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## Safety of Lancer<sup>®</sup> (lanthanide citrate) as a zootechnical additive for weaned piglets

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### Abstract

Following a request from the European Commission, the Panel on Additives and Products or Substances used in Animal Feed (FEEDAP) was asked to deliver a scientific opinion on the additional data submitted on Lancer<sup>®</sup> when used as a feed additive for weaned piglets. The FEEDAP Panel considered that uncertainty still remains on possible developmental neurotoxicity of Lancer<sup>®</sup> since it was unable to identify a no observed adverse effect level (NOAEL) for this specific endpoint applying a read-across strategy from the studies provided by the applicant. However, the FEEDAP Panel considered that the exposure to La and Ce from products of animals treated with Lancer<sup>®</sup> at 250 mg/kg feed would not add a significant contribution to the background exposure of these elements. The FEEDAP Panel concluded that the use of Lancer<sup>®</sup> in feed for weaned piglets (up to 120 days) according to the proposed conditions of use, does not represent a safety concern for the consumer and for the environment.

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**Keywords:** lanthanide citrate, Lancer<sup>®</sup>, zootechnical additive, weaned piglets, safety

**Requestor:** European Commission

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## 1. Introduction

### 1.1. Background and Terms of Reference as provided by the requestor

Regulation (EC) No 1831/2003<sup>1</sup> establishes the rules governing the Community authorisation of additives for use in animal nutrition. In particular, Article 9 of that Regulation defines the terms of the authorisation by the Commission.

The Applicant, Treibacher Industrie AG, is seeking a Community authorisation of Lanthanide citrate as feed additive to be used as zootechnical additive for piglets (weaned) (Table 1).

**Table 1:** Description of the substance

|                                     |                              |
|-------------------------------------|------------------------------|
| <b>Category of additive</b>         | Zootechnical additive        |
| <b>Functional group of additive</b> | Other zootechnical additives |
| <b>Description</b>                  | Lanthanide-citrate           |
| <b>Target animal category</b>       | Piglets (weaning)            |
| <b>Applicant</b>                    | Treibacher Industrie AG      |
| <b>Type of request</b>              | New opinion                  |

On 20 April 2016, the Panel on Additives and Products or Substances used in Animal feed of the European Food Safety Authority ("Authority"), in its opinion on the safety and efficacy of the product, could not conclude on the safety of Lanthanide-citrate. After the discussion with the Member States on the last Standing Committee, it was suggested to check for the possibility to demonstrate the safety for the environment.

The Commission gave the possibility to the applicant to submit complementary information in order to complete the assessment and to allow a revision of Authority's opinion. The new data have been received on 27 May 2019.

In view of the above, the Commission asks the Authority to deliver a new opinion on Lanthanide-citrate as feed additive for piglets (weaned) based on the additional data submitted by the applicant.

### 1.2. Additional information

Lancer® (lanthanide citrate) has not previously been authorised in the European Union (EFSA FEEDAP Panel, 2013, 2016).

## 2. Data and methodologies

### 2.1. Data

The present assessment is based on data submitted by the applicant in the form of additional information<sup>2</sup> to a previous application on the same product.<sup>3</sup>

### 2.2. Methodologies

The approach followed by the FEEDAP Panel to assess the safety for the consumer and the environment of lanthanide-citrate (Lancer®) is in line with the principles laid down in Regulation (EC) No 429/2008<sup>4</sup> and the relevant guidance documents: Guidance on the assessment of the safety of feed additives for the consumer (EFSA FEEDAP Panel, 2017) and Technical Guidance for assessing the safety of feed additives for the environment (EFSA, 2008).

## 3. Assessment

The additive Lancer® mainly consists of two rare earth elements, lanthanum (La) and cerium (Ce), in their citrate forms. It is intended to be used as a zootechnical additive (functional group: other

<sup>1</sup> 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.

<sup>2</sup> FEED dossier reference: FAD-2019-0040.

<sup>3</sup> FEED dossier reference: FAD-2015-0041.

<sup>4</sup> 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.

zootechnical additives) in feed for weaned piglets up to 120 days of age. This additive has not previously been authorised in the European Union.

In 2013, the EFSA FEEDAP Panel (2013) was unable to conclude on the safety of Lancer® (lanthanide citrate) for the target species, the consumer and the environment. In 2016, the FEEDAP Panel issued a new opinion (EFSA FEEDAP Panel, 2016) and concluded that the additive is safe for the target species. However, the FEEDAP Panel was unable to conclude on the safety of the additive for the consumer (due to the concern over the possible developmental neurotoxicity of La and the lack of residue study) and for the environment (due to inadequate data on plant and on earthworm ecotoxicity and lack of data on concentration of La and Ce in ground water).

The applicant has submitted additional information related to the safety of the additive for the consumer and the environment and this new information is the subject of this opinion.

### 3.1. Characterisation

The characterisation of the additive, the manufacturing process, stability and homogeneity were reviewed in a previous opinion (EFSA FEEDAP Panel, 2013).

La and Ce are present in the additive Lancer® as citrate chelates (water solubility: 85 g/L). According to the specification, the additive consists of 65% lanthanide citrate (La  $8.5 \pm 0.9\%$ ; Ce  $16.3 \pm 1.6\%$ ; citrate:  $40 \pm 5\%$ ). The rest of the additive consists of water ( $< 10\%$ ), sodium ( $10 \pm 2\%$ ), chloride ( $10 \pm 2\%$ ), other lanthanides (praseodymium (Pr) 2.0%, neodymium (Nd) 0.08%) and trace elements ( $< 0.45\%$ ) (EFSA FEEDAP Panel, 2013).

The applicant provided new analytical results on the purity measured on three batches of the additive indicating that the trace elements and minor rare earths (sum of Pr, Nd, iron, zinc and copper) represent  $< 0.35\%$  of the additive.<sup>5</sup>

Lancer® (lanthanide citrate) is intended for use in weaned piglets (up to 120 days of age) at a concentration of 250 mg/kg complete feedingstuffs either by direct addition to feed or via premixture (EFSA FEEDAP Panel, 2013).

### 3.2. Safety

#### 3.2.1. Safety for the consumer

The safety of the additive Lancer® for the consumer was assessed by the FEEDAP Panel considering the following: (i) the previous assessment of the EFSA FEEDAP Panel, (ii) the approach of the read-across proposed by the applicant and (iii) the results of the new residue study.

##### 3.2.1.1. Previous assessments by FEEDAP Panel

In 2013, the EFSA FEEDAP Panel could not conclude on the safety for the consumer due to some inconsistencies in the data available. One study demonstrated that after feeding piglets with lanthanide citrate at 2,500 mg/kg feed, no deposition of La and Ce in kidney, liver and muscles occurred (Von Rosenberg et al., 2013). However, other two studies available reported absorption and deposition of La and Ce after ingestion of rare earth elements (REE) supplementation, in bulls (in liver, kidney and bone) and rats (in liver, kidney, heart, spleen, brain, lung and bone) (Schwabe et al., 2012; Ji et al., 1985). The 90-day repeated dose oral toxicity study performed in rats did not allow to identify a no observed adverse effect level (NOAEL) for Lancer® since adverse effects (hyperplasia of the forestomach epithelium) were observed at all doses tested. In the absence of a NOAEL, the FEEDAP Panel was unable to relate any possible exposure to evidence of a safe dose.

Following the EFSA opinion in 2013, the applicant submitted a review of the histopathological findings of the 90-day study performed in rats exposed to Lancer®. The FEEDAP Panel evaluated the review proposed by the applicant and considered that the forestomach and its sensitivity to local irritants has no equivalent in humans, hence considered the effects described as not relevant for human risk assessment. The FEEDAP Panel identified a no observed effect level (NOEL) of 300 mg Lancer®/kg body weight (bw) per day (based on the effects observed in the forestomach) and a NOAEL of 600 mg Lancer®/kg bw per day (the highest dose tested). The FEEDAP Panel also noted that LaCl<sub>3</sub> induced adverse effects on neurobehavioural development in mice at doses of 25 mg LaCl<sub>3</sub>/kg bw per day (9.3 mg La/kg bw per day) or more. The same compound caused neurotoxicological effects at doses of 2 mg LaCl<sub>3</sub>/kg bw per day (0.73 mg La/kg bw per day) or more in rats exposed throughout gestation and

<sup>5</sup> Technical dossier/Annexes/Annex 1.

lactation and the first 6 months of life. This raised a concern about whether Lancer® could cause similar effects (Briner et al., 2000). The FEEDAP Panel considered that this would raise the need for an investigation of the possible reproduction/developmental toxicity of Lancer®, including a consideration of possible neurodevelopmental effects. Ce citrate was previously assessed by the US Environmental Protection Agency (EPA, 2009). The toxicological data available to the EPA did not allow the establishment of an acceptable daily intake (ADI) due to the paucity or absence of relevant data on genotoxicity, carcinogenicity, reproductive toxicity and target organ toxicity (EFSA FEEDAP Panel, 2016).

### 3.2.1.2. Assessment of the additional data received

In the current dossier, the applicant is proposing to use absorption, distribution, metabolism and excretion (ADME) and toxicological data available for La and Ce salts other than citrate within a read-across strategy, in order to fill the data gaps identified in previous EFSA evaluations as concern the safety for the consumer (EFSA FEEDAP Panel, 2013, 2016),<sup>6, 7</sup>

La and Ce are present in the additive Lancer® as citrate chelates. According to the applicant, 'these complexes dissociate and form the individual rare earths with citrate or other anions'. Citric acid is an intermediate in cellular oxidative metabolism, in the citric acid cycle. When supplemented in feedingstuffs, it is expected to be completely metabolised in the target species. Therefore, the use of citric acid in animal nutrition is safe for the consumer.

According to the applicant, for many metals, the metal ions are responsible for the toxicity, regardless of the counterparts. However, the FEEDAP Panel considers that this assumption is not applicable in general since counter ions or complexing agents may strongly affect toxicological properties and biochemical interactions for example by having an impact on the dissociation and solubility.

The FEEDAP Panel notes that, in the documentation provided by the applicant, data showing similarity of La/Ce citrate (the components of the additive Lancer®) as concern water solubility, dissociation, biochemical/toxicological properties with other La/Ce salts, are not present.

Furthermore, the FEEDAP Panel considers that for applying a read-across approach, a more detailed physicochemical characterisation of the additive would be needed, allowing a comparison of relevant parameters with those of other relevant La/Ce compounds (e.g. specification of molecular and structural formulas, including hydrates, ratio of the two components, indication of physicochemical parameters influencing kinetics such as solubility in water and at physiological pHs, dissociation, complex stability).

The applicant did not provide any study testing the additive Lancer®, however, submitted the results of some studies published in literature on the ADME of La salts.

Overall, for La, available kinetic studies performed with oral exposure refer exclusively to La carbonate, which is insoluble in water and therefore may differ in its kinetic behaviour from water-soluble La compounds (low potential of systemic absorption). Animal and human data show that La from orally administered La carbonate exhibits low gastrointestinal absorption (Damment and Pennick, 2007; D'Haese et al., 2019). The small fraction of La absorbed is distributed systemically to tissues, showing accumulation especially in the liver. This accumulation increases over time (Slatopolsky et al., 2005; D'Haese et al., 2019). An *in vitro* binding study demonstrated that La is bound to plasma proteins up to 99.7% (Damment and Pennick, 2007).

According to the study by Hollriegel et al. (2017), Ce citrate appears to be poorly absorbed after a single oral dose in human volunteers.

The applicant did not provide any study performed with the additive Lancer®, however presented findings from toxicological studies performed with La and Ce salts other than citrate, proposing a read-across strategy as described above as well as a literature search. The studies provided were performed in compliance with the OECD Guideline 414 and 422. Due to the non-applicability of the read-across strategy as described above and also in the light of the new data provided, the FEEDAP Panel considered that the concern on the possible developmental neurotoxicity of Lancer® (as highlighted in the previous EFSA opinion in 2016) remains.

Based on the above, the FEEDAP Panel is of the view that the read-across approach, as proposed by the applicant, is not acceptable to fill the data gaps identified in previous EFSA opinions.

<sup>6</sup> Technical dossier/Annexes/Annex 4.

<sup>7</sup> Technical dossier/Annexes/Annex 5.

### 3.2.1.3. Residue studies

In a good laboratory practice (GLP) study, 128 piglets (approximately 28 days old, 32 males and 32 females per treatment, 16 replicate pens per treatment, 8 castrated males and 8 females) were administered Lancer® at a nominal level of 250 mg/kg feed (confirmed by analysis) or basal diet (control), for 126 consecutive days. At days 42, 84 and 126, eight animals per treatment (4 females and 4 castrated males) were slaughtered for analysis of La and Ce contents in heart, liver, kidney, muscle, skin and subcutaneous fat and bone. Residues were analysed by inductively coupled plasma mass spectrometry (ICP-MS) (limit of detection (LoD): La 0.54 ng/kg, Ce 0.43 ng/kg; limit of quantification (LoQ): La 1.80 ng/kg, Ce 1.44 ng/kg). La and Ce contents in organ samples are reported in Table 2 (dry matter (DM) basis). The values expressed as DM were converted to fresh weight basis by the applicant (Table 3) (using the analysed DM content of the respective organ) and the values recorded at day 126 (Table 4) were used to estimate the human exposure to La and Ce by means of the exposure methodology described in the EFSA guidance on consumer safety (EFSA FEEDAP Panel, 2017). The results are shown in Table 5.

**Table 2:** Residues (expressed as ng lanthanum or cerium/kg tissue dry matter) measured in tissues from piglets (8 animals per treatment – 4 males and 4 females) fed 250 mg Lancer®/kg feed for 126 days

| Organs/tissues<br>Day of sampling | La (ng/kg DM)           |                           | Ce (ng/kg DM)           |                           |
|-----------------------------------|-------------------------|---------------------------|-------------------------|---------------------------|
|                                   | Lancer®<br>0 mg/kg feed | Lancer®<br>250 mg/kg feed | Lancer®<br>0 mg/kg feed | Lancer®<br>250 mg/kg feed |
| <b>Heart</b>                      |                         |                           |                         |                           |
| D42                               | 4,287                   | 8,133*                    | 5,860                   | 15,865*                   |
| D84                               | 1,203                   | 5,092**                   | 1,487                   | 10,541**                  |
| D126                              | 1,190                   | 2,948**                   | 2,280                   | 6,498**                   |
| <b>Liver</b>                      |                         |                           |                         |                           |
| D42                               | 5,937                   | 60,776**                  | 10,148                  | 96,410**                  |
| D84                               | 4,268                   | 145,183**                 | 6,280                   | 240,001**                 |
| D126                              | 17,803                  | 175,468**                 | 29,665                  | 294,275**                 |
| <b>Kidney</b>                     |                         |                           |                         |                           |
| D42                               | 1,623                   | 45,186**                  | 2,967                   | 83,258**                  |
| D84                               | 966                     | 14,433**                  | 1,112                   | 29,733**                  |
| D126                              | 3,060                   | 13,742**                  | 6,709                   | 28,187**                  |
| <b>Muscle</b>                     |                         |                           |                         |                           |
| D42                               | 2,369                   | 6,608**                   | 3,636                   | 10,840**                  |
| D84                               | 1,265                   | 4,505**                   | 1,680                   | 9,458**                   |
| D126                              | 3,188                   | 2,493*                    | 6,648                   | 3,902*                    |
| <b>Skin + subcutaneous fat</b>    |                         |                           |                         |                           |
| D42                               | 5,076                   | 61,377**                  | 9,080                   | 113,435**                 |
| D84                               | 1,263                   | 8,539**                   | 1,567                   | 16,740**                  |
| D126                              | 1,714                   | 5,449**                   | 3,863                   | 10,051**                  |
| <b>Bone</b>                       |                         |                           |                         |                           |
| D42                               | 1,828                   | 5,525**                   | 1,020                   | 2,356**                   |
| D84                               | 2,406                   | 12,022**                  | 1,782                   | 8,483**                   |
| D126                              | 923                     | 10,289**                  | 840                     | 5,183**                   |

DM: dry matter.

\*:  $p < 0.5$ .

\*\* :  $p < 0.01$ .

**Table 3:** Total residues (expressed as ng lanthanum or cerium/kg tissue fresh weight) measured in tissues from piglets (8 animals per treatment – 4 males and 4 females) fed 250 mg Lancer®/kg feed for 126 days

| Organs/tissues<br>Day of sampling | La (ng/kg fresh weight) |                           | Ce (ng/kg fresh weight) |                           |
|-----------------------------------|-------------------------|---------------------------|-------------------------|---------------------------|
|                                   | Lancer®<br>0 mg/kg feed | Lancer®<br>250 mg/kg feed | Lancer®<br>0 mg/kg feed | Lancer®<br>250 mg/kg feed |
| <b>Heart</b>                      |                         |                           |                         |                           |
| D42                               | 857                     | 1,627                     | 1,172                   | 3,173                     |
| D84                               | 217                     | 1,018                     | 268                     | 2,108                     |
| D126                              | 238                     | 590                       | 456                     | 1,300                     |
| <b>Liver</b>                      |                         |                           |                         |                           |
| D42                               | 1,840                   | 18,233                    | 3,146                   | 28,923                    |
| D84                               | 1,195                   | 46,459                    | 1,758                   | 76,800                    |
| D126                              | 5,341                   | 52,640                    | 8,900                   | 88,282                    |
| <b>Kidney</b>                     |                         |                           |                         |                           |
| D42                               | 357                     | 10,393                    | 653                     | 19,149                    |
| D84                               | 174                     | 3,031                     | 200                     | 6,244                     |
| D126                              | 612                     | 2,748                     | 1,342                   | 5,637                     |
| <b>Muscle</b>                     |                         |                           |                         |                           |
| D42                               | 569                     | 1,652                     | 873                     | 2,710                     |
| D84                               | 266                     | 1,081                     | 353                     | 2,270                     |
| D126                              | 765                     | 598                       | 1,596                   | 936                       |
| <b>Skin + subcutaneous fat</b>    |                         |                           |                         |                           |
| D42                               | 2538                    | 27,006                    | 4540                    | 49,911                    |
| D84                               | 606                     | 4,526                     | 752                     | 8,872                     |
| D126                              | 1,114                   | 3,487                     | 2,511                   | 6,433                     |
| <b>Bone</b>                       |                         |                           |                         |                           |
| D42                               | 877                     | 2,652                     | 490                     | 1,131                     |
| D84                               | 1,444                   | 7,213                     | 1,069                   | 5,090                     |
| D126                              | 591                     | 6,688                     | 538                     | 3,369                     |

The amount of both La and Ce deposited in all animal tissues analysed (heart, liver, kidney, muscle tissue, skin/subcutaneous fat, bone) is higher in animals receiving Lancer at 250 mg/kg feed, compared to the control.

**Table 4:** Residue data derived from the use of 250 mg Lancer/kg feed in piglets<sup>(1)</sup>

| Organs/tissues      | La (ng/kg fresh weight) | Ce (ng/kg fresh weight) |
|---------------------|-------------------------|-------------------------|
|                     | Lancer® 250 mg/kg feed  | Lancer® 250 mg/kg feed  |
| Fat tissue          | 3,487                   | 6,433                   |
| Liver               | 52,640                  | 88,282                  |
| Meat <sup>(2)</sup> | 1,175.8                 | 2,035                   |
| Offals              | 2,748                   | 5,637                   |

(1): EFSA FEEDAP Panel, 2016.

(2): The residue concentration in muscle and skin/fat will be applied to the intake of meat at the following proportions: 80% muscle and 20% skin/fat (EFSA FEEDAP Panel, 2017). This corresponds to 0.0886 mg/kg.



**Table 5:** Chronic dietary exposure of consumers to lanthanum and cerium residues in tissues and products of piglets fed 250 mg Lancer/kg feed – Summary statistics across European dietary surveys

| Exposure to Lanthanum |                   |                           |
|-----------------------|-------------------|---------------------------|
|                       | Number of surveys | Highest exposure estimate |
| Infants               | 6                 | 30.86                     |
| Toddlers              | 10                | 35.67                     |
| Other children        | 18                | 26.38                     |
| Adolescents           | 17                | 18.11                     |
| Adults                | 17                | 24.26                     |
| Elderly               | 14                | 16.44                     |
| Very elderly          | 12                | 15.18                     |
| Exposure to cerium    |                   |                           |
|                       | Number of surveys | Highest exposure estimate |
| Infants               | 6                 | 52.24                     |
| Toddlers              | 10                | 60.58                     |
| Other children        | 18                | 44.77                     |
| Adolescents           | 17                | 31.14                     |
| Adults                | 17                | 41.43                     |
| Elderly               | 14                | 28.50                     |
| Very elderly          | 12                | 25.52                     |

bw: body weight.

Based on the results obtained, toddlers (La: 35.67 ng/kg bw per day; Ce 60.58 ng/kg bw per day) and infants (La: 30.86 ng/kg bw per day; cerium 52.24 ng/kg bw per day) were identified as the population age groups most exposed to residues of Lancer®.

In order to estimate the background exposure, the applicant submitted an estimation of the exposure to La and Ce from other dietary sources using the Food Additive Intake Model (FAIM)<sup>8</sup> tool (version 2) model using as input data gathered from published literature.<sup>9</sup> The details on the literature search were provided in the application dossier. The total number of publications used for the exposure assessment of natural occurrence in food of La and Ce were 66.

In order to use the FAIM tool, each of the food items from the literature was assigned to a food category as described in Part E of Annex II to Regulation (EC) No 1333/2008<sup>10</sup> on food additives.

The results are given in Table 6. The Panel noted that, according to the calculation performed by the applicant, exposure to both La and Ce occur in all population age groups. The highest exposure (95th percentile) were reported in infants followed by toddlers and other children.

**Table 6:** Chronic dietary exposure to lanthanum and cerium from dietary sources (ng/kg bw per day)

| Population category   | Mean (min–max)        |                       | 95th (min–max)        |                       |
|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|
|                       | La (ng/kg bw per day) | Ce (ng/kg bw per day) | La (ng/kg bw per day) | Ce (ng/kg bw per day) |
| Infants               | 170–950               | 200–930               | 300–1720              | 350–1660              |
| Toddlers              | 310–500               | 380–580               | 440–940               | 590–1050              |
| Other children        | 250–400               | 290–480               | 300–630               | 450–700               |
| Adolescents           | 130–250               | 170–300               | 210–430               | 290–500               |
| Adults                | 130–240               | 150–250               | 210–420               | 260–440               |
| Elderly, very elderly | 150–240               | 160–260               | 230–420               | 250–420               |

bw: body weight.

<sup>8</sup> Available at: <https://dwh.efsa.europa.eu/bi/asp/Main.aspx?rwtrep=FAIM>

<sup>9</sup> Technical dossier/Annexes/Annex 3b.

<sup>10</sup> 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. 16–33.

The Panel notes that the background exposure of consumers to La and Ce from dietary sources of food (naturally containing La and Ce) is higher than that resulting from exposure to animal tissues of pig fed with Lancer®. The FEEDAP Panel considers that the additional exposure deriving from the consumption of products from animals (weaned piglets) treated with Lancer® at 250 mg/kg feed would not add a significant contribution to the background exposure of the consumer to La and Ce.

#### **3.2.1.4. Conclusions on the safety for the consumer**

The FEEDAP Panel considers that uncertainty still remains on possible developmental neurotoxicity of Lancer®. However, considering that the exposure to La and Ce from products of animals treated with Lancer® at 250 mg/kg feed would not add a significant contribution to the background exposure of these elements, the FEEDAP Panel concludes that Lancer® (at 250 mg/kg feed for weaned piglets) is not of concern for the safety for the consumer.

### **3.2.2. Safety for the environment**

For the current assessment, the applicant addressed the limitation of the previous opinions and provided (i) estimates of the predicted environmental concentrations of La(III) and Ce(III) for soil and ground water and (ii) ecotoxicity studies for the terrestrial compartment (earthworms, plants and microorganisms) performed with Lancer®<sup>11,12,13</sup> to address possible toxicological effects of La(III) and Ce(III).

#### **3.2.2.1. Previous assessments by FEEDAP Panel**

In 2013, the FEEDAP Panel was not able to conclude on the safety of Lancer® for the environment for the following reasons: (i) La is potentially toxic to environmental relevant species, but its toxicity is highly dependent on speciation, (ii) although the additive would probably not cause a concern for the aquatic environment (because of the low solubility of La and Ce in most situations), there were no data on toxicity of the additive to terrestrial organisms. In the absence of such data, a full environmental assessment could not be completed (EFSA FEEDAP Panel, 2013).

In 2016, the FEEDAP Panel assessed the additional data submitted to support the safety of Lancer® for the environment (EFSA FEEDAP Panel, 2016)<sup>14</sup> as follows:

A summary of the occurrence of La and Ce in the soil and surface water in Europe was provided to justify that the use of Lancer® would not increase the environmental levels of La and Ce. No clear information on measured concentrations of La and Ce in the ground water of EU Member States was provided.

In ecosystems, species may adapt to higher concentrations of naturally occurring elements (such as lanthanides). Therefore, the assessment of environmental risk for La and Ce should be based on the concentrations which will be added to the environmental concentrations. The background concentrations of La and Ce in soil in EU Member State geographic area varies between 1–109 and 1.6 and 266 mg/kg, respectively; however, no calculation on the expected increase of the environmental concentration (predicted environmental concentrations – PEC) of La and Ce was provided.

No prediction of environmental concentrations of La and Ce in ground water based on use of Lancer® was provided.

The applicant did not provide adequate data on plant ecotoxicity according to OECD 208 (Terrestrial Plants, Growth Test) and on earthworm ecotoxicity according to OECD 207 (Earthworm, Acute Toxicity Test) or according to OECD 222 (Earthworm Reproduction Test).

Consequently, the safe concentrations for soil (calculated as predicted no effect concentration – PNEC) could not be set. No PECs and no PNEC values were provided and therefore, no risk quotient could be determined. Therefore, in the absence of adequate data, the FEEDAP Panel could not conclude on the safety of Lancer® for the environment<sup>1</sup>.

#### **3.2.2.2. Assessment of the new data received**

##### *Predicted environmental concentrations*

Predicted environmental concentrations (PECs) were calculated according to the EFSA guidance on the safety of feed additives for the environment (EFSA, 2008).

<sup>11</sup> Technical dossier/Section III\_Annex 18.

<sup>12</sup> Technical dossier/Section III\_Annex 19.

<sup>13</sup> Technical dossier/Section III\_Annex 20.

<sup>14</sup> Technical dossier FAD-2015-0041/Environmental risk assessment Lancer.

### Physicochemical properties

The physical chemical properties of Ce(III) and La(III) are summarised in the Table 7.

**Table 7:** Physicochemical properties of cerium (III) and lanthanum (III)

| Property                       | Cerium (III)            | Lanthanum (III)         | Lancer® |
|--------------------------------|-------------------------|-------------------------|---------|
| Molecular weight               | 140.116 g/mol           | 138.91 g/mol            | –       |
| Water solubility               | –                       | –                       | 85 g/L  |
| Vapour pressure <sup>(1)</sup> | $4.9 \times 10^{-4}$ Pa | $3.2 \times 10^{-8}$ Pa | –       |

(1): EPI Suite (2015).

### Absorption/Desorption studies for lanthanum and cerium compounds

The applicant reviewed literature data from a considerable body of studies to address the adsorption characteristics of the two lanthanides.<sup>15</sup> Data were available for soil, sediment, and suspended matter taken from the field and laboratory studies. The partition coefficient ( $K_p$ ) in soil was reported in different studies for the two lanthanides.

Considering lanthanum, a study investigating adsorption in Chinese soils indicated that La(III) sorption is rather determined by the presence of oxides and silicate clays than by  $\text{CaCO}_3$  and organic matter. The  $K_p$  derived from batch equilibrium experiments varies according to soil and experiments from  $\log K_p$  of 3.61 (Du et al., 1998) to similar  $\log K_p$  values of 2.12 to 3.02 (Shan et al., 2002), 3.61 and 3.72 (Zuyi et al., 2000) and 3.41 to 4.43 (Wen et al., 2002). In addition, batch equilibrium experiments performed with Australian soils (Stokes et al., 1999) yielded  $\log K_p$  values between 2.3 and 2.8.

A generic  $\log K_p$  value of 3.2 for soil is suggested for deriving the organic carbon–water partitioning coefficient ( $K_{oc}$ ) value for La(III).

Considering cerium, an analogous variation of  $K_p$  is reported in the different studies provided as a weight of evidence. Based on data from Du et al. (1998), a  $\log K_p$  of 2.6 L/kg could be obtained for Ce (III) in cultivated Chinese soil. Another batch equilibrium experiment with four Chinese soils yielded  $\log K_p$  values of 3.54–4.46 L/kg (Wen et al., 2002). In a multi-tracer study, the adsorption of cerium to two Chinese soils, a calcareous soil and a sandy red earth, was investigated in a batch equilibrium experiment.  $\log K_p$  values were 4.43 and 2.60 L/kg for the calcareous soil and red earth, respectively (Zuyi et al., 2000). The adsorption of Ce(III) and Ce(IV) was studied on 16 Australian soils in batch equilibrium experiments (Cornelis et al., 2011). Median  $\log K_p$  values were 3.58 and 3.26 L/kg for Ce (III) and Ce(IV), respectively. Finally, a batch equilibrium experiment with 4 Chinese soils for Ce(III) showed  $\log K_p$  values varying between 3.7 and 4.5 L/kg (Li et al., 2001). To determine a final key value for adsorption of cerium to soil, a single value (arithmetic mean) was retained for each soil in each study.

A generic  $\log K_p$  value of 3.5 is suggested for deriving  $K_{oc}$  value for Ce(III).

The  $\log K_p$  for soil of La(III) (3.2 L/kg) and for Ce(III) (3.5 L/kg) were used to derive the  $K_{oc}$  to be used for PEC calculation. A generic 2% organic carbon content was used to derive a  $K_{oc}$  value of about 80,000 for La and 158,000  $\text{dm}^3/\text{kg}$  for Ce(III). These values were used for  $\text{PEC}_{\text{gw}}$  calculation.

### Phase I calculation

The highest dose recommended for weaned piglets was considered for PEC calculation in Phase I: 40.8 mg Ce(III)/kg feed and 21.3 mg La(III)/kg feed. The category 'Pigs for fattening' was used as a worst-case scenario. The calculated PEC values are given in Table 8.

**Table 8:** Initial predicted environmental concentration (PEC) of cerium (III) and lanthanum (III) in soil ( $\mu\text{g}/\text{kg}$ ) and groundwater ( $\mu\text{g}/\text{L}$ )

| Compartment  | PEC                         |                             |
|--------------|-----------------------------|-----------------------------|
|              | Cerium (III)                | Lanthanum (III)             |
| Soil         | 733 $\mu\text{g}/\text{kg}$ | 382 $\mu\text{g}/\text{kg}$ |
| Ground water | 0.06 $\mu\text{g}/\text{L}$ | 0.06 $\mu\text{g}/\text{L}$ |

PEC: predicted environmental concentration.

<sup>15</sup> Technical dossier/20190524 Lancer 2019 submission final KG, section 5.1.3.

The Phase I PEC trigger value is exceeded for the soil compartment, therefore a Phase II assessment for terrestrial organisms is considered necessary.

PEC groundwater is below the trigger value of 0.1 µg/L. No further assessment is necessary for groundwater and surface water compartment.

#### Phase II calculation

Considering that all the terrestrial ecotoxicological studies have been performed with the additive (see chapter below), a PEC in soil for the additive was calculated, considering that 250 mg/kg Lancer® is used in complete feedingstuffs for pig for fattening and that 65% of the additive is composed of lanthanides. The resulting PEC<sub>soil</sub> is reported in Table 9.

**Table 9:** Predicted environmental concentration in soil for Lancer®

| Compartment | PEC         |
|-------------|-------------|
| Soil        | 2,917 µg/kg |

PEC: predicted environmental concentration.

Considering that both La and Ce do not degrade, a PEC<sub>plateau</sub> in soil has to be evaluated taking into account a time to degradation of 50% of the original concentration of the compound (DT<sub>50</sub>) of 1,000 days. In order to calculate a PEC plateau for Lancer®, the amount of the product accumulating in soil has to be identified. Since the maximum amount of La(III) and Ce(III) in Lancer® are 9.4% and 17.9%, respectively, the amount expected to accumulate in soil is 27.3% of the calculated PEC of Lancer®. The resulting PEC<sub>plateau</sub> for lanthanides and Lancer® is reported in Table 10.

**Table 10:** Predicted environmental concentration in soil at plateau for lanthanides and Lancer®

|  | Value | Unit  |
|--|-------|-------|
| PEC <sub>soil initial</sub> Lancer®                    | 2,917 | µg/kg |
| PEC <sub>soil initial</sub> lanthanides <sup>(1)</sup> | 796   |       |
| PEC <sub>soil plateau</sub> lanthanides                | 3,564 |       |
| PEC <sub>soil plateau</sub> Lancer® <sup>(2)</sup>     | 6,481 |       |

PEC: predicted environmental concentration.

(1): Calculated as PEC<sub>soil initial</sub> × 0.273.

(2): Calculated as PEC<sub>soil initial</sub> Lancer® plus PEC<sub>soil plateau</sub> lanthanides.

This very worst-case PEC<sub>soil plateau</sub> for Lancer® value (6,481 µg/kg) was used for the risk assessment.

#### Toxicity of Lancer® to soil organisms

One batch of Lancer® was used in the three ecotoxicity studies reported below. It contained 80.8 g of La/kg additive, 155 g of Ce/kg additive and 366 g of citrate/kg additive.

#### Effect on earthworms

In an acute good laboratory practice (GLP) toxicity test performed on *Eisenia andrei*,<sup>16</sup> the additive under assessment was tested at concentrations of 62.5, 125, 250, 500 and 1,000 mg/kg soil dry weight in 6 treatment groups (one control group was untreated) with 4 replicates each containing 10 earthworms. The test was conducted in accordance with OECD 207 Guideline. Mortality and behaviour were assessed at 7 and 14 days after application and biomass at 14 days after application. The validity criteria for the control group were met. No mortality was seen at any concentration tested and there was no significant change in biomass (mean loss was 8.1%) compared to the control in any concentration tested. The LC<sub>50</sub> was estimated to be > 1,000 mg test item/kg soil dry weight. The NOEC for mortality and biomass was determined to be 1,000 mg test item/kg soil dry weight. Applying an assessment factor of 100 the PNEC<sub>earthworm</sub> corresponds to 10 mg Lancer®/kg soil dry weight (dw). This PNEC was used in the risk characterisation.

<sup>16</sup> Technical dossier/Section III\_18.

### Effects in terrestrial plants

In a GLP seeding emergence and seedling growth test,<sup>17</sup> three terrestrial plants (oat (*Avena sativa*, monocotyledon), oilseed rape (*Brassica napus*, dicotyledon) and soybean (*Glycine max*, dicotyledon)) were exposed to a concentration of 1,000 mg Lancer®/kg soil dry weight for 21 days. The results were compared with a control group that received water. The test was conducted in accordance with OECD 208 Guideline. There were 5 replicates (pots) with 5 seeds per replicate for oat; 7 replicates with 3 seeds per replicate for oilseed rape; and 12 replicates with 2 seeds per replicate for soybean. Plants were observed weekly for seedling emergence, survival/mortality and visual phytotoxicity. The validity criteria were met. End points observed at the end of the study were seedling emergence, survival of emerged seedlings, visual toxicity and biomass (shoot fresh weight). No adverse effects were seen on seedling emergence, survival of emerged seedlings and shoot fresh weight resulting in an overall NOEC of 1,000 mg test item/kg soil dry weight. For all species tested, the endpoints seedling emergence, survival of emerged seedlings and shoot fresh weight resulted in an EC<sub>10</sub>, EC<sub>20</sub> and EC<sub>50</sub> estimated to be higher than 1,000 mg test item/kg soil dry weight. Applying an assessment factor of 100 the PNEC<sub>plant</sub> corresponds to 10 mg Lancer®/kg soil dw. This PNEC was used in the risk characterisation.

### Effects on soil microorganisms

In a GLP nitrogen transformation test<sup>18</sup> performed in accordance with OECD 216 Guideline, biologically active agricultural soil (loamy sand/loam, pH 6.6, 1.45% Corg, water holding capacity (WHC) 37.39% dry soil) was either left untreated (control) or amended with Lancer® at 4.21 or at 42.1 mg/kg soil dry weight (test concentrations related to a soil depth of 5 cm and a soil density of 1.5 g/cm<sup>3</sup>). There were three replicates per treatment. Ammonia nitrogen, nitrate nitrogen and nitrite nitrogen were determined at 0, 7, 14 and 28 days of application. No adverse effects of the test item on nitrogen transformation in soil were observed at both test concentrations (deviation from control < 25%) after 28 days (time interval 14–28). The assessment factor for acute effects on microorganisms is 1; the PNEC is 42,100 µg/kg.

### Risk characterisation for Lancer®

The risk characterisation (PEC/PNEC ratio) for the terrestrial compartment is reported in Table 11.

**Table 11:** Risk characterisation (PEC/PNEC ratio) for Lancer® for the terrestrial compartment

|         | Taxa      | PEC <sub>soil</sub> (µg/kg) | PNEC (µg/kg) | PEC/PNEC |
|---------|-----------|-----------------------------|--------------|----------|
| Lancer® | Earthworm | 6,481                       | 10,000       | 0.65     |
|         | Plants    |                             |              |          |

PEC: predicted environmental concentration; PNEC: predicted no effect concentration.

Even considering a very worst-case approach, no negative effects are expected for the terrestrial organisms.

### 3.2.2.3. Conclusions on safety for the environment

The use of Lancer® in feed for weaned piglets according to the proposed conditions of use does not represent a safety concern for the environment.

## 3.3. 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<sup>19</sup> and Good Manufacturing Practice.

## 4. Conclusions

The FEEDAP Panel concludes that the use of Lancer® in feed for weaned piglets (up to 120 days) according to the proposed conditions of use does not represent a safety concern for the consumer and for the environment.

<sup>17</sup> Technical dossier/Section III\_19.

<sup>18</sup> Technical dossier/Section III\_20.

<sup>19</sup> Regulation (EC) No 1831/2003 of the European Parliament and of the Council of 22 September 2003 laying down requirements for feed hygiene. OJ L 35, 8.2.2005, p. 1.

## Documentation as provided to EFSA/Chronology

| Date       | Event   |
|------------|---|
| 28/05/2019 | Dossier received by EFSA. Supplementary information on the safety of lanthanide citrate as a zootechnical additive for weaned piglets under the conditions of Regulation (EC) No 1831/2003. Submitted by Treibacher Industrie AG. |
| 12/06/2019 | Reception mandate from the European Commission  |
| 19/06/2019 | Application validated by EFSA – Start of the scientific assessment  |
| 21/10/2019 | Spontaneous submission of information by the applicant. Issues: safety for the consumer   |
| 12/11/2019 | Opinion adopted by the FEEDAP Panel. End of the Scientific assessment   |

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## Abbreviations

|                  |  |
|------------------|--|
| ADI              | acceptable daily intake  |
| ADME             | absorption, distribution, metabolism and excretion                                     |
| Ce               | cerium   |
| DM               | dry matter   |
| DT <sub>50</sub> | time to degradation of 50% of the original concentration of the compound               |
| DW               | dry weight   |
| EC <sub>50</sub> | Concentration of the additive that has a given effect on 50% of the exposed population |
| FAIM             | Food Additive Intake Model   |
| GLP              | good laboratory practice   |
| HRP              | highest reliable percentile  |
| ICP-MS           | inductively coupled plasma mass spectrometry   |
| K <sub>oc</sub>  | organic carbon–water partitioning coefficient  |
| K <sub>p</sub>   | partition coefficient  |
| La               | lanthanum  |
| LC <sub>50</sub> | concentration of the additive that is lethal for 50% of the exposed population         |
| LoD              | limit of detection   |
| LoQ              | limit of quantification  |
| Nd               | neodymium  |
| NOAEL            | no observed adverse effect level   |
| NOEC             | no observed effects concentration  |
| NOEL             | no observed effect level   |
| OECD             | Organisation for Economic Co-operation and Development                                 |
| PEC              | predicted environmental concentration  |
| PNEC             | predicted no effect concentration  |
| Pr               | praseodymium   |
| RAC              | raw agricultural commodities   |
| REE              | rare earth elements  |
| WHC              | water holding capacity   |

## Annex A – Calculation of consumer exposure with FACE model

### Methodology

As described in the Guidance on the safety of feed additives for consumers (EFSA FEEDAP Panel, 2017), consumption data of edible tissues and products as derived from the EFSA Comprehensive European Food Consumption Database (Comprehensive Database) will be used to assess exposure to residues from the use of feed additives in different EU countries, age classes<sup>(20)</sup> and special population groups. For each EU country and age class, only the latest survey available in the Comprehensive Database will be used.

While the residue data reported for feed additives refer to organs and tissues (raw agricultural commodities (RAC)), the Comprehensive Database includes consumption data for foods as consumed. In order to match those consumption data with the available residue data for feed additives, the consumption data reported in the Comprehensive Database have been converted into RAC equivalents. For assessing the exposure to coccidiostats from their use in (non-reproductive) poultry, the following list of commodities is considered: meat, fat, liver, other offals (including kidney).

Depending on the nature of the health-based guidance derived, either a chronic or acute exposure assessment may be required.

For chronic exposure assessments, the total relevant residues will be combined for each individual with the average daily consumptions of the corresponding food commodities, and the resulting exposures per food will be summed in order to obtain total chronic exposure at individual level (standardised by using the individual body weight). The mean and the higher percentile (usually the 95th percentile) of the individual exposures will be subsequently calculated for each dietary survey (country) and each age class separately.

As opposed to the chronic exposure assessments, acute exposure calculation will be carried out for each RAC value separately. The higher percentile (usually the 95th percentile) exposures based on the consuming days only will be calculated for each food commodity, dietary survey and age class separately.

### Detailed results on chronic exposure calculation

**Table A.1:** Chronic exposure of consumers to lanthanum residues based on residue data in weaned piglets (ng/kg bw per day)

| Population class | Survey's country | Number of subjects | HRP value     | HRP description |
|------------------|------------------|--------------------|---------------|-----------------|
| Infants          | Bulgaria         | 523                | 7.3684746689  | 95th            |
| Infants          | Germany          | 142                | 11.5244593763 | 95th            |
| Infants          | Denmark          | 799                | 30.8662845021 | 95th            |
| Infants          | Finland          | 427                | 4.7680005671  | 95th            |
| Infants          | United Kingdom   | 1,251              | 5.2900720545  | 95th            |
| Infants          | Italy            | 9                  | 0.0171049620  | 50th            |
| Toddlers         | Belgium          | 36                 | 16.5095319605 | 90th            |
| Toddlers         | Bulgaria         | 428                | 16.0536334448 | 95th            |
| Toddlers         | Germany          | 348                | 15.5087477334 | 95th            |
| Toddlers         | Denmark          | 917                | 35.6780008503 | 95th            |
| Toddlers         | Spain            | 17                 | 7.3476836037  | 75th            |
| Toddlers         | Finland          | 500                | 10.0958136802 | 95th            |
| Toddlers         | United Kingdom   | 1,314              | 15.8058328988 | 95th            |
| Toddlers         | United Kingdom   | 185                | 30.7295381657 | 95th            |
| Toddlers         | Italy            | 36                 | 8.2286291280  | 90th            |
| Toddlers         | Netherlands      | 322                | 35.3634020314 | 95th            |
| Other children   | Austria          | 128                | 18.5743662370 | 95th            |
| Other children   | Belgium          | 625                | 20.7106553569 | 95th            |

<sup>20</sup> Infants: < 12 months old, toddlers: ≥ 12 months to < 36 months old, other children: ≥ 36 months to < 10 years old, adolescents: ≥ 10 years to < 18 years old, adults: ≥ 18 years to < 65 years old, elderly: ≥ 65 years to < 75 years old, and very elderly: ≥ 75 years old.



| Population class | Survey's country | Number of subjects | HRP value     | HRP description |
|------------------|------------------|--------------------|---------------|-----------------|
| Other children   | Bulgaria         | 433                | 20.2003163098 | 95th            |
| Other children   | Czech Republic   | 389                | 22.3060238900 | 95th            |
| Other children   | Germany          | 293                | 13.3052228786 | 95th            |
| Other children   | Germany          | 835                | 17.3377171460 | 95th            |
| Other children   | Denmark          | 298                | 21.2421492223 | 95th            |
| Other children   | Spain            | 399                | 16.2749021039 | 95th            |
| Other children   | Spain            | 156                | 21.1326908143 | 95th            |
| Other children   | Finland          | 750                | 22.7797307719 | 95th            |
| Other children   | France           | 482                | 14.7558766459 | 95th            |
| Other children   | United Kingdom   | 651                | 19.1334263735 | 95th            |
| Other children   | Greece           | 838                | 8.8964474825  | 95th            |
| Other children   | Italy            | 193                | 10.5431745496 | 95th            |
| Other children   | Latvia           | 187                | 22.0028657798 | 95th            |
| Other children   | Netherlands      | 957                | 26.3873793201 | 95th            |
| Other children   | Netherlands      | 447                | 16.2791446073 | 95th            |
| Other children   | Sweden           | 1,473              | 18.5760669991 | 95th            |
| Adolescents      | Austria          | 237                | 6.4039408898  | 95th            |
| Adolescents      | Belgium          | 576                | 7.0117959897  | 95th            |
| Adolescents      | Cyprus           | 303                | 3.9009657567  | 95th            |
| Adolescents      | Czech Republic   | 298                | 18.1104869102 | 95th            |
| Adolescents      | Germany          | 393                | 13.6576385128 | 95th            |
| Adolescents      | Germany          | 1,011              | 6.2761740912  | 95th            |
| Adolescents      | Denmark          | 377                | 9.9375215954  | 95th            |
| Adolescents      | Spain            | 651                | 9.4664301457  | 95th            |
| Adolescents      | Spain            | 209                | 10.7882492455 | 95th            |
| Adolescents      | Spain            | 86                 | 8.0976663814  | 95th            |
| Adolescents      | Finland          | 306                | 5.4334701638  | 95th            |
| Adolescents      | France           | 973                | 8.4807963118  | 95th            |
| Adolescents      | United Kingdom   | 666                | 4.4710932334  | 95th            |
| Adolescents      | Italy            | 247                | 5.7668844578  | 95th            |
| Adolescents      | Latvia           | 453                | 12.5589900986 | 95th            |
| Adolescents      | Netherlands      | 1,142              | 8.6264721929  | 95th            |
| Adolescents      | Sweden           | 1,018              | 7.3636916193  | 95th            |
| Adults           | Austria          | 308                | 6.3438966658  | 95th            |
| Adults           | Belgium          | 1,292              | 6.9507177251  | 95th            |
| Adults           | Czech Republic   | 1,666              | 13.2832216128 | 95th            |
| Adults           | Germany          | 10,419             | 6.7467413699  | 95th            |
| Adults           | Denmark          | 1,739              | 9.2629978717  | 95th            |
| Adults           | Spain            | 981                | 7.1892568618  | 95th            |
| Adults           | Spain            | 410                | 6.5130409067  | 95th            |
| Adults           | Finland          | 1,295              | 6.6104762816  | 95th            |
| Adults           | France           | 2,276              | 11.7604970830 | 95th            |
| Adults           | United Kingdom   | 1,265              | 4.4619348994  | 95th            |
| Adults           | Hungary          | 1,074              | 24.2620975609 | 95th            |
| Adults           | Ireland          | 1,274              | 4.6885591878  | 95th            |
| Adults           | Italy            | 2,313              | 4.2430683825  | 95th            |
| Adults           | Latvia           | 1,271              | 10.7639672581 | 95th            |
| Adults           | Netherlands      | 2,055              | 6.6830452838  | 95th            |
| Adults           | Romania          | 1,254              | 9.8512524326  | 95th            |
| Adults           | Sweden           | 1,430              | 6.1260304590  | 95th            |

| Population class | Survey's country | Number of subjects | HRP value     | HRP description |
|------------------|------------------|--------------------|---------------|-----------------|
| Elderly          | Austria          | 67                 | 13.1617389883 | 95th            |
| Elderly          | Belgium          | 511                | 8.8407752897  | 95th            |
| Elderly          | Germany          | 2,006              | 6.5921055026  | 95th            |
| Elderly          | Denmark          | 274                | 10.8324376260 | 95th            |
| Elderly          | Finland          | 413                | 6.5824447008  | 95th            |
| Elderly          | France           | 264                | 14.0973689355 | 95th            |
| Elderly          | United Kingdom   | 166                | 5.2712923080  | 95th            |
| Elderly          | Hungary          | 206                | 16.4485053221 | 95th            |
| Elderly          | Ireland          | 149                | 5.2812021760  | 95th            |
| Elderly          | Italy            | 289                | 3.5972950078  | 95th            |
| Elderly          | Netherlands      | 173                | 6.7035298546  | 95th            |
| Elderly          | Netherlands      | 289                | 6.0414089057  | 95th            |
| Elderly          | Romania          | 83                 | 6.8643072877  | 95th            |
| Elderly          | Sweden           | 295                | 7.9443620169  | 95th            |
| Very elderly     | Austria          | 25                 | 2.4978823108  | 75th            |
| Very elderly     | Belgium          | 704                | 8.1605923930  | 95th            |
| Very elderly     | Germany          | 490                | 6.4388113631  | 95th            |
| Very elderly     | Denmark          | 12                 | 4.6850144442  | 75th            |
| Very elderly     | France           | 84                 | 15.1899096970 | 95th            |
| Very elderly     | United Kingdom   | 139                | 10.4855061482 | 95th            |
| Very elderly     | Hungary          | 80                 | 13.8275189233 | 95th            |
| Very elderly     | Ireland          | 77                 | 5.1942126562  | 95th            |
| Very elderly     | Italy            | 228                | 3.1462833254  | 95th            |
| Very elderly     | Netherlands      | 450                | 5.8526410192  | 95th            |
| Very elderly     | Romania          | 45                 | 6.8873279455  | 90th            |
| Very elderly     | Sweden           | 72                 | 7.5447263349  | 95th            |

HRP: highest reliable percentile; bw: body weight.

**Table A.2:** Acute exposure of consumers to lanthanum residues based on residue data in weaned piglets (ng/kg bw per day)

| Raw primary commodity | Population class | Number of surveys | Maximum HRP    |
|-----------------------|------------------|-------------------|----------------|
| Mammals fat tissue    | Infants          | 4                 | 8.3218596154   |
| Mammals fat tissue    | Toddlers         | 11                | 8.3187274033   |
| Mammals fat tissue    | Other children   | 20                | 6.5090666667   |
| Mammals fat tissue    | Adolescents      | 20                | 5.3074581431   |
| Mammals fat tissue    | Adults           | 23                | 3.6519298955   |
| Mammals fat tissue    | Elderly          | 16                | 3.3799732673   |
| Mammals fat tissue    | Very elderly     | 14                | 3.5119560865   |
| Mammals liver         | Infants          | 4                 | 183.0080000000 |
| Mammals liver         | Toddlers         | 9                 | 141.0000000000 |
| Mammals liver         | Other children   | 20                | 270.9411764706 |
| Mammals liver         | Adolescents      | 18                | 144.2191780822 |
| Mammals liver         | Adults           | 22                | 197.1535580524 |
| Mammals liver         | Elderly          | 15                | 90.7586206897  |
| Mammals liver         | Very elderly     | 10                | 85.5400000000  |
| Mammals meat          | Infants          | 6                 | 12.3165050000  |
| Mammals meat          | Toddlers         | 11                | 13.2202258598  |
| Mammals meat          | Other children   | 20                | 19.0199647619  |
| Mammals meat          | Adolescents      | 20                | 14.7739270000  |
| Mammals meat          | Adults           | 23                | 8.6289571369   |

| Raw primary commodity                                       | Population class | Number of surveys | Maximum HRP   |
|---|------------------|-------------------|---------------|
| Mammals meat  | Elderly          | 16                | 7.2841806441  |
| Mammals meat  | Very elderly     | 14                | 7.4691432638  |
| Mammals offals and slaughtering products (other than liver) | Toddlers         | 5                 | 12.4909090909 |
| Mammals offals and slaughtering products (other than liver) | Other children   | 15                | 23.2816666667 |
| Mammals offals and slaughtering products (other than liver) | Adolescents      | 16                | 13.0857142857 |
| Mammals offals and slaughtering products (other than liver) | Adults           | 22                | 15.5015384615 |
| Mammals offals and slaughtering products (other than liver) | Elderly          | 13                | 11.9478260870 |
| Mammals offals and slaughtering products (other than liver) | Very elderly     | 12                | 10.5287356322 |

HRP: highest reliable percentile; bw: body weight.

**Table A.3:** Chronic exposure of consumers to cerium residues based on residue data in weaned piglets (ng/kg bw per day)

| Population class | Survey's country | Number of subjects | HRP value     | HRP description |
|------------------|------------------|--------------------|---------------|-----------------|
| Infants          | Bulgaria         | 523                | 12.8935679721 | 95th            |
| Infants          | Germany          | 142                | 19.9000039584 | 95th            |
| Infants          | Denmark          | 799                | 52.2433985436 | 95th            |
| Infants          | Finland          | 427                | 8.2521527080  | 95th            |
| Infants          | United Kingdom   | 1,251              | 9.2219581364  | 95th            |
| Infants          | Italy            | 9                  | 0.0296041825  | 50th            |
| Toddlers         | Belgium          | 36                 | 28.2485333459 | 90th            |
| Toddlers         | Bulgaria         | 428                | 28.2231677461 | 95th            |
| Toddlers         | Germany          | 348                | 26.5510728649 | 95th            |
| Toddlers         | Denmark          | 917                | 60.5895232478 | 95th            |
| Toddlers         | Spain            | 17                 | 12.7875445872 | 75th            |
| Toddlers         | Finland          | 500                | 17.5177772998 | 95th            |
| Toddlers         | United Kingdom   | 1,314              | 27.4713006358 | 95th            |
| Toddlers         | United Kingdom   | 185                | 52.2026075913 | 95th            |
| Toddlers         | Italy            | 36                 | 14.4563894213 | 90th            |
| Toddlers         | Netherlands      | 322                | 59.7724940091 | 95th            |
| Other children   | Austria          | 128                | 31.8674440988 | 95th            |
| Other children   | Belgium          | 625                | 35.6701222641 | 95th            |
| Other children   | Bulgaria         | 433                | 34.8028515050 | 95th            |
| Other children   | Czech Republic   | 389                | 37.9928529218 | 95th            |
| Other children   | Germany          | 293                | 23.1571022901 | 95th            |
| Other children   | Germany          | 835                | 29.4968280090 | 95th            |
| Other children   | Denmark          | 298                | 36.1440642641 | 95th            |
| Other children   | Spain            | 399                | 27.5535113742 | 95th            |
| Other children   | Spain            | 156                | 35.8998264033 | 95th            |
| Other children   | Finland          | 750                | 38.5577927265 | 95th            |
| Other children   | France           | 482                | 25.1781477376 | 95th            |
| Other children   | United Kingdom   | 651                | 32.4525040736 | 95th            |
| Other children   | Greece           | 838                | 15.3903475183 | 95th            |
| Other children   | Italy            | 193                | 18.2062633282 | 95th            |
| Other children   | Latvia           | 187                | 37.8773682217 | 95th            |
| Other children   | Netherlands      | 957                | 44.7755737187 | 95th            |

| Population class | Survey's country | Number of subjects | HRP value     | HRP description |
|------------------|------------------|--------------------|---------------|-----------------|
| Other children   | Netherlands      | 447                | 27.5417816610 | 95th            |
| Other children   | Sweden           | 1,473              | 31.8233947207 | 95th            |
| Adolescents      | Austria          | 237                | 11.1686329073 | 95th            |
| Adolescents      | Belgium          | 576                | 11.9461267004 | 95th            |
| Adolescents      | Cyprus           | 303                | 6.7515438976  | 95th            |
| Adolescents      | Czech Republic   | 298                | 31.1412500666 | 95th            |
| Adolescents      | Germany          | 393                | 23.2853430209 | 95th            |
| Adolescents      | Germany          | 1,011              | 10.8821366146 | 95th            |
| Adolescents      | Denmark          | 377                | 16.9256948255 | 95th            |
| Adolescents      | Spain            | 651                | 16.8397582441 | 95th            |
| Adolescents      | Spain            | 209                | 18.7230659622 | 95th            |
| Adolescents      | Spain            | 86                 | 13.9552291943 | 95th            |
| Adolescents      | Finland          | 306                | 9.6128115872  | 95th            |
| Adolescents      | France           | 973                | 14.5345388286 | 95th            |
| Adolescents      | United Kingdom   | 666                | 7.9883471130  | 95th            |
| Adolescents      | Italy            | 247                | 10.0036127896 | 95th            |
| Adolescents      | Latvia           | 453                | 21.4060110654 | 95th            |
| Adolescents      | Netherlands      | 1,142              | 14.8105652968 | 95th            |
| Adolescents      | Sweden           | 1,018              | 12.8622293052 | 95th            |
| Adults           | Austria          | 308                | 11.0259985538 | 95th            |
| Adults           | Belgium          | 1,292              | 11.9329089100 | 95th            |
| Adults           | Czech Republic   | 1,666              | 23.7117204076 | 95th            |
| Adults           | Germany          | 10,419             | 11.7100447467 | 95th            |
| Adults           | Denmark          | 1,739              | 15.7686274053 | 95th            |
| Adults           | Spain            | 981                | 12.4858294268 | 95th            |
| Adults           | Spain            | 410                | 11.2052458388 | 95th            |
| Adults           | Finland          | 1,295              | 11.5523019156 | 95th            |
| Adults           | France           | 2,276              | 20.0807408255 | 95th            |
| Adults           | United Kingdom   | 1,265              | 7.7734110438  | 95th            |
| Adults           | Hungary          | 1,074              | 41.4328701115 | 95th            |
| Adults           | Ireland          | 1,274              | 8.1588176125  | 95th            |
| Adults           | Italy            | 2,313              | 7.4366017416  | 95th            |
| Adults           | Latvia           | 1,271              | 18.5377333042 | 95th            |
| Adults           | Netherlands      | 2,055              | 11.5595094192 | 95th            |
| Adults           | Romania          | 1,254              | 16.9778785568 | 95th            |
| Adults           | Sweden           | 1,430              | 10.6586637668 | 95th            |
| Elderly          | Austria          | 67                 | 22.2620671117 | 95th            |
| Elderly          | Belgium          | 511                | 15.2601851336 | 95th            |
| Elderly          | Germany          | 2,006              | 11.5699507645 | 95th            |
| Elderly          | Denmark          | 274                | 18.2204656321 | 95th            |
| Elderly          | Finland          | 413                | 11.4839838903 | 95th            |
| Elderly          | France           | 264                | 23.7189744188 | 95th            |
| Elderly          | United Kingdom   | 166                | 8.9697963076  | 95th            |
| Elderly          | Hungary          | 206                | 28.5029266321 | 95th            |
| Elderly          | Ireland          | 149                | 9.1577951358  | 95th            |
| Elderly          | Italy            | 289                | 6.2765445989  | 95th            |
| Elderly          | Netherlands      | 173                | 11.4941750235 | 95th            |
| Elderly          | Netherlands      | 289                | 10.3085456304 | 95th            |
| Elderly          | Romania          | 83                 | 12.2447660700 | 95th            |
| Elderly          | Sweden           | 295                | 13.5910949558 | 95th            |

| Population class | Survey's country | Number of subjects | HRP value     | HRP description |
|------------------|------------------|--------------------|---------------|-----------------|
| Very elderly     | Austria          | 25                 | 4.3231761374  | 75th            |
| Very elderly     | Belgium          | 704                | 13.9442170489 | 95th            |
| Very elderly     | Germany          | 490                | 11.0462030954 | 95th            |
| Very elderly     | Denmark          | 12                 | 8.0120061563  | 75th            |
| Very elderly     | France           | 84                 | 25.5262814380 | 95th            |
| Very elderly     | United Kingdom   | 139                | 17.8926080282 | 95th            |
| Very elderly     | Hungary          | 80                 | 23.7121455361 | 95th            |
| Very elderly     | Ireland          | 77                 | 9.1569739837  | 95th            |
| Very elderly     | Italy            | 228                | 5.4453874529  | 95th            |
| Very elderly     | Netherlands      | 450                | 9.9910844858  | 95th            |
| Very elderly     | Romania          | 45                 | 11.6619898125 | 90th            |
| Very elderly     | Sweden           | 72                 | 13.6847930640 | 95th            |

HRP: highest reliable percentile; bw: body weight.

**Table A.4:** Acute exposure of consumers to cerium residues based on residue data in weaned piglets (ng/kg bw per day)

| Raw primary commodity                                       | Population class | Number of surveys | Maximum HRP    |
|---|------------------|-------------------|----------------|
| Mammals fat tissue  | Infants          | 4                 | 15.3526019231  |
| Mammals fat tissue  | Toddlers         | 11                | 15.3468234544  |
| Mammals fat tissue  | Other children   | 20                | 12.0082666667  |
| Mammals fat tissue  | Adolescents      | 20                | 9.7914764079   |
| Mammals fat tissue  | Adults           | 23                | 6.7372712985   |
| Mammals fat tissue  | Elderly          | 16                | 6.2355514851   |
| Mammals fat tissue  | Very elderly     | 14                | 6.4790402937   |
| Mammals liver   | Infants          | 4                 | 306.9208255319 |
| Mammals liver   | Toddlers         | 9                 | 236.4696428571 |
| Mammals liver   | Other children   | 20                | 454.3926470588 |
| Mammals liver   | Adolescents      | 18                | 241.8684931507 |
| Mammals liver   | Adults           | 22                | 330.6441947566 |
| Mammals liver   | Elderly          | 15                | 152.2103448276 |
| Mammals liver   | Very elderly     | 10                | 143.4582500000 |
| Mammals meat  | Infants          | 6                 | 21.3166250000  |
| Mammals meat  | Toddlers         | 11                | 22.8807276958  |
| Mammals meat  | Other children   | 20                | 32.9185476190  |
| Mammals meat  | Adolescents      | 20                | 25.5697750000  |
| Mammals meat  | Adults           | 23                | 14.9344512448  |
| Mammals meat  | Elderly          | 16                | 12.6069974576  |
| Mammals meat  | Very elderly     | 14                | 12.9271190184  |
| Mammals offals and slaughtering products (other than liver) | Toddlers         | 5                 | 25.6227272727  |
| Mammals offals and slaughtering products (other than liver) | Other children   | 15                | 47.7579166667  |
| Mammals offals and slaughtering products (other than liver) | Adolescents      | 16                | 26.8428571429  |
| Mammals offals and slaughtering products (other than liver) | Adults           | 22                | 31.7984615385  |
| Mammals offals and slaughtering products (other than liver) | Elderly          | 13                | 24.5086956522  |
| Mammals offals and slaughtering products (other than liver) | Very elderly     | 12                | 21.5977011494  |

HRP: highest reliable percentile; bw: body weight.