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Safety and efficacy of feed additives consisting of sodium ferrocyanide and potassium ferrocyanide for all animal species (Eusalt a.i.s.b.l.)

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Abstract

Following a request from the European Commission, EFSA was asked to deliver a scientific opinion on the safety and efficacy of potassium and sodium ferrocyanide as technological feed additives for all animal species. The additives sodium- and potassium ferrocyanide are intended to be used in sodium chloride with a maximum content of 80 mg ferrocyanide anion (anhydrous)/kg salt. The FEEDAP Panel concluded that the use of sodium ferrocyanide and potassium ferrocyanide is safe, when added to sodium chloride at a maximum content of 80 mg ferrocyanide anion/kg for: turkey for fattening and laying hens and other laying/breeding birds; all porcine species and categories, all ruminant species and categories, rabbit, horse, salmonids and other minor fin fish, dogs and cats. In the absence of a margin of safety, the use of sodium and potassium chloride according to the proposed conditions of use is not considered to be safe for chickens for fattening and other poultry species for fattening or reared for laying/breeding other than turkeys. In the absence of information on the use of sodium chloride in the diets for any other animal species, no conclusion on a potentially safe level of sodium chloride, supplemented with 80 mg ferrocyanide anions (anhydrous)/kg, could be made. The use of sodium and potassium ferrocyanide in animal nutrition under the conditions of use proposed is of no concern for consumer safety. The results of *in vivo* studies showed that sodium and potassium ferrocyanide are not irritant to skin and eye and are not skin sensitisers. However, owing to the presence of nickel, sodium ferrocyanide, is considered a dermal and respiratory sensitiser. No conclusions could be reached on the safety of the user exposed via inhalation for potassium ferrocyanide. The use of sodium and potassium ferrocyanide as feed additives is considered safe for the environment. The additives are considered to be efficacious as anticaking agents in sodium chloride at the proposed use level.

Keywords: technological additives, anticaking agents, sodium ferrocyanide, potassium ferrocyanide, safety, efficacy

Requestor: European Commission

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1. Introduction

1.1. Background and Terms of Reference

Regulation (EC) No 1831/2003[1] establishes the rules governing the Community authorisation of additives for use in animal nutrition. In particular, 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 a time limit or pursuant to Directive 82/471/EEC. In particular, Article 10(2) of that Regulation specifies that for existing products within the meaning of Article 10(1), an application shall be submitted in accordance with Article 7, within a maximum of seven years after the entry into force of this Regulation.

The European Commission received two requests from Eusalt Aisbl[2] for the re-evaluation of the authorisation of the additives consisting of Natrium hexacyanoferrate(II)-Ferrocyannatrium (sodium ferrocyanide) or of the additive consisting of Potassium hexacyanoterrate(II)-Ferrocyannatrium (potassium ferrocyanide), when used as feed additives for all animal species (category: technological additives; functional group: anticaking agent).

According to Article 7(1) of Regulation (EC) No 1831/2003, the Commission forwarded the applications to the European Food Safety Authority (EFSA) as applications under Article 10(2) (re-evaluation of an authorised feed additive). The particulars and documents in support of the applications were considered valid by EFSA as of 17 January 2014.

According to Article 8 of Regulation (EC) No 1831/2003, EFSA, after verifying the particulars and documents submitted by the applicant, shall undertake an assessment in order to determine whether the feed additives comply 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 on the efficacy of the feed additives consisting of potassium and sodium ferrocyanide, when used under the proposed conditions of use (see **Section 3.1.3**).

1.2. Additional information

Sodium ferrocyanide and potassium ferrocyanide are authorised as feed additives,[3] both with a maximum content of 80 mg/kg sodium chloride (NaCl) (calculated as ferrocyanide anion).

Sodium ferrocyanide and potassium ferrocyanide are currently authorised as food additives in accordance with Annex II to Regulation (EC) No 1333/2008[4], to be used in salt and salt substitutes. Specific purity criteria on sodium ferrocyanide and potassium ferrocyanide have been defined in Commission Regulation (EU) No 231/2012[5].

Sodium ferrocyanide and potassium ferrocyanide have not been previously assessed by EFSA as feed additives.

The Scientific Committee for Animal Nutrition (SCAN) delivered an opinion on potassium and sodium ferrocyanide as anticaking agents (EC, 2001).

Sodium ferrocyanide and potassium ferrocyanide were assessed by the Joint FAO/WHO Expert Committee on Food Additives (JECFA, 1970a,b, 1974a,b,c, 1975) and by the Scientific Committee for food (SCF) (EC, 1991). The EFSA Panel on Food Additives and Nutrient Sources added to Food (ANS) delivered an opinion on the safety of sodium ferrocyanide (E535) and potassium ferrocyanide (E536) (EFSA ANS Panel, 2018).

[1] Regulation (EC) No 1831/2003 of the European Parliament and of the council of 22 September 2003 on the additives for use in animal nutrition. OJ L 268, 18.10.2003, p. 29.
[2] Eusalt Aisbl, Square de Meeus 40 Brussels Belgium.
[3] Commission Regulation (EC) No 1810/2005 of 4 November 2005 concerning a new authorisation for 10 years of an additive in feedingstuffs, the permanent authorisation of certain additives in feedingstuffs and the provisional authorisation of new uses of certain additives already authorised in feedingstuffs. OJ L291, 5.11.2005, p. 5.
[4] Regulation (EC) No 1333/2008 of the European Parliament and of the Council of 16 December 2008 on food additives. OJ L 354, 31.12.2008, p. 16.
[5] Commission Regulation (EU) No 231/2012 of 9 March 2012 laying down specifications for food additives listed in Annexes II and III to Regulation (EC) No 1333/2008 of the European Parliament and of the Council. OJ L 83, 22.3.2012, p. 1–295.

2. Data and methodologies

2.1. Data

The present assessment is based on data submitted by the applicant in the form of two technical dossiers[6] in support of the authorisation request for the use of potassium and sodium ferrocyanide as feed additives.

The FEEDAP Panel used the data provided by the applicant together with data from other sources, such as previous risk assessments by EFSA or other expert bodies, peer-reviewed scientific papers, other scientific reports, to deliver the present output.

EFSA has verified the European Union Reference Laboratory (EURL) report as it relates to the methods used for the control of the potassium and sodium ferrocyanide in animal feed.

2.2. Methodologies

The approach followed by the FEEDAP Panel to assess the safety and the efficacy of potassium and sodium ferrocyanide is in line with the principles laid down in Regulation (EC) No 429/2008[7] and the relevant guidance documents: Guidance on studies concerning the safety of use of the additive for users/workers (EFSA FEEDAP Panel, 2012), Guidance on the identity, characterisation and conditions of use of feed additives (EFSA FEEDAP Panel, 2017a), Guidance on the assessment of the safety of feed additives for the target species (EFSA FEEDAP Panel, 2017b), Guidance on the assessment of the efficacy of feed additives (EFSA FEEDAP Panel, 2018) and Guidance on the assessment of the safety of feed additives for the environment (EFSA FEEDAP Panel, 2019).

3. Assessment

The present assessment is related to two additives, consisting of sodium and potassium hexacyanoferrate, respectively. They are both intended to be used as technological additives (functional group: anticaking agents) in sodium chloride (common salt feed grade) for all animal species.

3.1. Characterisation

3.1.1. Sodium ferrocyanide

3.1.1.1. Manufacturing of sodium ferrocyanide

The additive sodium ferrocyanide is synthesised from the reaction of sodium cyanide, spent acid and iron chloride. After reaction and filtration, sodium ferrocyanide is crystallised and dried to obtain the additive.

3.1.1.2. Characterisation of the additive

The additive is composed only of the active substance sodium ferrocyanide, (tetrasodium hexacyanoferrate(II) decahydrate, (chemical formula: $Na_4\ [Fe(CN)_6]\cdot 10H_2O$)) identified by the Chemical Abstracts Service (CAS) number 13601-19-9E and the European Inventory of Existing Chemical Substances (EINECS) number 237-081-9. The additive is a lemon-yellow coloured, fine crystallised and odourless powder. It has a molecular weight of 484.1 g/mol, its solubility in water is 180 g/L (at 20°C) and it has a density of 1,460 kg/m^3.

The applicant submitted three batches for infrared (IR) spectroscopy analysis which showed that the functional groups (CN and water) found were typical for sodium ferrocyanide decahydrate.[8]

The additive is manufactured to meet the specification set for its use as a food additive[9]: sodium ferrocyanide $\geq$ 99%, moisture $\leq$ 1%, water-insoluble matter $\leq$ 0.03%, chloride ion (Cl^-) $\leq$ 0.2%, sulfate (SO_4) $\leq$ 0.1%, lead $\leq$ 5 mg/kg, free cyanide not detectable and ferricyanide not detectable.

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6 FEED dossier reference: FAD-2011-0047 and FAD-2011-0048.

7 Commission Regulation (EC) No 429/2008 of 25 April 2008 on detailed rules for the implementation of Regulation (EC) No 1831/2003 of the European Parliament and of the Council as regards the preparation and the presentation of applications and the assessment and the authorisation of feed additives. OJ L 133, 22.5.2008, p. 1.

8 Technical dossier/Section II/Annexes/ Annex_II_3_Batch to Batch analysis.

9 Commission Regulation (EU) No 231/2012 of 9 March 2012 laying down specifications for food additives listed in Annexes II and III to Regulation (EC) No 1333/2008 of the European Parliament and of the Council. OJ L 83, 22.3.2012, p. 1–295.

Analytical data to confirm the specifications were provided for nine batches of the additive[8,10], and showed the following average values: 101.2% (99.55– 104) sodium ferrocyanide, 0.10% (0.05–0.21) moisture, 0.007–< 0.01% (LOQ) water-insoluble matter, 0.07% (0.03–0.10) chloride, and 0.05% (0.03–0.07) sulfate. Cyanide and ferricyanide were not detectable in five of these batches.

The same nine batches of the additive were analysed for impurities.[10,11] Cadmium, lead, mercury and arsenic concentrations were below the respective LOQ.[12] Nickel was analysed in four of these batches, resulting in a range of < 0.25 (LOQ)–5.58 mg/kg.[8]

Polychlorinated dibenzodioxins (PCDDs), polychlorinated dibenzofurans (PCDFs) and coplanar dioxin-like polychlorinated biphenyls (co-planar PCBs) were analysed in three batches.[13] The calculated (upper bound) levels of dioxins and the sum of dioxins and dioxin-like-PCBs were 1.10 ng WHO-PCDD/F-TEQ/kg and 0.13 ng WHO-PCDD/F-PCB-TEQ/kg, respectively. The results regarding impurities do not raise safety concerns.

The dusting potential of three batches of the additive was determined using the Stauber–Heubach method and showed values on average of 1,026 mg/m^3 (range 505–1,505 mg/m^3).[14]

3.1.2. Potassium ferrocyanide

3.1.2.1. Manufacturing of potassium ferrocyanide

The additive is produced by chemical synthesis. Calcium hexacyanoferrate is prepared from the reaction of hydrogen cyanide (HCN), iron (II) chloride ($FeCl_2$), and calcium hydroxide $Ca(OH)_2$. After filtration, the solution is concentrated by evaporation under reduced pressure, and the calcium hexacyanoferrate crystallises with 11 molecules of water. Two methods are used for the conversion of calcium hexacyanoferrate to the potassium salt, either the formation of a double potassium/calcium salt following the addition of stoichiometric amounts of potassium chloride, which is further treated with calcium carbonate to release the potassium salt, or the preparation of iron hexacyanoferrate by the addition of iron chloride followed by the addition of stoichiometric amounts of potassium cyanide.

3.1.2.2. Characterisation of the additive

The additive is composed only of the active substance potassium ferrocyanide (potassium hexacyanoferrate(II) trihydrate, (chemical formula: $K_4\,[Fe(CN)_6]\cdot 3H_2O$)), identified by the CAS number 14459-95-1 and EINECS number 237-722-2. The additive is a lemon-yellow coloured, fine crystallised and odourless powder. It has a molecular weight of 422.4 g/mol, its solubility in water is 289 g/L (at 20°C) and it has a density of 1,850 kg/m^3.

The additive is manufactured to meet the specifications set for its use as a food additive[9]: potassium ferrocyanide ≥ 99%, moisture ≤ 1%, water-insoluble matter ≤ 0.03%, chloride (Cl) ≤ 0.2%, sulfate (SO_4) ≤ 0.1%, lead ≤ 5 mg/kg, free cyanide not detectable and ferricyanide not detectable.

Analytical data to confirm the specifications were provided for five batches of the additive,[15] and showed the following average values: 99.61% (99.56–99.70) potassium ferrocyanide, 0.38% (0.32–0.4) moisture, < 0.01%(LOQ) water-insoluble matter, 0.02% (0.02–0.03) chloride, 0.04% (0.03–0.05) sulfate. Cyanide and ferricyanide were not detectable in five of these batches.

The same five batches of the additive were analysed for impurities. Cadmium, lead, arsenic and nickel concentrations were below the respective LOQ.[16] No information on the level of mercury in the additive was made available.

PCDDs, PCDFs and co-planar PCBs were analysed in three batches.[17] The calculated (upper bound) levels of dioxins and the sum of dioxins and dioxin-like-PCBs were 0.09 ng WHO-PCDD/F-TEQ/kg and 0.15 ng WHO-PCDD/F-PCB-TEQ/kg, respectively. The results regarding impurities do not raise safety concerns.

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[10] Technical dossier/FAD-2011-0047_SIn_Feb15/Annex_II_3 Certificates of analysis E535 Sodium ferrocyanide.

[11] Technical dossier/Section II/Annex_II_3_Batch to Batch analysis.

[12] Limit of quantification (LOQ) for four batches: < 0.01 mg/kg cadmium, < 0.05 mg/kg lead, < 0.005 mg/kg mercury and < 0.05 mg/kg arsenic. LOQ for five batches: < 1 mg/kg lead, < 1 mg/kg arsenic and < 1 mg/kg cadmium.

[13] Technical dossier/FAD-2011-0047_FAD-2011-0048_FAD-2013-0016_SIn_Oct18/ANNEX_SIN_2-1_N-BEFUND30_5-1651580_Vers_1.pdf.

[14] Technical dossier/FAD-2011-0047_SIn_Feb15/Annex_II_10_Physical state Dusting potential.

[15] Technical dossier/FAD-2011-0048_SIn_Feb15/Annex_II_3 Certificates of analysis E536 Potassium ferrocyanide.

[16] Limit of quantification (LOQ): < 1 mg/kg cadmium, < 1 mg/kg lead, < 1 mg/kg arsenic and < 1 mg/kg nickel.

[17] Technical dossier/FAD-2011-0047_FAD-2011-0048_FAD-2013-0016_SIn_Oct18/ANNEX_SIN_2-2_K-BEFUND30_5-1651603_Vers_1.pdf.

The dusting potential of three batches of the additive was determined using the Stauber–Heubach method and showed values on average of 40 mg/m^3 (range 15–60 mg/m^3).[18]

3.1.3. Conditions of use

The additives sodium and potassium ferrocyanide are intended to be used as anticaking agents in the feed material sodium chloride (NaCl, common salt feed grade) at a proposed maximum concentration of 80 mg ferrocyanide anion (anhydrous) from sodium ferrocyanide decahydrate/kg sodium chloride or of 80 mg ferrocyanide anion (anhydrous) from potassium ferrocyanide trihydrate/kg sodium chloride.

The feed material sodium chloride supplemented with either sodium ferrocyanide or potassium ferrocyanide is intended to be used in feed for all animal species.

3.2. Safety

No specific studies done for the current application were provided. The safety for use in food of ferrocyanides (sodium-, potassium- and calcium-) was assessed by JECFA (JECFA, 1970a, 1974b, 1975) and by EFSA (EFSA ANS Panel, 2018). To support the safety of the additive, the applicant referred to the conclusions reached in those evaluations and submitted the relevant studies. The main results of the previous assessments are summarised below, in the respective sections.

In addition, the applicant conducted an extensive literature search (ELS) to identify data which could support the safety of the additive.[19] The ELS was performed using PubMed/Medline, Scopus, CAB Direct, Science Direct and Google Scholar as database platform, covering the period between 1990 and 2021, and using as keywords ferrocyanide (and relevant synonyms) and toxicology related terms.

3.2.1. Absorption, distribution, metabolism and excretion (ADME)

A study (Nielsen et al., 1990a) performed in rats administered orally a single dose (10 mg) of labelled $K_4[^{59}Fe(^{14}CN)_6]$ indicated that: (i) ^{59}Fe was absorbed at a limited extent (up to 2.6%), most (about 95%) being recovered in the faeces and about 2.5% in the urine (^{14}C in urine amounting to about 2.8% of the administered dose) after 7 days; the limited absorption may be compared to the 0.22% absorption measured in humans administered 500 mg (Nielsen et al., 1990b); (ii) $K_4[^{59}Fe(^{14}CN)_6]$ was excreted essentially unchanged in the faeces, while in the urine up to 1.5% was unchanged and the rest appeared as Fe(II), cyanide and its main metabolite thiocyanate; exposure to free cyanide amounted to 0.06 mg/kg body weight (bw); (iii) the ^{14}C activity (related to the cyanide moiety) found in the urine was significantly higher compared to the excretion of $^{59}Fe(II)$, indicating that a fraction of the hexacyanoferrate(II) anion must have been hydrolysed either in the intestinal tract prior to the absorption of ferrous iron and cyanide or dissociated in the body after absorption of the anion; (iv) the $^{59}Fe/^{14}C$-ratios in the liver and kidney are close to 1.0, indicating that residues are likely non-dissociated $[Fe(CN)_6]^4$.

The ADME of ammonium ferric [^{14}C]hexacyanoferrate (AFCF) was studied in the cow (Arnaud et al., 1988) and previously assessed by EFSA FEEDAP Panel (2021). The results are summarised as follows: (i) *in vitro* incubation with rumen fluid showed that 9% of the compound was dissociated/metabolised to [^{14}C]hexacyanoferrate (89%) and thiocyanate (11%), (ii) most of the radioactivity orally administered (single dose of about 1.7 g) *in vivo* (two animals) was recovered after 9 days in the faeces (92% and 96%, respectively) with 0.5–0.2% in the urine and 0.07–0.07% in the milk. [^{14}C]hexacyanoferrate was identified as one of the main AFCF dissociation products/metabolites in the faeces (16%), which is consistent with the *in vitro* study, and in the urine (89%); (iii) average concentration of total radioactivity in milk was 300 Bq/L, equivalent to 0.025 mg/L; due to the very low levels of radioactivity, no direct identification of [^{14}C]hexacyanoferrate was possible; (iv) very low amounts of radioactivity ($\leq$ 6 Bq/kg above the background level, equivalent to 0.0005 mg/kg) were measured in the edible tissues analysed (i.e. liver and muscle) after 9-day withdrawal. The results of this experiment, done with a single oral dose about 10–12 times higher than the dose proposed for use, cannot be retained for a quantitative evaluation of the transfer of hexacyanoferrate to milk. However, they confirm the very limited absorption of this compound and its limited excretion in milk.

[18] Technical dossier/FAD-2011-0047_SIn_Feb15/Annex_II_10_Physical state Dusting potential.
[19] Technical dossier/FAD-2011-0047_Supplementary Information September 2021/Annex_SIn_ELS_Ferrocyanide_21–08-25,

3.2.2. Toxicological studies

Ferrocyanides were evaluated by JECFA (1969), which established a temporary acceptance of 0–0.00125 mg/kg bw per day. Subsequently a temporary acceptable daily intake (ADI) of 0–0.025 mg/kg bw per day (calculated as sodium ferrocyanide) was established by JECFA (1973), and confirmed in 1974 (JECFA, 1975).

The EFSA ANS Panel (EFSA ANS Panel, 2018) assessed the available information on ferrocyanides, in the context of the re-evaluation of ferrocyanides as food additives; in its assessment, the EFSA ANS Panel reviewed subchronic toxicity studies, genotoxicity studies and chronic toxicity studies, briefly summarised below.

The ANS Panel evaluated two subchronic toxicity studies, one in rats and one in dogs; treatment related effects on kidney (higher kidney weight, tubular damage and granular and calcified deposits) were observed in rats fed 450 or 4,500 mg sodium ferrocyanide/kg bw per day for 13 weeks, while no effects were observed in dogs receiving up to 25 mg sodium ferrocyanide/kg bw per day for 13 weeks.

With regards to genotoxicity, potassium ferrocyanide was negative in two Rec-assay system with *Bacillus subtilis* strains H17 and M45, in a SOS Chromotest with *Escherichia coli* strains PQ37 and PQ35, with or without metabolic activation. In an *in vitro* Comet assay in human lymphocyte cells, sodium ferrocyanide did not induce DNA damage, while potassium ferrocyanide significantly increased DNA damage at high concentrations. The ANS Panel noted 'that the effect may be related to an indirect mechanism, such as reactive oxygen species (ROS) generation under *in vitro* conditions which is based on the evidence that in food systems potassium ferrocyanide promotes lipid oxidation' and concluded that ferrocyanides are not of genotoxic concern. The FEEDAP Panel noted that in mammalian cells only an *in vitro* Comet assay is reported, a test not validated for regulatory purposes, while no studies on chromosomal aberrations are available. However, the Panel considered that the proposed mechanism is expected to be expressed at rather high exposure levels and is unlikely to be of concern in the proposed conditions of use of the feed additive. Therefore, integrating the available information, the FEEDAP Panel supports the conclusion reached by the ANS Panel.

In two chronic toxicity studies, rats were fed 0, 50, 500 or 5,000 mg/kg sodium ferrocyanide in the diet (corresponding to 0, 4.4, 45 and 450.7 mg/kg bw per day for males and 0, 6.2, 62.5 and 630.1 mg/kg bw per day for females) for either 49 weeks or 2 years. No carcinogenic effects were observed and none of the non-neoplastic findings observed was considered to be of toxicological relevance. However, in the 2-year study, rats fed the mid and high doses frequently showed higher cell excretion rate in 2-h urine samples. The ANS Panel considered 'the increased cell excretion rate indicative for occasional, transient kidney toxicity' and therefore, identified from this study a no observed adverse effect level (NOAEL) of 4.4 mg/kg bw per day in male rats and 6.2 mg/kg bw per day in female rats.

In one prenatal developmental toxicity study in rats, the highest dose tested of 1,000 mg sodium ferrocyanide/kg bw per day was considered to be the NOAEL.

The ANS Panel used the lowest NOAEL identified in the chronic toxicity study in rat (4.4 mg sodium ferrocyanide/kg bw per day for male rats) to derive an ADI of 0.044 mg sodium ferrocyanide/kg bw per day. Based on the assumption that the toxicity of sodium ferrocyanide is due to the ferrocyanide ion only, the ANS Panel established a group ADI for sodium, potassium and calcium ferrocyanide of 0.03 mg/kg bw per day expressed as ferrocyanide ion.

The FEEDAP Panel, having reviewed the relevant studies, supports the conclusions reached by the EFSA ANS Panel in 2018 and considers the ADI of 0.03 mg ferrocyanide ion/kg bw per day as adequate for the present assessment.

3.2.3. Safety for the target species

No specific studies aimed to demonstrate the safety of the additives for the target species were made available. The maximum safe concentration of the additive in complete feed can be derived using the results of the toxicological studies (EFSA FEEDAP Panel, 2017a,b,c). From the results of the toxicological studies available (see Section 3.2.2), the FEEDAP Panel considers that the NOAEL of 4.4 mg sodium ferrocyanide/kg bw per day (corresponding to 3 mg ferrocyanide ion/kg bw per day) in the chronic (2-year) toxicity study in rats is the appropriate value to calculate the safe level in feed for the target species. The NOAEL for ferrocyanide anion was used to calculate the maximum safe level for the different target species as per guidance. From the values obtained, the maximum safe levels for the feed material containing the additive were calculated. The results are shown in Table 1.

The maximum safe level of ferrocyanide ions, either from sodium or potassium ferrocyanide, in complete feed corresponds to: 0.33 mg/kg chickens for fattening and other poultry species for fattening or reared for laying/breeding; 0.45 mg/kg for turkey for fattening; 0.50 mg/kg for laying hens and other laying/breeding birds; 0.60 mg/kg for piglets; 0.72 mg/kg for pigs for fattening; 0.88 mg/kg for sows and minor porcine species; 1.40 mg/kg for veal calves (milk replacer); 0.86 mg/kg for dairy cows and other dairy ruminants; 1.32 mg/kg for cattle for fattening and other ruminants for fattening or for rearing, and horses; 0.53 mg/kg for rabbits; 1.51 mg/kg for salmonids and other fin fish, 1.58 mg/kg for dogs; 1.32 mg/kg for cats and 5.87 mg/kg for ornamental fish.

The maximum safe level of sodium chloride containing the additive requires comparison with the levels of NaCl used in the diets in order to establish a margin of safety. To this aim, the applicant was requested to provide practical data on the inclusion level of NaCl in complete feeds. The applicant submitted several publications concerning requirements/allowances/recommendations of Na for the relevant animal species/categories listed in the FEEDAP guidance on the safety of the feed additive for the target species (EFSA FEEDAP Panel, 2017a,b,c) and proposed to assume that all the required Na is supplemented by NaCl notwithstanding the contribution from the natural Na-content of feed materials. The FEEDAP Panel considered this proposal as a reasonable and conservative estimate of NaCl addition to complete feed. The data sources including the conversion of the different Na-dimensions used in the publications to a NaCl concentration in complete feed are listed in the Appendix A (Table A.1), and the proposed maximum NaCl supplementation levels are reported in Table 1.

Table 1: Maximum safe concentration of ferrocyanide anion in complete feed and of ferrocyanide-supplemented NaCl for different target animals

Animal category	Default values		Maximum safe concentration in complete feed[(1)]		Proposed maximum NaCl supplementation in complete feed (%)	Margin of safety[(2)]
	Body weight (kg)	Feed intake (g DM/day)	Ferrocyanide (mg/kg)	NaCl (%)		
Chicken for fattening	2	158	0.33	0.42	0.50	None
Laying hen	2	106	0.50	0.62	0.47	1.3
Turkey for fattening	3	176	0.45	0.56	0.37	1.5
Piglet	20	880	0.60	0.75	0.70	1.1
Pig for fattening	60	2,200	0.72	0.90	0.25	3.6
Sow lactating	175	5,280	0.88	1.09	0.50	2.2
Veal calf (milk replacer)	100	1,890	1.40	1.88	0.89	2.1
Cattle for fattening	400	8,000	1.32	1.65	0.18	9.2
Dairy cow	650	20,000	0.86	1.07	0.56	1.9
Sheep	60	1,200	1.32	1.65	0.13	12.7
Goat	60	1,200	1.32	1.65	0.20	8.3
Horse	400	8,000	1.32	1.65	1.42	1.2
Rabbit	2	100	0.53	0.66	0.51	1.3
Salmon	0.12	2.1	1.51	1.89	0.71	2.7
Dog	15	250	1.58	1.98	0.49	4.0
Cat	3	60	1.32	1.65	0.36	4.6
Ornamental fish	0.012	0.054	5.87	7.33	–	–

(1): Complete feed dry matter (DM) = 88%, milk replacer DM = 94.5%.
(2): Margin of safety calculated as the ratio between the proposed maximum NaCl supplementation and the maximum safe NaCl (containing the additive) level in complete feed.

When considering (i) the proposed conditions of use (80 mg ferrocyanide anions/kg sodium chloride), (ii) the default values used in Table 1 and (iii) the conservative assumption provided by the applicant on high salt supplementation of complete feed, the margin of safety denotes that the use of sodium ferrocyanide and potassium ferrocyanide is safe for: turkey for fattening and laying hens and other laying/breeding birds; all porcine species and categories, all ruminant species and categories, rabbit, horse, salmonids and other minor fin fish, dogs and cats. In the absence of a margin of safety, the use of sodium and potassium chloride according to the proposed conditions of use is not considered to be safe for chickens for fattening and other poultry species for fattening or reared for laying/breeding, except for turkeys. In the absence of information on the use of sodium chloride in the diets for any other animal species, no conclusion on a potentially safe level of sodium chloride, supplemented with 80 mg ferrocyanide/kg, can be made.

The FEEDAP Panel notes that the above assessment is based on the assumption that sodium chloride is the only dietary source of ferrocyanide anions, since safety estimate for maximum content of supplemented sodium chloride is derived from the ferrocyanide safety. Any other source of ferrocyanide would reduce the margin of safety given for the use of supplemented sodium chloride in the different animal species/categories. The only figure which is independent from the use of any other feed material containing or supplemented with ferrocyanide is the maximum dietary concentration of ferrocyanide in complete feed.

3.2.3.1. Conclusions on the safety for the target species

The maximum safe concentration of ferrocyanide ions, either from sodium- or potassium ferrocyanide, in complete feed corresponds to: 0.33 mg/kg chickens for fattening and other poultry species for fattening or reared for laying/breeding; 0.45 mg/kg for turkey for fattening; 0.50 mg/kg for laying hens and other laying/breeding birds; 0.60 mg/kg for piglets; 0.72 mg/kg for pigs for fattening; 0.88 mg/kg for sows and minor porcine species; 1.40 mg/kg for veal calves (milk replacer); 0.86 mg/kg for dairy cows and other dairy ruminants; 1.32 mg/kg for cattle for fattening and other ruminants for fattening or for rearing, and horses; 0.53 mg/kg for rabbits; 1.51 mg/kg for salmonids and other fin fish, 1.58 mg/kg for dogs; 1.32 mg/kg for cats and 5.87 mg/kg for ornamental fish.

The use of sodium ferrocyanide and potassium ferrocyanide is safe, when added to sodium chloride at a maximum content of 80 mg ferrocyanide anions (anhydrous)/kg for: turkey for fattening and laying hens and other laying/breeding birds; all porcine species and categories, all ruminant species and categories, rabbit, horse, salmonids and other minor fin fish, dogs and cats. In the absence of a margin of safety, the use of sodium and potassium ferrocyanide according to the proposed conditions of use is not considered to be safe for chickens for fattening and other poultry species for fattening or reared for laying/breeding, except for turkeys. In the absence of information on the use of sodium chloride in the diets for any other animal species, no conclusion on a potentially safe level of sodium chloride, supplemented with 80 mg ferrocyanide/kg, can be made.

3.2.4. Safety for the consumer

3.2.4.1. Assessment of consumer exposure and consumer safety

No residue data in tissues and products resulting from the use of sodium ferrocyanide decahydrate or potassium ferrocyanide trihydrate incorporated in NaCl in the target species were submitted by the applicant.

The applicant proposed instead to estimate consumer exposure on the basis of a theoretical worst-case model applied to dairy cows, the only target species for which ADME data are known for a similar additive (AFCF, see Section 3.2.1). The study of Arnaud et al. (1988) showed that ferrocyanide did not accumulate in edible tissues (e.g. liver and muscle) of dairy cows and that the small amount absorbed could be found in urine and milk. Consequently, it appears reasonable to base a consumer exposure model on the intake of cow's milk as the only source of ferrocyanide applying highly conservative uncertainties factors (UFs) at the different steps of the calculation. The FEEDAP Panel agreed to this proposal.

Default settings of the model proposed by the applicant were: (i) ferrocyanide is considered as the residue of concern, since the ADI is related to that anion of the additives under assessment, (ii) all ingested ferrocyanide is absorbed in the intestine and fully bioavailable (from the available information, less than 10% of the ingested ferrocyanides are absorbed (see 3.2.1), (iii) 10% of the ingested ferrocyanide is excreted unchanged via milk (published data on ferrocyanides show excretion of ferric ammonium hexacyanoferrate via milk of less than 0.1% of the total dose administered, see Section 3.2.1). The FEEDAP Panel accepted the above proposals of the applicant and added other proposals by setting default values as follows: (iv) the content of salt used in the target animal safety calculation is 5.6 g NaCl/kg complete feed, and (v) feed intake data and milk yield of dairy cows are based on equations derived from feeding studies with individual cows (assumptions: Simmental, 2nd lactation, 670 kg bw, 160 days in milk, 6.2 MJ NEL/kg forage DM, 6.7 MJ NEL/kg concentrate DM).[20]

The calculations were made considering the above assumption for a range of milk yields between 20 and 36 L/day, corresponding to a range of dry matter intake of 16.7 to 23.3 kg/day (calculations reported in Annex B). The highest concentration of ferrocyanide in milk (0.043 mg/L) resulted from cows with the lowest milk yield (20 L milk/day, 16.7 kg dry matter intake).

The FEEDAP Panel performed an exposure assessment following the methodology described in the Guidance on consumer safety (EFSA FEEDAP Panel, 2017a,b,c) (Appendix C), using the estimated residue data in milk from dairy cows.

The exposure of the consumer to ferrocyanide was calculated on the basis of the highest reliable percentile (HRP) of food consumption (raw agricultural food commodities), expressed in mg/kg bw per day for the different population categories and compared with the ADI established by EFSA ANS Panel (2018). The highest concentration of ferrocyanide in milk (0.043 mg/L) was used to estimate exposure of the consumer.

The results of the dietary exposure to ferrocyanide form dairy milk for the different population categories are reported in Table 2.

Table 2: Chronic human dietary exposure to ferrocyanide anion from milk of dairy cows fed with the additives sodium ferrocyanide or potassium ferrocyanide. Maximum highest reliable percentile expressed in mg/kg bw per day

Population class	Number of surveys	Maximum highest reliable percentile	% ADI*
Infants	6	0.0053	18
Toddlers	10	0.0053	18
Other children	18	0.0069	23
Adolescents	17	0.0025	8
Adults	17	0.0014	5
Elderly	14	0.0012	4
Very elderly	12	0.0014	5

*ADI: acceptable daily intake: 0.03 mg/kg bw day.

The calculated exposure resulted in values (maximum HRP) between 0.0012 and 0.0069 mg/kg bw per day for the different population classes, which corresponds to 4 and 23% of the ADI (0.03 mg ferrocyanide anion/kg body weight (EFSA ANS Panel, 2018)). The highest exposure, with a maximum HRP of 0.0069 mg/kg bw per day, was observed for 'other children', the maximum HRP for adults was 0.0014 mg/kg body weight per day.

In this context, it is noted that both additives can also be used as food additives. The EFSA ANS Panel (EFSA ANS Panel, 2018) estimated the exposure to ferrocyanides resulting from its use in food. The highest exposure to ferrocyanides (calculated based on regulatory maximum permitted level) was up to 0.009 mg/kg body weight per day in children and adolescents. The ANS Panel considered that the uncertainties identified indicate an overestimation of the exposure to ferrocyanides.

Considering both estimates, the exposure of consumers to ferrocyanides from the simultaneous use of sodium ferrocyanide and/or potassium ferrocyanide as food and feed additives would not exceed the ADI.

3.2.4.2. Conclusions on the safety for the consumer

The FEEDAP Panel concludes that the use of the feed additives sodium ferrocyanide or potassium ferrocyanide incorporated in sodium chloride (providing a maximum of 80 mg ferrocyanide/kg NaCl) does not raise concerns on the safety for the consumers.

3.2.5. Safety for the user

No specific information on the inhalation toxicity of sodium and potassium ferrocyanide was provided. The high dusting potential of sodium ferrocyanide (range 505–1,505 mg/m^3) makes exposure by inhalation likely. In contrast, the respiratory exposure to potassium-ferrocyanide is unlikely owning to its low dusting potential (range 15–60 mg/m^3).

[20] Futteraufnahme bei der Milchkuh, Bayerische Landesanstalt für Landwirtschaft (2006). https://www.lfl.bayern.de/mam/cms07/ite/dateien/zuteilungstabellen_fleckvieh_braunvieh.pdf

The highest nickel content analysed in the sodium ferrocyanide was 5.58 mg/kg. The highest dusting potential of the product was 1,505 mg/m^3, corresponding to about 0.001 mg Ni/m^3. This value would not exceed the transitional limit value of 0.1 mg Ni/m^3 for the inhalable fraction and 8 h time-weighted average (8 h TWA) exposure established in Directive (EU) 2022/431.[21] However, due to the presence of nickel, the additive should be considered as a respiratory and dermal sensitiser.

To test the irritation potential to skin and eye and the skin sensitisation potential of the additives, the applicant submitted studies done with sodium ferrocyanide.

The skin irritation potential of sodium ferrocyanide was tested in a study performed according to the OECD Guideline 404, which showed that it is not a skin irritant.[22]

The eye irritation potential of sodium ferrocyanide was tested in a study performed according to OECD Guideline 405, which showed that it is not an eye irritant.[23]

A local lymph node assay was performed to assess the skin sensitisation potential of sodium ferrocyanide, in line with the OECD Guideline 429[24] and the Method B42 Skin sensitization of Commission Regulation (EC) No 440/2008[25]. The results showed that sodium ferrocyanide is not a skin sensitiser.

The FEEDAP Panel notes that, since (i) the sodium salt and the potassium salt of ferrocyanide will dissociate to sodium and potassium ions and ferrocyanide anions when in contact with water, (ii) the additives have a high purity (> 99.5% active substance for both additives) and (iii) the toxicity of sodium and potassium ferrocyanide could be attributed to the ferrocyanide anion only, the FEEDAP Panel considered that the results of the studies obtained with sodium ferrocyanide could be used to conclude also on the safety for the user of potassium ferrocyanide.

3.2.5.1. Conclusions on safety for the user

In vivo studies showed that sodium and potassium ferrocyanide are not irritant to skin and eyes and are not skin sensitisers. However, owing to the presence of nickel, sodium ferrocyanide should be considered a dermal and respiratory sensitiser. No conclusions could be drawn on the potential effects on the respiratory system of potassium ferrocyanide.

3.2.6. Safety for the environment.

To assess the safety for the ferrocyanide ions for the environment, the maximum proposed inclusion levels in the diets of sodium chloride (see Table 1) supplemented with the maximum content of 80 mg ferrocyanide/kg NaCl was used to calculate the predicted environmental concentration (PEC) of ferrocyanide in soil, in line with the FEEDAP Guidance on the evaluation of the safety of feed additives for the environment (EFSA FEEDAP Panel, 2019).

The use of the additives under these conditions results in concentrations of ferrocyanide in soil below the trigger value of 10 µg/kg. In addition, the very limited ecotoxicity information available[26] do not highlight any concern for the environment. Therefore, the use of the additives in animal nutrition is considered safe for the environment.

3.3. Efficacy

Sodium and potassium ferrocyanide are used as food additives, as anticaking agents in sodium and potassium chloride. It is reasonable to expect that the effect seen in food will be observed in feed when these additives are used in sodium chloride used in animal nutrition. Therefore, the Panel concludes that the additives under assessment are efficacious as anticaking agents in sodium chloride.

4. Conclusions

The FEEDAP Panel concluded that the use of sodium ferrocyanide and potassium ferrocyanide is safe, when added to sodium chloride at a maximum content of 80 mg ferrocyanide anions (anhydrous)/kg for: turkeys for fattening and laying hens and other laying/breeding birds; all porcine

[21] Directive (EU) 2022/431 of the European Parliament and of the Council of 9 March 2022 amending Directive 2004/37/EC on the protection of workers from the risks related to exposure to carcinogens or mutagens at work. OJ L 88, 16.3.2022, p. 1–14.

[22] Technical dossier/FAD-2011-0047 and FAD-2011-0048_ Supplementary Information September 2022/Annex_SIN_2–3.

[23] Technical dossier/FAD-2011-0047 and FAD-2011-0048_ Supplementary Information September 2022/Annex_SIN_2–4.

[24] Technical dossier/FAD-2011-0047 and FAD-2011-0048_ SIn_Oct18/Annex_SIN_3–3.

[25] Available online: https://www.unece.org/fileadmin/DAM/trans/danger/publi/ghs/ghs_rev04/English/ST-SG-AC10-30-Rev4e.pdf

[26] Technical dossier/FAD-2011-0047 and FAD-2011-0048_ SIn_September 2022/Annex_SIN_3–3.

species and categories, all ruminant species and categories, rabbit, horse, salmonids and other minor fin fish, dogs and cats. In the absence of a margin of safety, the use of sodium and potassium chloride according to the proposed conditions of use is not considered to be safe for chickens for fattening and other poultry species for fattening or reared for laying/breeding other than turkeys. In the absence of information on the use of sodium chloride in the diets for any other animal species, no conclusion on a potentially safe level of sodium chloride, supplemented with 80 mg ferrocyanide anions (anhydrous)/kg, could be made.

The use of sodium and potassium ferrocyanide in animal nutrition under the conditions of use proposed is of no concern for consumer safety.

The results of *in vivo* studies showed that sodium and potassium ferrocyanide are not irritant to skin and eye and are not skin sensitisers. However, owing to the presence of nickel, sodium ferrocyanide is considered a dermal and respiratory sensitiser. No conclusions could be reached on safety for the user exposed via inhalation for potassium ferrocyanide.

The use of sodium and potassium ferrocyanide as feed additives is considered safe for the environment.

Sodium and potassium ferrocyanide are considered to be efficacious as anticaking agents when included in sodium chloride at the proposed use levels.

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Abbreviations

ADI	acceptable daily intake
ADME	absorption, distribution, metabolism and excretion
AFC	EFSA Scientific Panel on Food Additives, Flavourings, Processing Aids and Materials in Contact with Food
AFCF	[^{14}C]hexacyanoferrate
ANS	EFSA Scientific Panel on Additives and Nutrient Sources added to Food
bw	body weight
CAS	Chemical Abstracts Service
DM	dry matter
ECHA	European Chemicals Agency
EINECS	European Inventory of Existing Chemical Substances
ELS	extensive literature search
EURL	European Union Reference Laboratory
FAO	Food Agricultural Organization
FEEDAP	EFSA Scientific Panel on Additives and Products or Substances used in Animal Feed
JECFA	The Joint FAO/WHO Expert Committee on Food Additives
LOQ	limit of quantification
NOAEL	no observed adverse effect level
OECD	Organisation for Economic Co-operation and Development
SCAN	Scientific Committee on Animal Nutrition
SCF	Scientific Committee on Food
UF	uncertainty factor
WHO	World Health Organization

Appendix A – Sodium chloride supplementation in complete feedingstuffs

Table A.1: Sodium-requirements/allowances/recommendations for target species

Target species	Source	Data-type	Dimension	Na requirement	Na (%) in complete feed(1)	NaCl (%) in complete feed
Chicken for fattening	NRC (1994)	Requirements	% complete feed (90% DM(2))	0.20	0.20	0.50
Laying hen				0.19	0.19	0.47
Turkey for fattening				0.15	0.15	0.37
Piglet	NRC (2012)	Requirements	% complete feed (90% DM)	0.28	0.27	0.70
Pig for fattening				0.10	0.10	0.25
Sow				0.20	0.20	0.50
Calf (milk replacer)	NRC (2001)	Recommendation	% in DM	0.40	0.352	0.89
Dairy cow	NRC (2001)	Requirements derived from model diets	% in DM	0.22	0.22	0.56
Cattle for fattening	NRC 4	Requirements	% in DM	0.08	0.07	0.18
Sheep	NRC (2007)	Requirements	% in DM	0.06	0.05	0.13
Goat				0.09	0.08	0.20
Horse, work	FND (2016)	Exemplary ration	g/d	56	0.56	1.42
Rabbit	NRC (1977)	Adequate level	% in diet	0.2	0.2	0.51
Salmonids	Philip et al. (2022)	Trouw premix composition	% in diet	0.28	0.28	0.71
Dog	FEDIAF (2019)	Recommendation	g/100 g DM	0.22	0.19	0.49
Cat				0.16	0.14	0.36

(1): Complete feed with 88% DM (milk replacer 94.5%).
(2): DM: dry matter.

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Appendix B – Calculated ferrocyanide content in milk

Table B.1: Ferrocyanide anion (FC) intake and content in milk of dairy cows at different yielding stages when fed complete feed containing 0.56% NaCl, supplemented with 80 mg ferrocyanide form sodium or potassium ferrocyanide, with the assumption that 10% of ingested FC is excreted via milk

FC in NaCl (mg/kg)	NaCl in feed (g/kg)	DM intake (kg/day)	Feed intake (kg/day)	NaCl intake (g/day)	FC intake (mg/day)	Milk yield (L/day)	FC in milk (mg/L)
80	5.6	16.7	19.0	106	8.5	20	0.043
80	5.6	18.6	21.1	118	9.5	24	0.039
80	5.6	20.5	23.3	130	10.4	28	0.037
80	5.6	22.4	25.5	143	11.4	32	0.036
80	5.6	23.3	27.6	155	12.4	36	0.034

Appendix C – Detailed results of chronic exposure calculation

Table C.1: Chronic dietary exposure of consumers to residues of ferrocyanide anion per population class, country and survey (mg/kg bw per day) based on residue data

Population class	Survey's country	Number of subjects	Highest reliable percentile value	Highest reliable percentile description
Infants	Bulgaria	523	0.00534	95th
Infants	Germany	142	0.00290	95th
Infants	Denmark	799	0.00409	95th
Infants	Finland	427	0.00334	95th
Infants	Italy	9	0.00141	50th
Infants	United Kingdom	1,251	0.00255	95th
Toddlers	Belgium	36	0.00442	90th
Toddlers	Bulgaria	428	0.00425	95th
Toddlers	Germany	348	0.00414	95th
Toddlers	Denmark	917	0.00444	95th
Toddlers	Spain	17	0.00249	75th
Toddlers	Finland	500	0.00526	95th
Toddlers	Italy	36	0.00331	90th
Toddlers	Netherlands	322	0.00388	95th
Toddlers	United Kingdom	1,314	0.00430	95th
Toddlers	United Kingdom	185	0.00417	95th
Other children	Austria	128	0.00692	95th
Other children	Belgium	625	0.00384	95th
Other children	Bulgaria	433	0.00342	95th
Other children	Germany	293	0.00345	95th
Other children	Germany	835	0.00248	95th
Other children	Denmark	298	0.00331	95th
Other children	Spain	399	0.00252	95th
Other children	Spain	156	0.00272	95th
Other children	Finland	750	0.00379	95th
Other children	France	482	0.00352	95th
Other children	Greece	838	0.00344	95th
Other children	Italy	193	0.00269	95th
Other children	Latvia	187	0.00248	95th
Other children	Netherlands	957	0.00315	95th
Other children	Netherlands	447	0.00260	95th
Other children	Sweden	1,473	0.00305	95th
Other children	Czechia	389	0.00382	95th
Other children	United Kingdom	651	0.00269	95th
Adolescents	Austria	237	0.00184	95th
Adolescents	Belgium	576	0.00135	95th
Adolescents	Cyprus	303	0.00112	95th
Adolescents	Germany	393	0.00183	95th
Adolescents	Germany	1,011	0.00138	95th
Adolescents	Denmark	377	0.00159	95th
Adolescents	Spain	651	0.00139	95th

Population class	Survey's country	Number of subjects	Highest reliable percentile value	Highest reliable percentile description
Adolescents	Spain	209	0.00155	95th
Adolescents	Spain	86	0.00110	95th
Adolescents	Finland	306	0.00182	95th
Adolescents	France	973	0.00179	95th
Adolescents	Italy	247	0.00154	95th
Adolescents	Latvia	453	0.00161	95th
Adolescents	Netherlands	1,142	0.00167	95th
Adolescents	Sweden	1,018	0.00182	95th
Adolescents	Czechia	298	0.00252	95th
Adolescents	United Kingdom	666	0.00129	95th
Adults	Austria	308	0.00130	95th
Adults	Belgium	1,292	0.00116	95th
Adults	Germany	10,419	0.00121	95th
Adults	Denmark	1,739	0.00105	95th
Adults	Spain	981	0.00109	95th
Adults	Spain	410	0.00108	95th
Adults	Finland	1,295	0.00141	95th
Adults	France	2,276	0.00119	95th
Adults	Hungary	1,074	0.00093	95th
Adults	Ireland	1,274	0.00091	95th
Adults	Italy	2,313	0.00096	95th
Adults	Latvia	1,271	0.00100	95th
Adults	Netherlands	2,055	0.00116	95th
Adults	Romania	1,254	0.00084	95th
Adults	Sweden	1,430	0.00107	95th
Adults	Czechia	1,666	0.00122	95th
Adults	United Kingdom	1,265	0.00088	95th
Elderly	Austria	67	0.00094	95th
Elderly	Belgium	511	0.00125	95th
Elderly	Germany	2,006	0.00115	95th
Elderly	Denmark	274	0.00103	95th
Elderly	Finland	413	0.00121	95th
Elderly	France	264	0.00101	95th
Elderly	Hungary	206	0.00092	95th
Elderly	Ireland	149	0.00106	95th
Elderly	Italy	289	0.00082	95th
Elderly	Netherlands	173	0.00106	95th
Elderly	Netherlands	289	0.00101	95th
Elderly	Romania	83	0.00070	95th
Elderly	Sweden	295	0.00106	95th
Elderly	United Kingdom	166	0.00097	95th
Very elderly	Austria	25	0.00068	75th
Very elderly	Belgium	704	0.00141	95th
Very elderly	Germany	490	0.00124	95th

Population class	Survey's country	Number of subjects	Highest reliable percentile value	Highest reliable percentile description
Very elderly	Denmark	12	0.00064	75th
Very elderly	France	84	0.00095	95th
Very elderly	Hungary	80	0.00109	95th
Very elderly	Ireland	77	0.00093	95th
Very elderly	Italy	228	0.00090	95th
Very elderly	Netherlands	450	0.00105	95th
Very elderly	Romania	45	0.00075	90th
Very elderly	Sweden	72	0.00123	95th
Very elderly	United Kingdom	139	0.00113	95th