when used up to the currently authorised maximum content of total iodine in complete feed, with the exception of horses and dogs, for which maximum tolerated levels are 3 and 4 mg I/kg complete feed, respectively. The limited data available on the iodine tolerance in cats support a provisional tolerated level of 5 mg I/kg complete feed.

The exposure of consumers was calculated in two scenarios applying the currently authorised maximum iodine contents in feed and reduced contents. The iodine content of food of animal origin, if produced taking account of the currently authorised maximum content of iodine in feed, would represent a substantial risk to high consumers. The risk would originate primarily from the consumption of milk and to a minor extent from consumption of eggs. The upper tolerable level (UL) for adults (600 µg/day) would be exceeded by a factor of 2, and that for toddlers (200 µg/day) by a factor of 4. If the authorised maximum iodine concentrations in feed for dairy cows and laying hens were reduced to 2 and 3 mg I/kg feed, respectively, the exposure of adult consumers to iodine from food of animal origin would be below the UL. However, iodine intake in high-consuming toddlers would remain above the UL (1.6-fold).

In the absence of data, calcium iodate is considered as irritant to the eye, skin and respiratory tract, and as a dermal sensitiser. Exposure by inhalation should be avoided.

The use of calcium iodate in animal nutrition is not expected to pose a risk to the environment.

Calcium iodate is an efficacious source of iodine to meet animal requirements.

The FEEDAP Panel recommended that some of the currently authorised maximum iodine contents in complete feed be modified as follows: dairy cows and minor dairy ruminants, 2 mg I/kg; laying hens, 3 mg I/kg; horses, 3 mg I/kg; dogs, 4 mg I/kg; cats, 5 mg I/kg. The Panel made another recommendation concerning the specifications of the additive.

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BACKGROUND

Regulation (EC) No 1831/2003[5] 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 the company Calibre Europe SPRL/BVBA[6] for re-evaluation of authorisation, of the iodine-containing additive *calcium iodate anhydrous*, 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 applicants the technical dossiers in support of this application.[7] 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 8 December 2011.

The additive "Calcium iodate, anhydrous" had been authorised in the EU under the element Iodine-I for all animal species "Without a time limit" (Commission Regulation (EC) No 1459/2005).[8] 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".[9]

The FEEDAP Panel adopted an opinion on the use of iodine in feedingstuffs (EFSA, 2005).

[5] 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.

[6] Calibre Europe SPRL/BVBA. 500 Avenue Louise. 1050-Brussels. Belgium.

[7] EFSA Dossier reference: FAD-2010-0223.

[8] Commission Regulation (EC) No 1459/2005 of 8 September 2005 amending the conditions for authorisation of a number of feed additives belonging to the group of trace elements. OJ L 233, 9.9.2005, p. 8.

[9] European Union Register of Feed Additives pursuant to Regulation (EC) No 1831/2003 available from http://ec.europa.eu/food/food/animalnutrition/feedadditives/comm_register_feed_additives_1831-03.pdf

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 calcium iodate anhydrous, when used under the conditions described in Table 1.

Table 1: Description and conditions of use of the additive as proposed by the applicant Calibre Europe SPRL/BVBA

Additive	Calcium iodate, anhydrous
Registration number/EC No/No (if appropriate)	E 2
Category(-ies) of additive	Nutritional additives
Functional group(s) of additive	Compounds of trace elements

Description			
Composition, description	Chemical formula	Purity criteria (if appropriate)	Method of analysis (if appropriate)
Calcium iodate, Anhydrous	$Ca(IO_3)_2$		

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		
- Equine - Dairy cows and laying hens - Fish - Other species or categories			4 mg/kg 5 mg/kg 20 mg/kg 10 mg/kg	

Other provisions and additional requirements for the labelling	
Specific conditions or restrictions for use (if appropriate)	
Specific conditions or restrictions for handling (if appropriate)	
Post-market monitoring (if appropriate)	
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

The FEEDAP Panel considers in the current opinion the highest dietary iodine levels tolerated by target animals in order to derive a safe maximum content of iodine in feed. It considers further the consequences of feeding iodine, at safe levels to the target animals, on consumer exposure to iodine resulting from the consumption of food of animal origin. The Panel examines if, and in which cases, the maximum content of iodine in feed should be further reduced to minimise the risk to consumers. The Panel does not consider the use of iodine in animal nutrition as a tool to potentially increase the supply of iodine to that part of the population which might have a deficient or marginal intake.

This opinion is based in part on data provided by an applicant involved in the production/ distribution of iodine-containing compounds. It should be recognised that these data covers only a fraction of the existing calcium iodate anhydrous.

1. Introduction

Iodine occurs in nature as iodide and iodate. Its mineral forms occur ubiquitously in igneous rocks and soils, most commonly as impurities in saltpetre and natural brines. Iodine is an essential trace element for animals and humans. The only known role of iodine in metabolism is its incorporation into the thyroid hormones, thyroxine (T_4; 3,5,3′,5′-tetraiodothyronine) and triiodothyronine (T_3; 3,5,3′-triiodothyronine) as well as the precursor iodothyrosines. Both hormones have multiple functions as regulators of cell activity (energy metabolism) and growth and as transmitters of nervous stimuli and play an important role in brain development.

The application under assessment is for the use of calcium iodate anhydrous in feed for all animal species, which use is already authorised in the EU as a nutritional additive.

A compilation of risk assessments carried out on iodine, including opinions from EFSA's Panels other than the FEEDAP Panel, can be found in Appendix B. A list of authorisations of iodine in the EU, other than as feed additive, is reported in Appendix C.

EFSA commissioned the University of Gent (Belgium) to carry out a study by of selected trace and ultratrace elements, and a technical report was subsequently submitted to EFSA (Van Paemel et al., 2010); iodine was included in this study. Information from this report has been used in the development of this opinion.

2. Identity and characterisation

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

2.1. Identity of the additive

Calcium iodate (IUPAC name calcium diiodate; other name lautarite) is identified by the CAS number 7789-80-2, and the EINECS number 232-191-3. It has a molecular weight of 389.88 g/mol and its molecular formula is $Ca(IO_3)_2$. The theoretical content of iodine and calcium is 65.1 and 10.5 %, respectively. The molecular structure is shown in Figure 1.

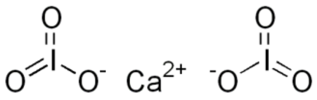

Figure 1. Molecular structure of calcium iodate anhydrous

According to the specification, the minimum calcium iodate, iodine and calcium contents are 97.5, 63.5 and 9.7 %, respectively. Analysis of five batches showed a mean calcium iodate content of 98.1 % (range: 97.7–98.5 %), iodine 63.9 % (range: 63.6–64.2 %)[10] and calcium 9.8 % (range: 9.7–9.8 %).[11]

2.1.1. Impurities

Analytical data of heavy metals and arsenic in five batches raise no concerns (Pb< 4, Cd< 2, Hg< 0.1 mg/kg and As< 3 mg/kg).[12] Levels of dioxins (≤ 0.05 ng WHO PCDD/F-TEQ/kg) and the sum of dioxins plus dioxin-like PCBs (≤ 0.1 ng WHO PCDD/F-PCB-TEQ/kg) measured in four batches[13] are compliant with EU legislation. Control methods are in place.

2.2. Physical state of the product

The additive is a white to off-white odourless crystalline powder. Its melting point is 540 ºC, the pH in water solution is between 6 and 7 and the solubility in water approximately 4 g/L at 30 ºC. Bulk density is 1.6 g/cm^3.

Particle size distribution, measured by sieving in three batches, showed that 52 % (w/w) of particles (range 47–55 %) have a diameter < 63µm, and 89 % (range 88–90 %) < 90 µm.[14] The dusting potential, measured by the Stauber-Heubach method in three batches, was 6.1 g/m^3 (range: 2.5–9.4 g/m^3).[15]

2.3. Manufacturing process

The manufacturing process of the additive is fully described in the technical dossier. Material safety data sheets (MSDS) of the additive and of the raw materials used in the manufacturing process are enclosed in the dossier.

2.4. Stability and homogeneity

Stability data are not required for inorganic compounds of trace elements. The applicant submitted stability data for one batch stored for three years and four months in polyethylene bags at ambient temperature. Iodine was fully recovered at the end of the test period and no change in the physical properties of the additive was observed.[16]

To test the capacity of the additive to homogenously distribute in premixtures, one batch of calcium iodate anhydrous was mixed with calcium carbonate. The analysis of ten subsamples showed a coefficient of variation of 4 %.[17] No further data on the distribution of the additive in other premixtures or feeds were submitted.

[10] Technical Dossier/Section II/Annex_II_1.
[11] Technical Dossier/Supplementary Information.
[12] Technical Dossier/Section II/Annex_II_1.
[13] Technical Dossier/Section II/Annex_II_1 and Technical Dossier/Supplementary Information.
[14] Technical Dossier/Supplementary Information.
[15] Technical Dossier/Supplementary Information.
[16] Technical Dossier/Section II/Annex_II_13.
[17] Technical Dossier/Supplementary Information.

2.5. Physico-chemical incompatibilities in feed

Based on current knowledge, no incompatibilities resulting from the use of calcium iodate anhydrous in compound feed are expected.

2.6. Conditions of use

Calcium iodate anhydrous is intended to be used as a source of the trace element iodine for all animal species and categories up to maximum total content of 10 mg I/kg complete feed, except for the following: dairy cows and laying hens, 5 mg I/kg complete feed; equines, 4 mg I/kg complete feed; and fish, 20 mg I/kg complete feed.

2.7. 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 calcium iodate anhydrous in animal feed. The Executive Summary of the EURL report can be found in the Appendix A.

3. Safety

3.1. Safety for the target species

3.1.1. Iodine tolerance in animals

Scientific committees (e.g. the National Research Council (NRC) in the USA and the Society of Nutrition Physiology (GfE) in Germany) have established iodine requirements for food producing animals of between 0.16 (pigs) and 0.60 mg/kg DM (breeding sows) (see also Flachowsky, 2007). From a study of Wedekind et al. (2010) the requirement of cats can be derived as 0.46 mg I/kg DM diet. For growing and adult dogs, the NRC (2006) considered data from 1970 and 1975 and concluded that the requirement would be 0.175 mg I/1000 kcal ME; taking into account variation in energy intake and goitrogenic substances, an allowance of 125 % of the requirement is recommended.

The upper tolerated levels of dietary iodine as previously published by the FEEDAP Panel (EFSA, 2005) are 5 mg/kg feed for laying hens, 3 mg/kg feed for horses and 4 mg/kg feed for dogs. No upper tolerance limits have been established for farmed fish; however, no effects have been observed at levels as high as 60 mg/kg feed. The iodine tolerance of pigs and fish is far above the EU regulations. The upper safe level for dairy cows, calves, chickens for fattening, turkeys, sheep, goat, rabbits and cats could not be determined at that time by the FEEDAP Panel.

Since the first EFSA opinion on iodine (EFSA, 2005) only a few papers dealing with effects of iodine feed levels close to or at maximum authorised EU levels on animals have been published. Schöne et al. (2009) did not observe any adverse effect of a diet containing 10.1 mg I/kg DM as calcium iodate-hexahydrate when fed to lactating Holstein cows (11 months after calving, mean body weight 674 kg and average milk yield 22.1 kg/day) for only two weeks.

In a study carried out in cattle for fattening, in which iodine from calcium iodate at a level of 8.3 mg/kg feed DM and given until slaughter, zootechnical performance was not significantly different in supplemented animals (11 or 12 animals per treatment) and animals given unsupplemented feed (weight gain 1453, 1419 and 1343 g per day for 0.8, 3.5 and 8.3 mg I/kg DM, respectively). The weight of the thyroid gland increased significantly with the highest iodine dosage (32, 26 and 42 g per animal for 0.8, 3.5 and 8.3 mg I/kg DM, respectively) (Meyer et al., 2008). This increased thyroid weight, together with the lower weight gain, albeit non significant, supports the conclusion that the upper iodine level for cattle for fattening is near to the highest dose tested.

In a study in pigs (initial body weight 27 kg, final 115 kg) fed diets supplemented with iodine from calcium iodate anhydrous at 0, 0.5, 1.0, 2.0 and 5.0 mg/kg, no effects of iodine dose on zootechnical endpoints were observed (Franke et al., 2008). Supplementation with 5 mg I/kg significantly increased the weight of the thyroid gland (by 57 %) compared with the unsupplemented control group (background 0.17 mg I/kg). Thyroid, offal and muscle showed a dose-dependent increase in iodine content, with levels in the group receiving the highest dietary iodine dose being significantly different to those of the control group. In another study, supplementation of a grower finisher diet for pigs with 8 mg I/kg feed resulted in a similar increase in the weight of the thyroid gland (Berk et al., 2008).

In another study in pigs (initial body weight 33 kg, final weight 115 kg), Li et al. (2012) compared different supplementation levels (4 and 10 mg I/kg feed) from two iodine sources (potassium iodide or potassium iodate) with a control feed (0.15 mg I/kg). There was a significant negative effect of increasing levels of dietary iodine on growth rate during the grower phase (33–70 kg bw) which could not be seen in the finisher period (70–115 kg bw). Cumulative gain over the entire period was lower in the groups receiving potassium iodate ($P < 0.05$). The iodine concentrations in the thyroid, liver, kidney, muscle and skin increased dose dependently. However, this increase was different in the individual tissues, muscle iodine showing no response at 4 mg I/kg feed. Neither the plasma thyroid hormone levels (T_3, T_4) nor the T_3/T_4 ratio were affected.

A study in chickens for fattening comparing various levels of iodine supplementation (0, 1.0, 2.5 and 5.0 mg I/kg feed) from two sources (potassium iodide and calcium iodate), did not show any adverse effect of iodine supplementation on performance and thyroid weight (Röttger et al., 2011). The data revealed a dose-dependent increase in iodine concentration in muscle, liver and thyroid gland.

In two dose-effect experiments conducted in laying hens, KI or $Ca(IO_3)_2$ was added in different quantities to feed (0, 0.25, 0.5, 2.5 and 5 mg/kg complete feed; measured data: 0.44, 0.75, 1.98, 2.44 and 4.01 mg I/kg). After four weeks of experimental feeding no effects on laying performance or the composition of the eggs (other than iodine concentration) were registered in the first study with 60 hens (Röttger et al., 2012). The second study was carried out as a long term experiment (164 days). Hens of two breeds (Lohmann Selected Light (white feathers) and Lohmann Brown (brown feathers); 432 hens each) were fed with or without 10 % rapeseed cake as source of an iodine antagonist (glucosinolate content: 13.8 µmol/g) in the feed. The laying performance of hens was not significantly influenced by iodine supplementation. Rapeseed cake significantly reduced feed intake and daily egg mass production, but did not influence feed to egg mass ratio. Only in diets containing 10 % rapeseed cake, which by itself increased thyroid weight, did iodine supplementation of 2.5 and 5 mg/kg feed result in a significant increase in thyroid gland weight (Röttger, 2012).

Forty-two healthy euthyroid castrated cats (14 males and 28 females; 1.6–13.6 years old) were fed a dry diet (0.23 mg I /kg) for a minimum of one month (pre-test), then switched to the experimental diets supplemented with seven levels of potassium iodide for one year (experimental period) (Wedekind et al., 2010). The analysed iodine concentrations in the 1-year study were 0.15, 0.2, 0.5, 1.1, 3.1, 8.2 and 9.2 mg/kg DM diet. Response variables included iodine concentrations in serum, urine and faeces, urinary iodine:creatinine ratio, iodine balance, technetium-99m ($^{99}Tc^{m}$) pertechnetate thyroid:salivary ratio, complete blood count and serum chemistry parameters as well as serum thyroid hormone profiles. No significant changes in food intake, body weight or clinical signs were noted. Serum iodine, daily urinary iodine, daily faecal iodine and urinary iodine:creatinine ratio were linear functions of iodine intake. The authors considered 9.2 mg I/kg feed DM as the lowest observed adverse effect level (LOAEL) of the study indicated by a significant reduction of free plasma thyroxine at week 48 and a tendency for reduced total T_3 and T_4. No comparable findings were identified at the next lower dose (8.2 mg I/kg DM). Hence, it appeared that 8.2 mg I/kg DM was tolerated by the cats. However, statistical analysis of the iodine concentration in food DM during the course of the study showed that 8.2 mg I/kg was not significantly different from 9.2 mg I/kg, the highest concentration tested. Accounting for the apparent steep response curve above 8.2 mg I/kg (see Figure 2) and the diversity of cat breeds, the FEEDAP Panel considers that the maximum safe level of iodine to cats is less than 8.2 mg I/kg DM. On the other hand, the concentration considered safe was 3.1 mg I/kg DM; it cannot be ruled out that concentrations higher than 3.1 are also safe. A proposal for a maximum safe content could take into consideration the safe level (3.1 mg I/kg DM) and the newly identified LOAEL of 8.2 mg I/kg DM, along with the relatively high iodine content of feed materials used for cat food. The Panel proposes a provisional maximum iodine content of 5 mg/kg complete feed (88 % DM).

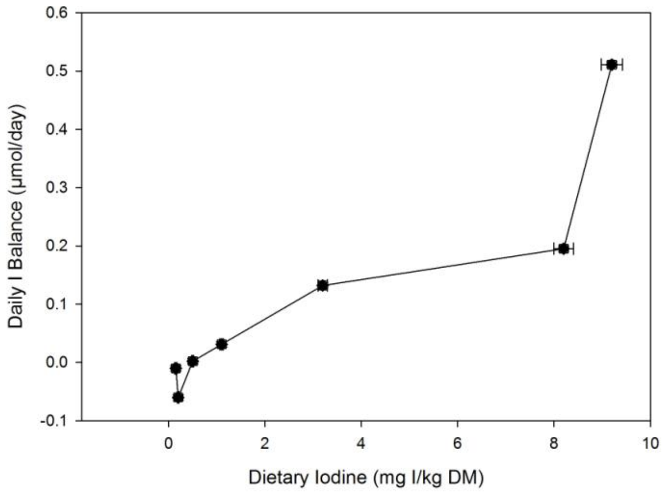

Figure 2: Iodine balance in cats fed diets containing different concentrations of iodine. Horizontal error bars show the standard deviation of iodine concentration in cat food. (Data extracted from a 1-year experiment described in Wedekind et al., 2010)

3.1.2. Conclusions on the safety for target species

In the absence of new data, the FEEDAP Panel reiterates the maximum iodine levels in complete feed considered safe for target animals in 2005: higher than 60 mg/kg feed for farmed fish, 3 mg/kg feed for horses and 4 mg/kg feed for dogs.

Newer findings in chickens for fattening identified the highest dietary concentration tested (5 mg/kg) as safe for these target animals. The FEEDAP Panel does not expect that the currently authorised maximum level for chickens for fattening (10 mg/kg complete feed) poses concerns for the safety of these target animals. The upper safe level concluded in 2005 for laying hens (5 mg I/kg feed) was based on egg quality criteria. More recent findings applying increased thyroid weight as an endpoint do not essentially modify the former conclusion. This upper safe limit complies with current EU legislation.

In two studies in pigs for fattening no significant effects on the weight of the thyroid gland were observed at levels up to 8 mg I/kg feed. This observation is considered consistent with the currently established EU regulation for the maximum content of iodine in feed (10 mg I/kg) which is likely coincident with the upper tolerated level.

The available studies with dairy cows did not raise any concern over the safety of the currently established maximum content in feed. However, recent experimental data obtained in cattle for fattening also indicate that the currently established maximum iodine content in feed (10 mg/kg) coincides with the upper tolerated level.

The iodine tolerance of fish is above the current EU regulation (maximum content 20 mg I/kg complete feed for fish).

The limited published data on the iodine tolerance in cats support a provisional tolerated level of 5 mg I/kg complete feed.

The FEEDAP Panel emphasises that the above estimates of the upper safe level, with the exception of that for fish, do not include a margin of safety.

Finally, the FEEDAP Panel concludes that the use of calcium iodate anhydrous as source of iodine in animal nutrition is safe for all animal species/categories provided the above estimates of the upper tolerated levels of iodine in complete feed are respected.

3.2. Safety for the consumer

Iodine metabolism in food-producing animals is well-known and has been summarised by EFSA (2005). Owing to its physiological function the thyroid gland is the tissue with the highest iodine concentration, containing 60–90 % of the body pool of the element.

3.2.1. Iodine deposition studies in food-producing animals

No specific studies were provided by the applicant. The FEEDAP Panel published a comprehensive review on tissue deposition of iodine (EFSA, 2005). In the current opinion only studies published after that opinion are reviewed. The FEEDAP Panel considers that, based on the available data, no meaningful differences in bioavailability are expected among calcium iodate, potassium iodide or other inorganic iodine compounds. For consumer safety assessment, the available studies on iodine deposition in edible tissues and products after supplementation of feed with inorganic iodine compounds were considered together.

3.2.1.1. Ruminants

Dairy ruminants

Average values from bulk sample analysis of various European studies were between 100 and 200 µg I/L milk (EFSA, 2005). These values are generally confirmed by recent studies; for details see Tables D1 and D2 in Appendix D.

Values between 100 and 240 µg I/L milk (Haug et al. 2012) are also given in various Food Tables of North European countries (Norway: 190; Denmark: 243; Sweden: 140; Finland: 170; Iceland: 112 µg I/L). Much lower values (20 to 60 µg I/L cow milk) are given in the “Food Composition and Nutrition Tables” of Souci et al. (2008). Only data from the Czech Republic (Kursa et al., 2004; Travnicek et al., 2006a) are higher (mean values 324 and 489 µg I/L milk, respectively), likely due to a specific feed supplementation program.

The data in Appendix D indicate that (i) milk produced by organic farming shows consistently lower iodine concentrations than milk from conventional farms and (ii) milk collected during the summer (outdoor feeding) shows lower iodine concentrations than winter samples (indoor feeding). Differences in feeding practices in summer and winter may contribute to the differences in iodine concentration in milk in summer and winter. Previous findings indicate that ambient temperatures also influences the iodine concentration in milk (which increases with increasing environmental temperature: Lengemann, 1979; Lengemann and Wentworth, 1979). The use of iodine as a disinfectant (udder hygiene, teat dipping, disinfection of the milking machine and other equipment) may also influence iodine content in milk (reviewed in EFSA, 2005; Flachowsky et al., 2007; Borucki Castro et al., 2012; see also Table D3 in Appendix D).

In its previous opinion (EFSA, 2005), the FEEDAP Panel also calculated the expected iodine concentrations in milk from feed intake using regression formulas taken from publications by Binnerts (1958) and Alderman and Stranks (1967). These results are not in accordance with more recent findings, likely because of the development of new analytical techniques (e.g. ICP-MS). In a study with 32 dairy cows, Franke et al. (2009) taking into consideration various influencing factors (e.g. two iodine sources, six iodine dosages, rape seed meal as source of glucosinolates), derived the following linear regression equations (x= mg I/kg feed dry matter, y= µg I/kg milk):

y= 342.2x – 73.1 (R^2= 0.98): Low glucosinolate diet (without rapeseed meal, calcium iodate)
y= 298.3x – 64.0 (R^2= 0.97): Low glucosinolate diet (without rapeseed meal, potassium iodide)
y= 112.0x – 24.3 (R^2= 0.96): High glucosinolate diet (with rapeseed meal, calcium iodate)
y= 136.5x – 67.1 (R^2= 0.94): High glucosinolate diet (with rapeseed meal, potassium iodide)

Table 2 summarises the expected iodine concentrations in milk based on the above equations.

Table 2: Milk iodine concentrations (µg/kg) at various feed concentrations of iodine considering different glucosinolate contents in complete feed of dairy cows (calculations based on regression equations by Franke, 2009 and Franke et al., 2009)

Diet type	**Iodine (mg/kg feed DM)**					
	0.5	**1**	**2**	**3**	**4**	**5**
No glucosinolates	90	250	560	880	1200	1500
High glucosinolates[1]	20	80	200	330	450	580

[1] 0.58 mmol glucosinolates/kg DM or 11.0-13.7 mmol glucosinolates/cow and day from rape seed

The data in Table 2 also indicate that feed manufacturers do not make use of the high iodine feed supplementation as permitted by EU legislation, as already concluded by the FEEDAP Panel in the previous iodine opinion (EFSA, 2005). Considering the values observed in bulk milk, the mean supplementation is not likely to exceed 2 mg iodine per kg DM. This conclusion is confirmed by a similar consideration based on German feed samples (Grünewald et al., 2006).

Cattle for fattening

The iodine content of beef muscles in the "Food Composition and Nutrition Tables" (Souci et al., 2008) was reported to be 20−70 µg/kg fresh weight, the value in liver being 140 µg/kg.

The effect of iodine supplementation on the iodine content of beef was investigated in a dose-response experiment with 34 growing/fattening German Holstein bulls with body weight ranging between 223 and 550 kg (Meyer et al., 2008). The animals were fed a maize silage/concentrate (free of glucosinolate) ration containing one of three iodine doses (0.79, 3.52 or 8.31 mg iodine per kg DM). After slaughtering, the iodine content of liver, kidney, meat (*M. longissimus dorsi*, *M. glutaeus medius*) and thyroid gland was determined by ICP-MS. Iodine concentration in muscle, liver and kidney (Table 3) showed a statistically significant dose-related increase. However, when considering absolute values for meat, the data confirmed the previous assessment by the FEEDAP Panel (EFSA, 2005) that meat is not a major source of dietary iodine for the consumer.

Table 3: Iodine concentration (µg/kg fresh weight) of meat (beef) and liver at various feed concentrations of iodine in complete feed of growing/fattening bulls (calculations based on data of Meyer et al., 2008)

Food of animal origin	**Iodine (mg/kg feed DM)**		
	0.5	**4**	**10**
Meat (beef)	25	65	115
Liver	75	150	250
Kidney	95	230	450

3.2.1.2. Pigs

The iodine content of pork meat in the "Food Composition and Nutrition Tables" (Souci et al., 2008) was reported to be with 30−50 µg I/kg fresh matter, and of liver 140 µg I/kg fresh matter. Pork muscle from iodine-unsupplemented pigs is reported to contain about 28 µg I/kg fresh matter (Kaufmann and Rambeck, 1998; He et al., 2002).

Herzig et al. (2005) investigated the iodine concentration in pork meat collected from 18 herds in 10 districts of the Czech Republic during 2004, and found it to range from 5 to 66 µg I/kg, with an average of 26 µg I/kg.

Schöne et al. (2006), Berk et al. (2008) and Franke et al. (2008) found a close correlation between iodine supplementation and thyroid iodine stores, iodine concentration in blood serum, liver and meat (see also Table 4). It should be noted that the absolute values for iodine concentrations in meat are lower by one dimension than those in liver, independent of the level of dietary iodine.

Table 4: Iodine concentration (µg/kg fresh weight) of meat and liver at various feed concentrations of iodine in complete feed of growing/fattening pigs (calculations based on data of Berk et al., 2008 and Franke et al., 2008)

Food of animal origin	Iodine (mg/kg feed DM)				
	0.5	1	2	5	8
Meat	5	10	15	20	30
Liver	60	140	200	250	300

3.2.1.3. Poultry

Chickens for fattening

The "Food Composition and Nutrition Tables" of Souci et al. (2008) do not contain data on the iodine concentration in meat and liver of poultry.

Two experiments were performed in chickens for fattening, using calcium iodate or potassium iodide (Röttger et al., 2011). In each experiment, 288 one-day-old broiler chickens were divided into four groups (72 birds/group) and fed diets supplementated with 0–5 mg I/kg feed. Six birds per group were slaughtered at 35 days: samples of blood, thyroid gland, liver, pectoral and thigh meat were taken. Results are summarised in Table 5.

Table 5: Iodine concentration (µg/kg fresh weight) of meat and liver at various feed concentrations of iodine in complete feed of growing/fattening broilers (calculations based on data of Röttger et al., 2011)

Food of animal origin	Iodine (mg/kg feed DM)			
	0.5	1	2.5	5
Meat	5	10	40	60
Liver	20	40	100	180

Since the highest iodine concentration was 5 mg/kg, the study does not allow extrapolations to iodine concentrations in edible tissues at the maximum EU authorised iodine concentrations in feed of 10 mg/kg.

Laying hens

The iodine content of eggs in the "Food Composition and Nutrition Tables" (Souci et al. 2008) was reported to be with 85–100 µg/kg fresh weight.

Travnicek et al. (2006b) found a higher iodine content in eggs from large flocks (31.2 µg/egg; corresponding to 500 µg/kg fresh weight) than in eggs from small flocks (10 µg/egg; corresponding to

160 µg/kg fresh weight). The authors suggest that the differences may be caused by higher iodine supplementation in commercial compound feed used in large farms.

Röttger et al. (2012) fed diets (for details see Section 3.1.1) with iodine contents of between 0.44 and 4.01 mg/kg from potassium iodide or calcium iodate to hens (six per group) for four weeks. At the end of the experiment, the hens were slaughtered and samples were taken from various organs and tissues. Eggs were collected during the fourth week. The iodine concentration increased in all tissue samples, but the highest increase was found in eggs (from 144 to 1304 µg I/kg fresh weight). Comparative regression analyses showed that, at a similar iodine intake, iodine supplementation in the form of KI resulted in significantly higher iodine deposition in eggs than supplementation from $Ca(IO_3)_2$.

Röttger (2012) performed a long-term experiment (164 days) in laying hens (for details see Section 3.1.1) with four variables: two iodine sources (KI and $Ca(IO_3)_2$), five iodine concentrations in feed (unsupplemented, 0.25, 0.5, 2.5 and 5 mg/kg mixed feed), with and without glucosinolate-containing feed (10 % rape seed cake in mixed feed), and two breeds. All the analysed factors had a certain influence on the iodine content of the eggs, which cannot be described in detail here. Table 6 summarises the influence of the iodine concentration of feed and rape seed cake as glucosinolate source on the iodine content of eggs. Insignificant differences were measured between iodine sources: Lohmann Brown hens laid eggs with significantly higher iodine content than eggs from Lohmann Selected Light.

Table 6: Iodine concentration (µg/kg fresh weight)[1] of eggs produced by laying hens receiving various feed concentrations of iodine and considering different glucosinolate contents in complete feed (calculations based on data of Röttger, 2012 and Röttger et al., 2012)

Diet type	Iodine (mg/kg feed DM)			
	0.5	1	2.5	5
No glucosinolates	300	500	900	1 500
With glucosinolates[2]	200	350	600	1 100

[1] Average from KI and $Ca(IO_3)_2$ supplementation and two hen breeds (see Röttger, 2012)
[2] 1.4 mmol/kg complete feed

3.2.1.4. Fish

No data were available on the relation between dietary iodine and iodine deposition in flesh in farmed salmonids and other fish. Data from "Food Composition and Nutrition Tables" (Souci et al. 2008) are listed in Table D4 of Appendix D.

3.2.1.5. Conclusion on iodine deposition studies in food producing animals

The content of iodine in animal tissues and products is related to the iodine intake and, thus, to the iodine concentration in the feed. In response to feed supplementation with iodine sources, the iodine level in edible tissues/products is generally found to be highest in milk and eggs, followed by kidney and liver, whereas in muscle tissue it is rather low. Dietary factors (e.g. glucosinolates), animal management practices (e.g. teat disinfection) and environmental conditions (temperature) may also influence the iodine deposition.

3.2.2. Toxicological studies

Excess iodine primarily causes hyperthyroidism and may trigger autoimmune thyroiditis especially in previously iodine-deficient populations and may eventually lead to goitre and hypothyroidism, especially in fetuses and people already suffering from thyroid problems (EC, 2002). Secondary effects include changes in the levels and metabolism of steroid hormones and amenorrhea.

Iodine compounds have generally produced negative results in mutagenicity assays. Results of epidemiological studies, in which the relationship between iodine intake and the incidence of thyroid cancer was investigated, suggest that high iodine intake may be a risk factor particularly in populations with previous iodine deficiency; this effect is related to tumour promotion resulting from chronic hormone imbalance in the gland tissue, whereas the available evidence does not indicate a direct carcinogenic effect of iodine.

The Scientific Committee on Food (SCF) established an upper intake level (UL) of 600 µg I/day for adults on the basis of the biochemical changes in thyroid-stimulating hormone (TSH) levels and the TSH response to thyrotropin-releasing hormone (TRH) administration, and applying an uncertainty factor of 3 (EC, 2002). This UL was also considered to be acceptable for pregnant and lactating women based on evidence of a lack of adverse effects at exposures significantly in excess of this level. Since there is no evidence of increased susceptibility in children, the ULs for children were derived by the SCF (EC, 2002) adjustment of the adult UL on the basis of body surface area (body weight$^{0.75}$), i.e. 200 µg I/day for toddlers.

3.2.3. Assessment of consumer safety

The FEEDAP Panel considers that the new studies on iodine in edible tissues and products do not modify substantially the deposition values used by EFSA (2005). However, the FEEDAP Panel considers that the consumers exposure assessment should be performed using the EFSA comprehensive food consumption database as well as the approach laid down in the FEEDAP guidance on consumer (EFSA, 2012).

Based on the assumptions of the FEEDAP Panel's opinion on iodine in feed, up to 180 µg iodine/day may be provided by a consumption of 9 g iodised salt in adults (EFSA, 2005); the balance is given by food of animal origin, which represent the major iodine source for the general population. However, the contribution of supplements or special functional foods (seaweed) can be important in some groups, but it is currently difficult to assess.

The EFSA comprehensive food consumption database provides conservative figures for the intake of the main relevant food items (95th percentile, consumers only); in adults: meat 290 g/day, egg 70 g/day, milk 1.5 L/day, and in toddlers: meat 90 g/day, egg 35 g/day, milk 1.05 L/day.

According to the FEEDAP Panel's guidance on consumer safety, the two food sources resulting in the highest iodine consumption figures should be used for estimating consumer exposure based on 95th percentile/consumers only figures. Food processing should be considered before estimating consumer exposure. Several publications indicate that milk pasteurization results in an approximate reduction in the iodine concentration of at least 27% (Wheeler et al., 1983; Aumont et al., 1987; Pedriali et al., 1997; Norouzian, 2011).

A further assumption is made regarding iodine concentration in milk, considering that about 50 % of dairy cows receive diets containing rapeseed derived feed materials and taking into account the larger collection areas of dairy industries (Johner et al., 2012a). The FEEDAP Panel uses as iodine concentration in milk the average of the values calculated for low and high glucosinolate diets (Table 2). This assumption is further supported by the values observed in bulk milk throughout Europe (except in the Czech Republic) which are in the 60–250 µg/L range (see Tables D1 and D2), depending on feed, season and type of farming. According to Table 2, the outcome of the calculation at 2 mg total iodine in DM for dairy cows would be 380 µg I/L milk, indicating that the FEEDAP model is conservative. With a similar reasoning the values obtained in eggs from hens fed diets with or without glucosinolates can be averaged.

The following values are used for exposure scenarios: at 2 and 5 mg I/kg DM feed for dairy cow: 280 and 760 µg I/L milk (also considering a loss by pasteurisation), respectively; at 10 mg I/kg DM feed for cattle for fattening: 100 µg I/kg beef meat (pork meat is lower); at 3 and 5 mg I/kg feed for laying hens: 825 and 1300 µg I/kg egg.

The calculations identified that in both population groups, adults and toddlers, milk is by far the main source of iodine exposure, this being in agreement with consumption surveys (Gireli et al., 2004; Bader et al., 2005; Hampel et al., 2009; Johner et al., 2011, 2012a,b; Soriguer et al., 2011). In both groups of consumers, egg is the second largest iodine source of animal origin.

Based on the currently authorised maximum contents of total iodine in complete feed, the exposure of 95th percentile adult consumers from milk and eggs would be 1230 µg/day, which exceeds by more than twice the UL; reducing the maximum iodine concentrations for dairy cows from 5 to 2 mg/kg feed and for laying hens from 5 to 3 mg/kg feed would reduce the exposure of 95th percentile consumers to 480 µg/day. If adding 180 µg I/day from 9 g iodised salt per person and day, the maximum iodine intake would amount to 660 µg I/day.

In the case of toddlers, the analogous exposure of 95th percentile consumers from milk and eggs would result in an intake of 840 µg/day at the currently authorised maximum contents of total iodine in complete feed for cows and laying hens. This amount exceeds by more than four times the UL. Reducing the maximum iodine concentrations for dairy cows from 5 to 2 mg/kg feed and for laying hens from 5 to 3 mg/kg feed would reduce the exposure of 95th percentile consumers to 320 µg/day. For details on consumer exposure calculations, see Appendix E.

The FEEDAP Panel reiterates its above statement that the exposure data are based on a conservative consumption model that includes high consumers only and which assume that all feed compounders use the maximum authorised iodine content in complete feed. Except in areas adopting specific programmes of feed supplementation, such as the Czech Republic (reported iodine concentrations in milk of about 500 µg I/L milk: Travnicek et al., 2011), practical supplementation levels in dairy ruminants would probably not exceed 2 mg iodine per kg DM, depending also on the goitrogen content of feed materials. This conclusion is confirmed by similar considerations based on German feed samples (Grünewald et al., 2006). A consideration of the values observed in bulk milk throughout Europe (60–250 µg/L milk; see Tables D1 and D2) and the model developed by Franke et al. (2009) indicates (see also Table 2) that maximum supplementation levels in practice would be 1 mg/kg (low-glucosinolate feed) and somewhat higher than 2 mg/kg (high-glucosinolate feed).

The FEEDAP Panel also notes that iodine-deficient populations are recognised as more susceptible to iodine excess (EC, 2002) and that there are indications of persisting subclinical iodine deficiency in Europe, particularly among some sub-groups such as pregnant women, children and consumers of organic products (Bath et al., 2011; Vanderpump et al., 2011; Zimmermann and Andersson, 2011; Andersson et al., 2012; Raverot et al., 2012).

Recent biomonitoring studies in humans, based on urinary iodine as an established biomarker, do not indicate that the EU population is generally exposed to excess levels of iodine (Gireli et al., 2004; Remer et al., 2006; Remer, 2007; Thamm et al., 2007; Mazzarella et al., 2009; Andersson et al., 2010; Hampel et al., 2010; Hilty and Zimmermann, 2011; Raverot et al., 2012).

3.2.4. Conclusions on consumer safety

The iodine content of food of animal origin, if produced from animals receiving the currently authorised maximum contents of total iodine in complete feed for dairy cows and laying hens (5 mg/kg), would represent a substantial risk to consumers, mainly for high-consuming (95th percentile) adults and toddlers. The risk would originate primarily from the consumption of milk and, to some extent, from consumption of eggs. The ULs would for adults be exceeded by a factor of 2 (1230 *vs.* 600 µg I/day), and for toddlers by a factor of 4 (840 *vs.* 200 µg I/day).

Exposure of adult consumers to iodine from foods of animal origin would be below the UL (480 *vs.* 600 µg I/day) if the maximum iodine concentrations in feed for dairy cows and laying hens are reduced to 2 and 3 mg I/kg feed, respectively. However, iodine intake would remain above the UL (1.6-fold) for high-consuming toddlers (320 *vs.* 200 µg I/day).[18]

3.3. Safety for the users/workers

No specific studies on irritation, sensitisation or inhalation toxicity were provided by the applicant. In the absence of any information, it would be prudent to consider calcium iodate anhydrous as irritant to eyes, skin and the respiratory tract, and as a dermal sensitiser.

Calcium iodate anhydrous has a high dusting potential (2.5–9.4 g/m^3). Although the potential for inhalation exposure is high, data on inhalation toxicity were not available; consequently the additive should be considered as hazardous by inhalation.

3.4. Safety for the environment

Iodine is a naturally occurring element. Its content in soil depends on geological origin. The lowest iodine concentrations are found in granites, and the highest in boulder clay (Anke et al., 1993). The iodine content ranges from 6 to 10 mg/kg in soils derived from igneous rocks, from 2.2 to 4.5 mg/kg in soils derived from sedimentary rocks and is approximately 5 mg/kg in soils from all types of metamorphic rocks. In soils from Germany, the iodine content was 2.4 mg/kg in a loam soil, 3.2 mg/kg in a sandy loam soil, 3.6 mg/kg in a loamy sand soil and 1.8 mg/kg in sand. In Ireland, peaty soil contained 32 mg iodine/kg, whereas soil derived from limestone and red sandstone contained 3.5 and 2.4 mg iodine/kg, respectively (Anonymous, 1956). The iodine concentration in 42 soils in County Wexford (Ireland) ranged from 3 to 30 mg/kg. Loam and clay loam soils had consistently higher values than loamy sand and sandy loam soils. The average iodine concentration in soil increased in the order: loamy sand (3.73 mg/kg) < sandy loam (4.74 mg/kg) < sandy clay loam (6.26 mg/kg) < loam (12.17 mg/kg) < clay loam (19.01 mg/kg). The iodine concentration was not related to the distance from the sea (McGrath and Fleming, 1988). In rainwater the iodine concentration is around 1 µg/L.

The forms of aqueous iodine found in natural environments depend on pH and electrochemical potential (E_h). The dominant forms are the inorganic species iodate (IO_3^-), iodide (I^-), and molecular iodine (I_2). Thermodynamically, under typical pH and E_h ranges found in natural soil environments, I^- ion should be the most prevalent phase, while IO_3^- exists under more oxidising conditions. Soil solution measurements support thermodynamic predictions in that I^- ion is the prevalent form in soil solutions under most conditions and IO_3^- is usually present only in soil solutions associated with oxidised conditions found in alkaline desert soils. Aqueous dissolved I^- ion in soil sorbs to clays, hydrous oxides, and soil organic matter, with sorption generally increasing with decreasing pH. In alkaline soils, I^- ion is mobile and has even been evaluated as an inert tracer in soil water studies (as reviewed by Mackowiak et al., 2005).

In culture studies on rice (*Oryza sativa*), a nutrient solution containing 1.7 mg IO_3^- per litre had no effect on rice biomass but 17 mg IO_3^- per litre had a small negative effect (Mackowiak and Grossl, 1999). There are few data available on the toxicity of any of the iodine species to soil and aquatic organisms. In general, iodate appears to be less toxic than iodide.

Fish appear not be very sensitive to I^- ion and IO_3^-, with species average LC_{50} values in rainbow trout of 4190 and 336 mg/L, respectively (US EPA Ecotox Database;[19] Laverock et al., 1995). *Daphnia magna* is more sensitive to I^- ion (species average 48h LC_{50} of 0.84 mg/L) than to IO_3^- (species average 48h LC_{50} of 72 mg/L) (US EPA Ecotox Database; Laverock et al., 1995). Several other species are similarly tolerant to I^- ion, the 24h LC_{50} value in zebra mussel being 226 mg/L and the no observed effect concentration (NOEC) for bluegreen algae (*Scenedesmus quadricauda*) being 66 mg/L (Bringmann and Kuhn, 1978). In contrast to elemental iodine, iodide and iodate have very low antibacterial activity.

[18] An iodine exposure of toddlers at the level of the UL would be achieved only if iodine for dairy cows fed glucosinolate-free diets were reduced further to 1 mg I/kg DM.
[19] Available online: http://cfpub.epa.gov/ecotox/ecotox_home.cfm

Iodine from iodate in feed can enter the environment via direct excretion of manure or urine on pasture or spreading of sludge and slurry collected from intensively reared animals. Based on the calculation method provided in the technical guidance on environmental risk assessment (EFSA, 2008), the highest increase of iodine in soil is around 180 μg/kg after a one-year application of manure from pigs from fattening assuming that 100 % of the intake via feed will be excreted. This concentration is well below the background concentration and is therefore not expected to pose an environmental risk.

Conclusions on safety for the environment

The use of calcium iodate in animal nutrition will not increase the iodine concentration in the environment considering the background concentration of iodine in the different compartments. It is not expected to pose a risk to the environment.

4. Efficacy

Iodine is an established essential trace element (Mc Dowell, 2003; Suttle, 2010). The use of calcium iodate anhydrous as iodine source in animal nutrition is extensively documented in scientific literature. The compound is efficacious to meet the animal needs of iodine. The additive under application does not require further confirmation of efficacy.

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[20] and Good Manufacturing Practice.

CONCLUSIONS AND RECOMMENDATIONS

CONCLUSIONS

The use of calcium iodate anhydrous as a source of iodine is considered safe for all animal species/categories when used up to the currently authorised maximum content of total iodine in complete feed, with the exception of horses and dogs, for which maximum tolerated levels are 3 and 4 mg I/kg complete feed, respectively. The limited data available on the iodine tolerance in cats support a provisional tolerated level of 5 mg I/kg complete feed.

The iodine content of food of animal origin, if produced taking account the use of the currently authorised maximum content of total iodine in complete feed, would represent a substantial risk to consumers, mainly high-consuming adults and toddlers. The risk would originate primarily from the consumption of milk and, to some extent, from consumption of eggs. The UL for adults would be exceeded by a factor of 2 and for toddlers by a factor of 4. If the authorised maximum iodine concentrations in feed for dairy cows and laying hens were reduced to 2 and 3 mg I/kg feed, respectively, the exposure of adult consumers to iodine from food of animal origin would be below the UL. However, iodine intake in high-consuming toddlers would remain above the UL (1.6-fold).

In the absence of data, calcium iodate is considered as irritant to the eyes, skin and respiratory tract, and as dermal sensitiser. Exposure by inhalation should be avoided.

The use of calcium iodate in animal nutrition is not expected to pose a risk to the environment.

Calcium iodate is an efficacious source of iodine to meet animal requirements.

[20] 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.

RECOMMENDATIONS

The specification of the additive as proposed by the applicant should be part of the authorisation of calcium iodate anhydrous: “ minimum 63.5 % iodine”.

Based on considerations of animal and consumer safety, the FEEDAP Panel recommends to modify some of the currently authorised maximum iodine contents in complete feed as follows:

- dairy cows and minor dairy ruminants: 2 mg I/kg complete feed
- laying hens: 3 mg I/kg complete feed
- horses: 3 mg I/kg complete feed
- dogs: 4 mg I/kg complete feed
- cats: 5 mg I/kg complete feed

To prevent the release of elemental iodine under the acidic conditions of the stomach by the comproportionation reaction, the simultaneous use of different iodine sources should be avoided.

The FEEDAP Panel recommends that calcium iodate anhydrous should be incorporated into compound feedingstuffs only via premixtures.

Regarding the outcome of the risk assessment in toddlers, the FEEDAP Panel recommends that the consequences of a potential reduction in the iodine content of feed should be accompanied by monitoring the iodine status of toddlers.

DOCUMENTATION PROVIDED TO EFSA

1. Dossier Calcium iodate, anhydrous, for all animal species. October 2010. Submitted by Calibre Europe SPRL/BVBA

2. Dossier Calcium iodate, anhydrous, for all animal species. Supplementary information. June 2011. Submitted by Calibre Europe SPRL/BVBA.

3. Evaluation report of the European Union Reference Laboratory for Feed Additives on the methods(s) of analysis for Iodine.

4. Comments from Member States received through the ScienceNet.

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APPENDICES

APPENDIX A

Executive Summary of the Evaluation Report of the European Union Reference Laboratory for Feed Additives on the Method(s) of Analysis for Iodine[21]

In the current application authorisation is sought under articles 4(1) and 10(2) for *Potassium iodide* and *Calcium iodate anhydrous* 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 additives* for all categories and species.

According to the Applicants *Potassium iodide* is a white to yellow crystalline powder with a minimum content of 67 % *total iodine* and 21 % potassium, while *Calcium iodate anhydrous* is a white crystalline powder with a minimum content of 63 % *total iodine* and 10 % calcium.

The *feed additives* are intended to be incorporated into *premixtures*, *feedingstuffs* and *water* (only for KI). All Applicants proposed the maximum *total iodine* levels in *feedingstuffs* set in the previous legislation: 4 mg/kg for equine; 5mg/kg for diary cows and laying hens; 20 mg/kg for fish and 10 mg/kg for other species and categories.

For the characterisation of *Potassium iodide* in the *feed additive*, Applicants (FAD-2010-0148 and FAD-2010-0231) suggested the titrimetric method described in the European Pharmacopoeia (Eur.Ph. 6 01/2008:0186) and in the Food Chemicals Codex (FCC) monographs. For the characterisation of *Calcium iodate* in the *feed additive*, all Applicants suggested the same titrimetric method, based on the iodate conversion to tri-iodide as described in the European Pharmacopoeia (Eur.Ph. 6 01/2008:20504) and in the FCC monographs. Even though no performance characteristics are available, the EURL recommends for official control the titrimetric methods described in the European Pharmacopoeia and the FCC monographs for the characterisation of *Potassium iodide* and *Calcium iodate* in the *feed additives*.

For the quantification of *total calcium*, and *total potassium* in the *feed additives*, the EURL identified two ring-trial validated methods - EN ISO 6869:2000, based on atomic absorption spectrometry (AAS) after dilution in hydrochloric acid; and - EN 15510:2007, based on inductively coupled plasma atomic emission spectrometry (ICP-AES) after dilution in hydrochloric acid, for which relative precisions were reported ranging from 4 to 25 %. Based on these performance characteristics, the EURL recommends for official control the two methods (EN ISO 6869:2000 and EN 15510:2007) for the quantification of *total calcium* and *total potassium* in the *feed additives.*

For the quantification of *total iodine* in *premixtures* and *feedingstuffs*, Applicant (FAD-2010-0148) submitted the ring-trial validated CEN method EN 15111:2007 designed for the quantification of iodine in foodstuffs by inductively coupled plasma mass spectrometry (ICP-MS). The following performance characteristics are reported for a total iodine concentration ranging from 0.2 to 40 mg/kg:

- a relative standard deviation for *repeatability* (RSD_r) ranging from 0.7 to 7.8 %; and

[21] The full report is available on the EURL website: http://irmm.jrc.ec.europa.eu/SiteCollectionDocuments/FinRep-IodineGroup.pdf

- a relative standard deviation for *reproducibility* (RSD_R) ranging from 6.2 to 19 %.

The Applicant applied the above mentioned CEN method to analyse *premixtures* and two *feedingstuffs* (including a mineral feed) containing *Potassium iodide* or *Calcium iodate* with iodine concentrations ranging from 4 to 1000 mg/kg. The reported recovery rates range from 95 to 105 % while the reported relative precisions (ranging from 2 to 15%) are in good agreement with those of the EN 15111:2007 method. This demonstrates the applicability (cf. extension of scope) of the CEN method to *premixtures* and *feedingstuffs*. Based on the experimental evidence provided, the EURL recommends for official control the EN 15111:2007 method for the quantification of *total iodine* in *premixtures* and *feedingstuffs.*

Applicant FAD-2010-0231 provided no experimental data for the quantification of *total iodine* in *water*. Hence, the EURL could not evaluate nor recommend any method for official control to determine *total iodine* in *water*.

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.

APPENDIX B

List of Risk Assessment Reports on iodine

In addition to the reports cited in the Background section, risk assessments from other EU bodies and Institutions have been carried out (see list below).

1. EC Health and Consumers Scientific Committees Opinions

Opinion of the Scientific Committee on Food on the Tolerable Upper Intake Level of Iodine. (http://ec.europa.eu/food/fs/sc/scf/out146_en.pdf)

2. EU Risk Assessment Reports

Risk Assessment Iodine. Expert Group on Vitamins and Minerals 2003. (http://www.food.gov.uk/multimedia/pdfs/evm_iodine.pdf)

3. EFSA-NDA Panel Opinions

Scientific Opinion on the substantiation of health claims related to iodine and thyroid function and production of thyroid hormones (ID 274), energy-yielding metabolism (ID 274), maintenance of vision (ID 356), maintenance of hair (ID 370), maintenance of nails (ID 370), and maintenance of skin (ID 370) pursuant to Article 13(1) of Regulation (EC) No 1924/2006 - EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA). (http://www.efsa.europa.eu/en/efsajournal/pub/1214.htm)

Scientific Opinion on the substantiation of a health claim related to Iodine and the growth of children pursuant to Article 14 of Regulation (EC) No 1924/2006 - EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA). (http://www.efsa.europa.eu/en/efsajournal/pub/1359.htm)

Scientific Opinion on the substantiation of health claims related to various food(s)/food constituent(s) and improved bioavailability of nutrients (ID 384, 1728, 1752, 1755), energy and nutrient supply (ID 403, 413, 457, 487, 667, 1675, 1710, 2901, 4496) and presence of a nutrient in the human body (ID 720) pursuant to Article 13(1) of Regulation (EC) No 1924/2006 - EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA). (http://www.efsa.europa.eu/en/efsajournal/pub/1743.htm)

Scientific Opinion on the substantiation of health claims related to iodine and contribution to normal cognitive and neurological function (ID 273), contribution to normal energy-yielding metabolism (ID 402), and contribution to normal thyroid function and production of thyroid hormones (ID 1237) pursuant to Article 13(1) of Regulation (EC) No 1924/2006 - EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA) (http://www.efsa.europa.eu/en/efsajournal/pub/1800.htm)

APPENDIX C

List of authorisations of iodine compounds other than feed additive

The following iodine compounds are authorised for use in food (Regulation (EC) No 1170/2009):[22] sodium iodide, sodium iodate, potassium iodide and potassium iodate which may be used in the manufacture of food supplements and may be added to food.

The following iodine compounds can be used for the manufacturing of dietetic foods (Commission Regulation (EC) No 953/2009[23]): sodium iodide, sodium iodate, potassium iodide and potassium iodate.

The following iodine compounds can be used for the manufacturing of processed cereal-based foods and baby foods for infants and young children (Commission Directive 2006/125/EC):[24] sodium iodide, sodium iodate, potassium iodide and potassium iodate.

The following iodine compounds are listed in Table 1 of the Annex of Regulation 37/2010[25] as *Allowed substances, no MRL required*: 3,5-Diiodo-L-thyrosine, iodine and iodine inorganic compounds (sodium iodide, sodium iodate, potassium iodide, potassium iodate and iodophors including polyvinylpyrrolidoneiodine) and iodine organic compounds such as iodoform.

The following iodine compounds are listed in Annex of Commission Implementing Regulation (EU) No 540/2011[26] as "Active substances approved for use in plant protection products": 6-iodo-2-propoxy-3-propylquinazolin-4(3H)-one, 4-iodo-2-[3-(4-methoxy-6- methyl-1,3,5-triazin-2-yl)-ureidosulfonyl]benzoate and 4- hydroxy- 3,5- di-iodobenzonitrile.

The following iodine compounds are "Active substances identified as existing" listed in Annex I of the Commission Regulation (EC) No 1457/2007:[27] iodoform/triiodomethane, iodine, iodine in the form of iodophor, iodine complex in solution with non-ionic detergents, polyvinylpyrrolidone iodine, alkylaryl polyether alcohol-iodine complex, iodine complex with ethylene-propylene block co-Polymer (pluronic), iodine complex with poly alkylenglycol, iodinated Resin/polyiodide Anion Resin, potassium iodide, iodine monochloride, p-[(diiodomethyl)sulphonyl]toluene, 3-iodo-2-propynyl butylcarbamate and quaternary ammonium iodides. According to Annex II of the same Regulation, the following iodine compounds are "Active substances to be examined under the review programme": iodine, p-[(diiodomethyl)sulphonyl] toluene, 3-iodo-2-propynyl butylcarbamate, quaternary ammonium iodides and polyvinylpyrrolidone iodine.

[22] 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.

[23] 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.

[24] Commission Directive 2006/125/EC of 5 December 2006 on processed cereal-based foods and baby foods for infants and young children. OJ L 339, 6.12.2006, p. 16.

[25] 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.

[26] Commission Implementing Regulation (EU) No 540/2011 of 25 May 2011 implementing Regulation (EC) No 1107/2009 of the European Parliament and of the Council as regards the list of approved active substances. OJ L 153, 11.6.2011, p. 1.

[27] Commission Regulation (EU) No 1457/2007 of 4 December 2007 on the second phase of the 10-year work programme referred to in Article 16(2) of Directive 98/8/EC of the European Parliament and of the Council concerning the placing of biocidal products on the market. OJ L325, 11.12.2007, p.3.

The following iodine compounds will not be added to the Annex I, IA or IB of the Directive 98/8/EC[28] according to the Commission Decision of 14 October 2008:[29] iodine, p-[(diiodomethyl]sulphonyl] toluene and quaternary ammonium iodides.

The following iodine compounds can be used for cosmetic purposes (Regulation (EC) No 1223/2009 of the European Parliament and of the Council[30]): Disodium 2-(2,4,5,7-tetraiodo-6-oxido-3-oxoxanthen-9-yl) benzoate and its insoluble barium, strontium and zirconium lakes, salts and pigment; and 3-Iodo-2-propynylbutylcarbamate. However, the following iodine compounds are prohibited in cosmetic products use, under the above mentioned Regulation: [4-(4-hydroxy-3-iodophenoxy)-3,5-diiodophenyl]acetic acid (Tiratricol (INN)) and its salts, piprocurarium iodide (INN), N-(3-Carbamoyl-3,3-diphenylpropyl)-N,N-diisopropylmethylammonium salts, e. g. isopropamide iodide (INN), furfuryltrimethylammonium salts, e. g. furtrethonium iodide (INN), iodine, gallamine triethiodide (INN), 5,5'-Di-isopropyl-2,2'-dimethylbiphenyl-4,4'-diyl dihypoiodite (thymol iodide), trifluoroiodomethane, iodomethane (methyl iodide), 4,4′-thiodianiline and its salts.

According to the Annex of Regulation (EC) No 432/2012[31] the following health claims can be made only for food which is at least a source of iodine 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:[32] iodine contributes to normal cognitive function, iodine contributes to normal energy-yielding metabolism, iodine contributes to normal functioning of the nervous system, iodine contributes to the maintenance of normal skin and iodine contributes to the normal production of thyroid hormones and normal thyroid function.

[28] Directive 98/8/Ec of the European Parliament and of the Council of 16 February 1998 concerning the placing of biocidal products on the market. OJ L123, 24.4.98, p. 1.

[29] Commission Decision of October 2008 concerning the non-inclusion of certain substances in Annex I, IA or IB to Directive 98/8/EC of the European Parliament and of the Council concerning the placing of biocidal products on the market. OJ L 281, 24.10.2008, p. 16.

[30] 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.

[31] 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.

[32] Regulation (EC) No 1924/2006 of the European Parliament and of the council of 20 December 2006 on nutrition and health claims made for food. OJ L 404, 30.12.2006, p.9.

APPENDIX D

Iodine in milk and fish. Data from recent literature

Table D1: Influence of type of farming on the iodine content of bulk milk (µg/kg) in some European studies.

Author(s)	Country	Type of farming		Remarks
		Organic	Conventional	
Rey Crespo et al. (2012)	Spain	78	157	
Bath et al. (2012)	UK	144	250	
Johner et al. (2012)	Germany	58	112	
Köhler et al. (2012)	Germany	92	143	
Rozenska et al. (2011)	Czech Republic	302	350	Sheep milk

Table D2: Influence of summer (outdoor, grazing) and winter (indoor) animal feeding/keeping on the iodine content of bulk milk (µg/kg) in some European studies.

Author(s)	Country	Type of animal feeding/keeping		Remarks
		Outdoor	Indoor	
Dahl et al. (2003)	Norway	88	232	
Travnicek et al. (2006)	Czech Republic	351	494	
Paulikova et al. (2008)	Slovakia	155	127	Cow milk
Paulikova et al. (2008)	Slovakia	56	198	Sheep milk
Paulikova et al. (2008)	Slovakia	48	89	Goat milk
Hampel et al. (2009)	Germany	108	134	
Rozenska et al. (2011)	Czech Republic	38	72	Sheep milk
Soriguer et al. (2011)	Spain	247	270	
Rey Crespo et al. (2012)	Spain	35	73	Organic farming
Haug et al. (2012)	Norway	92	122	
Johner et al. (2012)	Germany	87	110	

Table D3: Influence of iodine concentration of teat-disinfectant and application form on the increase of iodine concentration of milk by various authors

Author(s)	Available iodine in disinfectants (g/L)	Application of disinfectants[1]	Increase of iodine in milk (µg/L)
Galton et al. (1986)	1	A	35
Ryssen et al. (1985)	2	A	11-60
Berg and Padgitt (1985)	2.5	A	7
Rasmussen et al. (1991)	2.5	A	54
Rasmussen et al. (1991)	2.5	B/A	69
Falkenberg et al. (2002)	2.7	B	30
Flachowsky et al. (2007)	3	A	54
Rasmussen et al. (1991)	5	A	20
Borucki Castro et al. (2012)	5	B (complete cleaning)	25
Galton (2004)	5	A	27-32
Galton et al. (1984)	5	A	36
Rasmussen et al. (1991)	5	B/A	41
Borucki Castro et al. (2012)	5	B (incomplete cleaning)	88
Hamann and Heeschen (1982)	5	A	120
Berg and Padgitt (1985)	10	A	7
Swanson et al. (1990)	10	A	46
Galton et al. (1984)	10	A	90
Galton et al. (1986)	10	A	76
Galton et al. (1984)	10	B,A	150
Galton et al. (1986)	10	B,A	110
Conrad and Hemken (1978)	10	A	88
Borucki Castro et al. (2012)	10	A	49
Borucki Castro et al. (2012)	10	A (spraying)	409
Borucki Castro et al. (2012)	10	B (complete cleaning)	54

1: A: after milking; B: before milking

Table D4: Iodine concentration (µg/kg fresh weight) of salt- and fresh water fish, crustaceans and molluscs ("Food Composition and Nutrition Tables", Souci et al. (2008)).

Species	Average	Minimum	Maximum
Salt-water fish			
Flounder	260	44	1 540
Halibut	370	220	520
Herring	470	240	670
Cod	2 290	1 210	5 480
Mackerel	500	390	820
Sardine	320	130	540
Haddock	1 350	600	5 100
Plaice	530	260	2 400
Alaska pollack	880	570	1 030
Tuna	500	400	500
Fresh-water fish			
Eel	40		
Perch	40		
Trout	35	30	36
Carp	17		
Salmon	340		
Crustaceans and molluscs			
Oyster	580		
Brown shrimp	910	510	1 300
Lobster	1 000		
Mussel	1 500	1 010	4 470
Soft clam	1 200		

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APPENDIX E.

Exposure to iodine of adults and toddlers resulting from consumption of food produced from animals administered different dietary iodine concentrations[1]

Scenario I: Currently authorised iodine concentration in feed: at total iodine level in feed of 5 (dairy cows, laying hens) or 10 (cattle for fattening) mg/kg complete feed

ADULTS

Food	Intake (kg)	Iodine level (µg/kg)	Iodine intake (µg/day)
Meat	0.290	100	29
Milk*	1.500	760	1140
Egg*	0.070	1300	91
			1231

(*) Only the two items contributing at the highest amount to the iodine intake are summed

TODDLERS

Food	Intake (kg)	Iodine level (µg/kg)	Iodine intake (µg/day)
Meat	0.090	100	9
Milk*	1.050	760	798
Egg*	0.035	1300	46
			844

Scenario II: Reduced iodine concentrations in feed, as proposed by the FEEDAP Panel: at total iodine level in feed of 2 (dairy cows), 3 (laying hens) and 10 (cattle for fattening) mg/kg complete feed

ADULTS

Food	Intake (kg)	Iodine level (µg/kg)	Iodine intake (µg/day)
Meat	0.290	100	29
Milk*	1.500	280	420
Egg*	0.070	825	58
			478

(*) Only the two items contributing at the highest amount to the iodine intake are summed

TODDLERS

Food	Intake (kg)	Iodine level (µg/kg)	Iodine intake (µg/day)
Meat	0.090	100	9
Milk*	1.050	280	294
Egg*	0.035	825	29
			323

[1] Exposure calculated according to the Guidance on Consumer safety (EFSA, 2012) based on the EFSA Comprehensive European Food Consumption Database.