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Re-evaluation of calcium carbonate (E 170) as a food additive in foods for infants below 16 weeks of age and follow-up of its re-evaluation as food additive for uses in foods for all population groups

EFSA Panel on Food Additives and Flavourings (FAF),
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Abstract

Calcium carbonate (E 170) was re-evaluated in 2011 by the former EFSA Panel on Food Additives and Nutrient sources added to Food (ANS). As a follow-up to this assessment, the Panel on Food Additives and Flavourings (FAF) was requested to assess the safety of calcium carbonate (E 170) for its uses as a food additive in food for infants below 16 weeks of age belonging to food category 13.1.5.1 (Dietary foods for infants for special medical purposes and special formulae for infants) and as carry over in line with Annex III, Part 5 Section B to Regulation (EC) No 1333/2008. In addition, the FAF Panel was requested to address the issues already identified during the re-evaluation of the food additive when used in food for the general population. The process involved the publication of a call for data to allow the interested business operators (IBOs) to provide the requested information to complete the risk assessment. The Panel concluded that there is no need for a numerical acceptable daily intake (ADI) for calcium carbonate and that, in principle, there are no safety concern with respect to the exposure to calcium carbonate *per se* at the currently reported uses and use levels in all age groups of the population, including infants below 16 weeks of age. With respect to the calcium intake resulting from the use of E 170 in food for the general population and infants < 16 weeks of age, the Panel concluded that it contributes only to a small part to the overall calcium dietary exposure. However, the unavoidable presence of aluminium in E 170 is of concern and should be addressed. In addition, the Panel concluded that the technical data provided by the IBO support further amendments of the specifications for E 170 laid down in Commission Regulation (EU) No 231/2012.

Keywords: calcium carbonate, E 170, food additive, infants

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Summary

In accordance with Regulation (EU) No 257/2010, the European Food Safety Authority (EFSA) is currently re-evaluating the safety of food additives already permitted in the Union before 20 January 2009 and issuing scientific opinions on their safety when used in food as per Annexes II and III to Regulation (EC) No 1333/2008. The risk assessment approach followed in the re-evaluation has not covered the use of food additives in food for infants below 12 weeks of age. Additionally, while re-evaluating the safety of food additives referred to above, EFSA identified some concerns, namely (1) Data gaps that have triggered recommendations in the published scientific opinions; and/or; (2) Data gaps that have increased uncertainties linked to the risk assessment and/or which prevented the Panel from concluding on some aspects of it.

On 31 May 2017, EFSA published a guidance on the risk assessment of substances present in food intended for infants below 16 weeks of age, thus enabling EFSA to assess the safety of food additive used in food for infants below this age. The age up to 16 weeks was selected in the guidance because infants are exposed to formula feeding until this age as the only source of food since complementary feeding is not supposed to be introduced before.

As follow-up of the above, this Opinion addresses the data gaps previously identified during the re-evaluation of calcium carbonate (E 170) as a food additive and the safety in the special sub-population of infants below 16 weeks of age.

The process followed involved the publication of a dedicated call for data allowing all interested parties to provide the requested information for completing the assessment and to confirm that the additive is present as carry over in food category 13.1.5.1 (Dietary foods for infants for special medical purposes and special formulae for infants). The data submitted in response to the call for data on calcium carbonate (E 170) comprised technical information and clinical studies, post marketing surveillance reports and literature studies.

Calcium carbonate is an inorganic salt with CAS Registry Number 471-34-1, Colour Index No. 77220. Calcium carbonate is practically insoluble in water and ethanol (FCC 7, 2010). According to the available information in the REACH Registration dossier the solubility of calcium carbonate (conventional) in water tested according to the OECD TG 105 is 16.6 mg/L (20°C, pH 9–9.4).

Specifications for calcium carbonate (E 170) have been defined in Commission Regulation (EU) No 231/2012.

In response to a public call issued by EFSA in 2018 in support of the present assessment, data from interested business operators (IBOs) were made available to EFSA for Dietary foods for infants for special medical purposes and special formulae for infants (FC 13.1.5.1). Exposure to calcium carbonate (E 170) as a food additive from infant formulae (FC 13.1.5.1) was estimated for infants below 16 weeks of age, using the highest value and the mean of the reported typical use level. Using the highest value of the reported typical use level, calcium carbonate (E 170) exposure ranged between 85 mg/kg body weight (bw) per day (mean consumption) and 110 mg/kg bw per day (at the high-level consumption). Using the mean value of the reported typical use level, calcium carbonate (E 170) exposure ranged between 71 mg/kg bw per day (mean consumption) and 92 mg/kg bw per day (at the high-level consumption).

For the general population (from infants > 16 weeks of age to the elderly), mean dietary exposure to calcium carbonate (E 170) ranged from 0.6 mg/kg bw per day for infants to 37.7 mg/kg bw per day for toddlers; at the 95th percentile, dietary exposure to calcium carbonate (E 170) ranged from 4.2 mg/kg bw per day for adolescents to 80.9 mg/kg bw per day for toddlers. Exposure to calcium carbonate as a source of calcium ranged at the mean from 0.4 mg/kg bw per day for the elderly to 58.6 mg/kg bw per day for infants; at the 95th percentile, it ranged from 2.2 mg/kg bw per day from the elderly to 245.7 mg/kg bw per day for infants. Considering both uses of calcium carbonate as a food additive (E 170) and as a source of calcium, mean exposure would range from 5.9 mg/kg bw per day for the elderly to 91.9 mg/kg bw per day for toddlers, while exposure at the 95th percentile would range from 13.9 mg/kg bw per day for the elderly to the 311.5 mg/kg bw per day for infants.

Based on these estimates, the mean intake of calcium from the use of calcium carbonate as a food additive (E 170) and as a source of calcium is estimated to be from 56 mg/day for infants up to 1,058 mg/day for the elderly. At the 95th percentile, intake of calcium ranged from 183 mg/day for infants to 2,935 mg/day for the elderly. In addition, for the consumers of food supplements (and considering also their whole diet), mean intake of calcium ranged from 271 to 3,530 mg/day for the elderly. At the 95th percentile, intake of calcium ranged from 945 mg/day for children to 10,553 mg/day for adults.

Analytical data on toxic elements were provided by one IBO for levels of Pb, Cd, As, Hg and Al in the calcium carbonate ground calcium carbonate (GCC) and PCC used as a food additive E 170. The Panel noted that the occurrence data submitted by the IBOs for Pb, Cd, As in E 170 are substantially lower than the current limits in the EU specifications. The Panel further observed that there are no substantial differences between the levels of Pb, Cd, As, Hg and Al provided for GCC and PCC E 170. However, the Panel further noted that the level of Al strongly depends on the sample preparation method used (i.e. partial extraction or full digestion).

The same IBO proposed a maximum limit for Pb, Hg, Cd, As and Al in E 170 separately for uses in food for the general population and for food for infants < 16 weeks of age. The proposals differ only in the levels of Al being 500 mg/kg for infants < 16 weeks of age and 700 mg/kg for all population groups. The IBO proposed that the maximum limit in the EU specifications for E 170 for Al should be set based on the total aluminium content in this food additive.

Considering the data provided by the IBO on the Al levels, the fact that Al is a part of the structure of calcium carbonate PCC and that E 170 up to the concentration tested in the dissolution rate tests is expected to be fully dissolved under the stomach conditions the Panel concurs with the IBO that the maximum limits for Al in the EU specifications for E 170 should be based on the total-Al content in E 170.

The Panel performed the risk assessment that would result if Pb, Hg, Cd, As and Al were present in E 170 at (i) the maximum current limit in the EU specification; (ii) limits proposed by the IBO; (iii) at the 90 percentile values, using the upper bound levels, calculated by the Panel based on the analytical data submitted for Pb, Cd and As, the highest measured value for Hg, i.e. 0.05 mg/kg and for Al rounded to 250 mg/kg.

Considering that calcium carbonate may also be used in the manufacture of foods as a source of calcium for nutritional purposes and that the same purity criteria established for the use as a food additive would apply also to the use as a source of calcium, the Panel has assumed that the data provided by the IBO on impurities in E 170 may apply equally to calcium carbonate when used as a source of calcium.

For infants below 16 weeks of age, the Panel considered the highest mean and 95th percentile of the refined exposure estimates based on the maximum and mean use levels of E 170 reported by the IBOs. For the infants from 16 weeks to 1 year of age and toddlers' consumers only of food for special medical purpose (FSMP), the dietary exposure to calcium carbonate (E 170) at the highest mean and 95th percentile estimates were considered.

As currently calcium carbonate (E 170) as a food additive is allowed at *quantum satis* in FSMP (FC 13.1.5.1) and considering that calcium carbonate may also be used for nutritional purposes as a source of calcium in infant formula and FSMP and that it needs to meet the specifications of E 170, the Panel considered two additional dietary exposure estimates to E 170 for infants < 16 weeks of age: if calcium carbonate was used in infant formula and FSMP at the allowed maximum calcium level as set in the respective Regulations EU No 2016/127 and EU 2016/128, and at the highest consumption value of 260 mL formula/kg bw per day as recommended in the relevant EFSA guidance considering the highest energy requirement 70 kcal/100 mL (EU 128/2016). The Panel noted that the same assumption was considered by the IBO to calculate the concentration to be tested in the dissolution rate test. However, the illustrative calculations described above would result in an overestimation, noting that calcium carbonate might not be the only source of calcium in infant formula and FSMPs.

With regard to the dietary exposure to calcium carbonate for the general population, the Panel considered the highest mean and 95th percentile which was calculated in three scenarios:

i) calcium carbonate used as a food additive E 170 only (highest mean and 95th percentile 49.3 and 108.1 mg/kg bw per day for toddlers)
ii) calcium carbonate used as a food additive (E 170) and a source of calcium from fortified food (highest mean and 95th percentile 91.9 and 311.5 mg/kg bw per day for toddlers and infants, respectively) and
iii) calcium carbonate used as a food additive (E 170) and a source of calcium for consumers only of food supplements (highest mean and 95th percentile 167 for elderly and 458 mg/kg bw per day for adolescents).

The resulting figures show, that at the current EU Specifications limits and at the limits proposed by the IBO, the exposure to toxic elements Pb, Cd, Hg, As and Al from the consumption of E 170 could be substantial and would give raise to concern. For some of the population groups the exposure to Al from the use of the calcium carbonate exceeds substantially (up to circa 4 fold) the tolerable weekly

intake (TWI) in the case that Al would be present at the limit proposed by the IBO. Furthermore, the Panel noted that at the highest measured value for Al of 1,120 mg/kg reported by the IBO, the TWI would be greatly exceeded (up to 890%).

The Panel noted that already in 2008, the AFC Panel concluded that the TWI of 1 mg/kg bw per week for Al is likely to be exceeded in a significant part of the European population. The AFC Panel considered that the major route of exposure to aluminium compounds for the general population was through food, both as a consequence of the natural occurrence of aluminium in food and the use of aluminium compounds in food processing, including food additives. Considering this and the outcome of the current risk assessment for aluminium present in E 170 (as above) and the fact that there are other dietary sources of aluminium, the Panel is of the opinion that limiting the content of aluminium in foods should be considered.

The Panel noted that the maximum limits in the EU specifications for toxic elements should be established based on actual levels in the commercial food additive. Therefore, the Panel recommended that the maximum limits should be lowered for Pb, Cd and As and that maximum limits for Hg and Al should be introduced on the basis of the information provided by the IBO and on the considerations of the Panel.

Additionally, the Panel calculated the impact of the potential level of the toxic elements lead and cadmium in the food additive (i.e. up to the specifications limit values) on the final product and compared that with the legal limits for these elements in the final formula for infants below 16 weeks of age set by Commission Regulation (EU) 2023/915. Considering the results of these estimations and the fact that the food additive is not the only potential source of toxic elements in the infant formula the Panel emphasises the need to reduce the specification limit values for lead and cadmium in Regulation (EU) No 231/2012.

Regarding particle size the Panel considered that, based on the data provided, the presence of small particles including nanoparticles in the pristine GCC and PCC calcium carbonate used as a food additive (E 170) cannot be excluded. One IBO further provided dissolution rate tests results for GCC and PCC E 170, performed at pH 3 and pH 6 mimicking the stomach conditions of adults and infants, respectively. Based on that data the Panel considered that there is no concern with regard to the exposure to small particles, including nanoparticles, present in E 170 when used as a food additive up to the concentrations tested and that the previous risk assessment completed by the ANS Panel in 2011 does not need to be complemented with nano-specific considerations. Consequently, also with respect to the evaluation of the safety in infants below 16 weeks of age, this is considered to be adequately covered by the applicable guidance of the EFSA Scientific Committee.

In view of the additional information submitted by IBOs on the form of calcium carbonate (E 170) used as a food additive, the Panel considers that the definition of the food additive E 170 should be revised in the current EU specifications for calcium carbonate (E 170) (Commission Regulation (EU) No 231/2012) indicating that: calcium carbonate (E 170) has no surface treatments or coatings and is not an intentionally engineered nanomaterial.

Based on the similarity of the data provided on the levels of toxic elements and the dissolution tests rates for GCC and PCC E 170 and the fact that these two forms can be used interchangeably, the Panel does not see the need to introduce separate technical specifications for GCC and PCC E 170.

An overview of the toxicological studies provided in the REACH registration dossier together with the relevant study reports/publications was provided by one IBO. The only study not considered in the ANS Panel opinion on the re-evaluation was a 90-day oral toxicity study with nano calcium carbonate in Sprague–Dawley rats. Based on the absence of toxicologically relevant effects, the Panel agreed with the study authors that a no-observed-adverse-effect level (NOAEL) of 1,000 mg/kg bw per day (highest dose tested). The Panel noted that the toxicological studies provided had not investigated endpoints of relevance for infants below 16 weeks of age and that none of the studies was performed in a relevant animal model (i.e. piglet). Hence, the submitted information does not contribute to the assessment of calcium carbonate as a food additive for use in food for infants below 16 weeks of age.

Results from six clinical studies were provided by one IBO. Three trials were performed in infants and children with underlying health conditions (chronic renal failure, recovering from undernutrition) and were, therefore, considered not relevant for the current assessment. In the three remaining publications the content of calcium carbonate as a food additive was not given and, therefore, the exposure could not be assessed by the Panel. Of note, the provided clinical trials did not address endpoints related potential adverse effects of calcium carbonate, e.g. hypercalcaemia. Hence, the information in these studies was considered not useful for the assessment of the safety of calcium carbonate (E 170) as a food additive in food for infants and young children.

In the context of the re-evaluation of calcium carbonate, the ANS Panel agreed with the group acceptable daily intake (ADI) 'not specified' assigned by the Scientific Committee on Food (SCF) to a group of carbonates including calcium carbonate, when considering the use of calcium carbonate as a food additive. The ANS Panel also noted that the estimated exposures to calcium from all sources, including the use of calcium carbonate as a food additive, taken together with intakes of calcium from supplements and from food fortification are below 2,500 mg/day. In the current assessment, the Panel noted that, after the adoption of the conceptual framework in 2014, the conclusion 'ADI not specified' was no longer considered fit for purpose and concluded that there is no need for a numerical ADI for calcium carbonate and that, in principle, there are no safety concern with respect to the exposure to calcium carbonate *per se* at the currently reported uses and use levels in all age groups of the population, including infants below 16 weeks of age. However, the unavoidable presence of aluminium in E 170 is of concern and should be addressed, in the first instance, by the introduction of a limit in the purity criteria of the EU specifications for E 170 but also by the reduction of the intake of this toxic element resulting from the dietary exposure to E 170.

With respect to the calcium intake resulting from the use of E 170 in food for the general population and infants $<$ 16 weeks of age, the Panel noted that the exposure to calcium in the scenario which takes into account consumers only of food supplements (all age groups above 3 years) is greatly exceeding the Tolerable Upper Intake Level (UL) and may be of concern given the known adverse effects of high-dose calcium supplementation (gastrointestinal side effects, kidney stones, cardiovascular effects). The Panel noted that the high exposures associated with the use of food supplements are not because of the exposure from the food additive which is only 10–20% of the overall exposure. Therefore, the Panel considered that the exposure to calcium from calcium carbonate as a food additive (E 170) does not raise concerns.

Table of contents

1. Introduction

The present opinion deals with:

- the risk assessment of calcium carbonate (E 170) in food for infants below 16 weeks of age in the food category (FC) 13.1.5.1 (Dietary foods for infants for special medical purposes and special formulae for infants).
- the follow-up on issues that have been expressed in the conclusions and recommendations of the Scientific Opinion on the re-evaluation of calcium carbonate (E 170) as a food additive (EFSA ANS Panel, 2011).

1.1. Background and terms of reference as provided by the requestor

1.1.1. Background

The composition of food intended for infants and young children, as defined by Regulation (EU) No 609/2013[1], is regulated at EU level and such rules include requirements concerning the use of substances as food additives.

The use of food additives is regulated by Regulation (EC) No 1333/2008 on food additives. Only food additives that are included in the Union list, in particular in Annex II and III to that Regulation, may be placed on the market and used in food under the conditions of use specified therein.

In accordance with Regulation (EU) No 257/2010[2], EFSA is currently re-evaluating the safety of food additives already permitted in the Union before 20 January 2009 and issuing scientific opinions on their safety when used in food as per Annexes II and III to Regulation (EC) No 1333/2008. However, the risk assessment approach followed until now has not covered the use of food additives in food for infants below 12 weeks of age. Consequently, EFSA published several scientific opinions on the re-evaluation of the safety of food additives permitted in food category 13.1 but not addressing their use in food for infants below 12 weeks of age.

In addition, in these opinions EFSA identified some concerns, namely (1) Data gaps that have triggered recommendations in the (to be) published scientific opinions, and/or; (2) Data gaps that have increased uncertainties linked to the risk assessment and/or which prevented the EFSA from concluding on some aspects of it.

On 31 May 2017, EFSA published a guidance document (EFSA Scientific Committee, 2017) on the risk assessment of substances present in food intended for infants below 16 weeks of age, thus enabling EFSA to assess the safety of food additives used in food for infants below 12 weeks of age.[3] Now EFSA is expected to launch dedicated calls for data to be able to perform such risk assessments.

The EC considers it is more effective that EFSA, in the context of these dedicated calls for data, also addresses all the issues and data gaps already identified in the relevant (to be) published scientific opinions on the re-evaluation of the safety of food additives permitted in food category 13.1.

In accordance with the current EC approach for the follow-up of EFSA"s scientific opinions on the re-evaluation of the safety of permitted food additives for which some concerns have been identified, a specific call for data would be published by the EC on DG SANTE"s website[4] on food additives and additional (missing) information would then be provided by interested business operators to the EC.

However, for those scientific opinions on the re-evaluation of the safety of permitted food additives in food category 13.1 for which the risk assessment does not address their uses in food for infants below 12 weeks of age and for which some concerns have been identified by EFSA, the EC considers that for the sake of efficiency it would be appropriate to streamline the approach as described above.

Therefore, the EC requests EFSA to address all the issues and data gaps already identified in the relevant published scientific opinions of those food additives (or groups of additives that can be

[1] Regulation (EU) No 609/2013 of the European Parliament and of the Council of 12 June 2013 on food intended for infants and young children, food for special medical purposes, and total diet replacement for weight control and repealing Council Directive 92/52/EEC, Commission Directives 96/8/EC, 1999/21/EC, 2006/125/EC and 2006/141/EC, Directive 2009/39/EC of the European Parliament and of the Council and Commission Regulations (EC) No 41/2009 and (EC) No 953/2009. OJ L 181, 29.6.2013, pp. 35–56.

[2] Commission Regulation (EU) No 257/2010 of 25 March 2010 setting up a program for the re-evaluation of approved food additives in accordance with Regulation (EC) No 1333/2008 of the European Parliament and of the Council on food additives. OJ L 80, 26.3.2010, pp. 19–27.

[3] See Section 1.1.3.

[4] https://ec.europa.eu/food/safety/food_improvement_agents/additives/re-evaluation_en.

addressed simultaneously) as part of the upcoming work on the safety assessment of food additives uses in food for infants below 12 weeks of age.

This follow-up aims at completing the re-evaluation of the food additives in question for all food categories and includes calls for data covering the actual use and usage levels of food additives in food for both infants below 12 or 16 weeks of age as well as for older infants, young children and other groups of the population for which EFSA has already finalised its assessment.

The future evaluations of EFSA should systematically address the safety of use of food additives for all age groups, including the infants below 12 or 16 weeks of age.

1.1.2. Terms of reference

In accordance with Article 29(1)(a) of Regulation (EC) No 178/2002[5], and as part of EFSA's work in completing its risk assessments concerning the use of food additives in food for infants below 12 weeks of age,[5] covered by the re-evaluation programme and its terms of reference, the European Commission requests the European Food Safety Authority to address all the data gaps specified in the recommendations made in this scientific opinions on the re-evaluation of the safety of food additives permitted in food category 13.1 (food for infants and young children) of annex II to Regulation (EC) No 1333/2008.

1.1.3. Interpretation of terms of reference

Before the publication of the EFSA Scientific Committee Guidance on the risk assessment of substances present in food intended for infants below 16 weeks of age (EFSA Scientific Committee, 2017), EFSA has taken 12 weeks as a cut off age for the applicability of the safety assessment. However, according to EFSA Scientific Committee (2017), the assessment will include infants up to 16 weeks of age because they are exposed to formula feeding until this age as the only source of food since complementary feeding is not supposed to be introduced before this age (see EFSA Scientific Committee, 2017).

Calcium carbonate produced as nanomaterial (engineered nanomaterial) as well as calcium carbonate coated or functionalised and with chemically modified surfaces are not used as the food additive E 170, according to the available information, and therefore, are not considered in this evaluation.

The current assessment addresses the safety of calcium carbonate (E 170) in its technological function as a food additive and not the safety of calcium carbonate as a source of calcium (food fortification and food supplements). However, noting that, in absence of specifications for the use of calcium carbonate as a source of calcium, the purity criteria set in the EU specifications for calcium carbonate as a food additive (E 170; see Table 2) apply also to calcium carbonate when used as a source of calcium,[6,7,8] the exposure to toxic elements (Pb, Hg, Cd, As and Al) was performed considering also this use (see Sections 3.3.6 and 3.4).

1.2. Previous evaluations of calcium carbonate (E 170) as a food additive

Calcium carbonate was evaluated by JECFA in 1965 (JECFA, 1965, 1966). JECFA established an acceptable daily intake (ADI) 'not limited'. In 1991, the Scientific Committee on Food (SCF) evaluated calcium carbonate as part of a group of carbonates and concluded that both calcium and carbonate are natural constituents of man, animals and plants and occur naturally in foodstuffs. The Committee noted that exhaustive systematic toxicological studies had not been carried out with the individual ions (or their salts) but concluded that *'no safety problems are likely to arise from their use in food, provided the contributions from food intake do not disturb the homeostatic mechanisms controlling the*

[5] Regulation (EC) No 178/2002 of the European Parliament and of the Council of 28 January 2002 laying down the general principles and requirements of food law, establishing the European Food Safety Authority and laying down procedures in matters of food safety. OJ L 31, 1.2.2002, pp. 1–24.

[6] Directive 2002/46/EC of the European Parliament and of the Council of 10 June 2002 on the approximation of the laws of the Member States relating to food supplements (Text with EEA relevance), OJ L 183, 12.7.2002, pp. 51–57.

[7] Regulation (EC) No 1925/2006 of the European Parliament and of the Council of 20 December 2006 on the addition of vitamins and minerals and of certain other substances to foods, OJ L 404, 30.12.2006, pp. 26–38.

[8] Regulation (EC) No 108/2008 of the European Parliament and of the Council of 15 January 2008 amending Regulation (EC) No 1925/2006 on the addition of vitamins and minerals and of certain other substances to foods. OJ L 39, 13.2.2008, pp. 11–13.

electrolyte balance of the body.' Consequently, the Committee assigned a group ADI 'not specified' for carbonates (SCF, 1991).

Under the frame of Regulation (EC) No 257/2010, the EFSA Panel on Food Additives and Nutrient Sources added to Food (ANS) re-evaluated the safety of calcium carbonate (E 170) when used as a food additive (EFSA ANS Panel, 2011). In its scientific opinion, the ANS Panel reviewed available technical, biological and toxicological data on calcium carbonate (E 170), when used as a food additive (EFSA ANS Panel, 2011). Overall, the ANS Panel considered that the available toxicological database on calcium carbonate was limited but did not give rise to concerns. The ANS Panel agreed with the group ADI 'not specified' assigned by the SCF when considering the use of calcium carbonate as a food additive and food colour (SCF, 1991). The ANS Panel concurred with the JECFA definition of 'ADI not specified' (JECFA, 1965, 1966) and considered it applicable to calcium carbonate (E 170) when used as a food additive.

The following issues relevant for this assessment were noted by the ANS Panel:

- Calcium carbonate is currently permitted at *quantum satis* (*QS*) in the vast majority of food categories (generally permitted in all foods with certain exceptions), however, information gathered by the ANS Panel for this re-evaluation has shown that calcium carbonate is only used at defined amounts in a number of food categories. The ANS Panel thus recommended the legislation to be updated to reflect actual usage levels evaluated in its 2011 opinion.
- The presence of unintentional nanoscale particles at trace levels in food additive grade calcium carbonates could not be excluded. Whilst the data were inadequate to reach definitive conclusions on calcium carbonate predominantly in the nanoscale, the ANS Panel concluded that the available data were sufficient to conclude that the current levels of adventitious nanoscale material within microscale calcium carbonate would not be an additional toxicological concern.
- JECFA specification for lead in calcium carbonate is $\leq$ 3 mg/kg whereas the European Commission specification is $\leq$ 10 mg/kg.
- Limestone (a source of calcium carbonate) may contain variable amounts of aluminium. The ANS Panel noted that aluminium intake from use of calcium carbonate (E 170) as a food additive could significantly contribute (50–100%) to the weekly intake of aluminium, for which a tolerable weekly intake (TWI) of 1 mg aluminium/kg body weight (bw)/week had been established, and therefore specifications for the maximum level of aluminium in calcium carbonate may be required.

In the absence of a specific guidance, the ANS Panel in its 2011 re-evaluation opinion, did not address the safety of the use of calcium carbonate (E 170) as a food additive in food for infants below the age of 16 weeks of age.

1.3. Calcium dietary reference values and tolerable upper intake levels

In 2012, the EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA Panel) issued a scientific opinion on the tolerable upper intake level (UL) of calcium. In its opinion, the NDA Panel concluded that:

- No new data were available which would require a revision of the UL of 2,500 mg/day, previously established by the SCF in 2003 for adults, including pregnant and lactating women.
- No new data had become available which would allow the setting of a UL for infants, children or adolescents.

The NDA Panel also reported that the data from the EU population indicated that intakes of calcium in high consumers among adult males could be close to the UL and noted that, although available data did not allow the setting of a UL for infants, children or adolescents, no risk had been identified with the highest current levels of calcium intake in these age groups (EFSA NDA Panel, 2012). In that opinion, the NDA Panel further noted that in the general adult population calcium intakes up to about 2,400 mg/day had not been associated with an increased risk of chronic hypercalciuria or impaired kidney function, and that calcium intakes up to 3,000 mg/day had not been associated with an increased risk of nephrolithiasis (EFSA NDA Panel, 2012).

In 2015, the NDA Panel derived the average requirements (ARs) and population reference intakes (PRIs) for calcium (EFSA NDA Panel, 2015). Additionally, in its opinion on the essential composition of infant formulae (IF) and follow-on formulae (FOF) (EFSA NDA Panel, 2014), the NDA Panel established

an adequate intake (AI) for the population up to 6 months of age of 200 mg/day based on calcium intakes from breast milk. Considering the lower absorption efficiency of calcium in formula as compared to breast milk, the NDA Panel recommended a minimum calcium content in IF and FOF of 50 mg/100 kcal.

An overview of the ARs, PRIs, AIs and UL for calcium is provided in Table 1.

Table 1: Summary of the dietary reference values and for tolerable upper intake level for calcium (EFSA NDA Panel, 2012, 2014, 2015; EFSA, 2017)

Age	AI (mg/day)	AR (mg/day)	PRI (mg/day)	UL (mg/day)
< 6 months	200			_(c)
7–11 months	280			_(c)
1–3 years		390	450	_(c)
4–10 years		680	800	_(c)
11–17 years		960	1,150	_(c)
Adult		860(a);750(b)	1,000(a);950(b)	2,500
Pregnant women		860(a);750(b)	1,000(a);950(b)	2,500
Lactating women		860(a);750(b)	1,000(a);950(b)	2,500

AR: average requirement; PRI: population reference intake; AI: adequate intake; UL: tolerable upper intake level.
(a): 18–24 years.
(b): ≥ 25 years.
(c): No adequate data to derive a UL.

2. Data and methodologies

2.1. Data

For the current opinion, the Panel based its assessment on the:

- Information submitted by interested business operators (IBOs) in response to the EFSA public call for data[9] and subsequent requests for clarifications and/or additional information, and the conclusions and recommendations from previous evaluations
- Information on the use levels submitted in the context of the re-evaluation of calcium carbonate (E 170; EFSA ANS Panel, 2011)[10]
- Information from Mintel's Global New Products Database (GNPD) to identify the use of the food additive calcium carbonate (E 170) in food products

2.2. Methodologies

This opinion was formulated following the principles described in the EFSA Guidance on transparency with regard to scientific aspects of risk assessment (EFSA Scientific Committee, 2009) and following the relevant existing guidance documents from the EFSA Scientific Committee and in particular the EFSA Guidance of the Scientific Committee on the risk assessment of substances present in food intended for infants below 16 weeks of age (EFSA Scientific Committee, 2017).

In order to conclude on the safety of calcium carbonate (E 170) for all population groups and to address the data gaps identified during the re-evaluation in 2011, the FAF Panel assessed the information provided:

- for the risk assessment of calcium carbonate (E 170) in food for infants below 16 weeks of age in the food category (FC) 13.1.5.1 (Dietary foods for special medical purposes and special formulae for infants);
- for the follow-up on issues that have been raised in the conclusions and recommendations of the Scientific Opinion on the re-evaluation of calcium carbonate (E 170) as a food additive (EFSA ANS Panel, 2011).

[9] Call for technical and toxicological data on calcium carbonate (E 170) as a food additive for uses in foods for all population groups including infants below 16 weeks of age. Published: 18 October 2018. Available from: https://www.efsa.europa.eu/de/consultations/call/call-technical-and-toxicological-data-calcium-carbonate-e-170-uses.

[10] Re-evaluation of food colours: call for data https://wayback.archive-it.org/12090/20070108033129/http://www.efsa.europa.eu/en/science/afc.html.

Dietary exposure to calcium carbonate (E 170) from its use as a food additive in foods for infants below 16 weeks of age was estimated combining the mean and high-level consumption values for infant formulae reported for the period of 14–27 days of life which correspond, respectively, to 200 and 260 mL/kg bw per day (EFSA Scientific Committee, 2017, see Section 3.3.3.1), with the maximum levels according to Annex II and reported use levels submitted to EFSA following a call for data. Different scenarios were used to calculate exposure (see Section 3.3.1). Uncertainties on the exposure assessment were identified and discussed.

Dietary exposure to calcium carbonate (E 170) as a food additive was estimated combining the food consumption data available within the Comprehensive Database with reported use levels submitted to EFSA (EFSA ANS Panel, 2011; Documentation provided to EFSA n. 13). The exposure was estimated according to different exposure scenarios (EFSA ANS Panel, 2011). Uncertainties in the exposure assessment were identified and discussed (Section 3.3.5). Dietary exposure to calcium carbonate was also estimated from its uses as a source of calcium using the same data (food consumption and nutrient level) and both sources (food additive and source of calcium) were also summed up.

3. Assessment

3.1. Identity and specifications

Calcium carbonate is an inorganic salt with CAS Registry Number 471-34-1, Colour Index No. 77220. Synonyms are carbonic acid calcium salt, calcite, chalk, CI Pigment White 18, INS No. 170(i). Calcium carbonate is practically insoluble in water and ethanol (FCC 7, 2010). According to the available information in the REACH Registration dossier,[11] the solubility of calcium carbonate (conventional) in water tested according to the OECD TG 105 (OECD, 1995) is 16.6 mg/L (20°C, pH 9–9.4).

Specifications for calcium carbonate (E 170) have been defined in Commission Regulation (EU) No 231/2012 as described in Table 2. The JECFA specifications are reported in the same table.

Table 2: Specifications for calcium carbonate (E 170) according to Commission Regulation (EU) No 231/2012 and JECFA (2006)

	Commission Regulation (EU) No 231/2012	**JECFA Specification 2006**
Definition	Calcium carbonate is the product obtained from ground limestone or by the precipitation of calcium ions with carbonate ions	
Colour Index No	77220	
EINECS	Calcium carbonate: 207-439-9 Limestone: 215-279-6	
CAS number	–	471-34-1
Chemical name	Calcium carbonate	
Chemical formula	$CaCO_3$	$CaCO_3$
Molecular weight	100.1	100.09
Assay	Content not less than 98% on the anhydrous basis	Not less than 98.0% after drying
Description	White crystalline or amorphous, odourless and tasteless powder	Odourless, white micro-crystalline powder
Identification		
Solubility	Practically insoluble in water and in alcohol. Dissolves with effervescence in diluted acetic acid, in diluted hydrochloric acid and in diluted nitric acid, and the resulting solutions, after boiling, give positive tests for calcium	Insoluble in water and ethanol
Purity		
Loss on drying	Not more than 2% (200°C, 4 hours)	Not more than 2% (200°C, 4 hours)
Acid-insoluble substances	Not more than 0.2%	Not more than 0.2%

[11] https://echa.europa.eu/registration-dossier/-/registered-dossier/16050/4/9 accessed on 30.05.2023.

	Commission Regulation (EU) No 231/2012	JECFA Specification 2006
Magnesium and alkali salts	Not more than 1%	Not more than 1%
Free alkali	–	Not more than 0.05%
Fluoride	Not more than 50 mg/kg	Not more than 50 mg/kg
Antimony (as Sb)	Not more than 100 mg/kg single or in combination	
Copper (as Cu)		
Chromium (as Cr)		
Zinc (as Zn)		
Barium (as Ba)		Not more than 0.03%
Arsenic	Not more than 3 mg/kg	Not more than 3 mg/kg
Lead	Not more than 3 mg/kg	Not more than 3 mg/kg
Cadmium	Not more than 1 mg/kg	–

CAS: Chemical Abstract Service; EINECS: European Inventory of Existing Commercial Substances.

The Panel noted that in the EU specifications no maximum level for mercury and aluminium is set and no CAS number is included. The Panel noted that the JECFA specifications include the CAS number representing only precipitated calcium carbonate (PCC), the EU specifications include EINECS number for the ground limestone and PCC.

3.2. Technical data submitted

In order to support a revision of the existing specifications, the Panel has assessed the data provided by the IBOs in response to the EFSA call for data.[12]

In the response to the call for technical data and in response to the additional data requests from EFSA, two IBOs (Documentation provided to EFSA n. 1–3, 5–11) provided information. One IBO submitted analytical data on the levels of toxic elements: lead (Pb), mercury (Hg), cadmium (Cd), arsenic (As) and aluminium (Al); particle size and dissolution rates of calcium carbonate used as E 170 and the other IBO provided information on the fate and the reaction products of calcium carbonate (E 170) in ready to use formulae.

3.2.1. Characterisation of calcium carbonate used as E 170

As stated by one IBO (a consortium; Documentation provided to EFSA n. 2 and 5), calcium carbonate (E 170) is produced by grinding limestone ((geologic) ground calcium carbonate, GCC[13]) and by the precipitation of calcium ions with carbonate ions (PCC). The impurities found in GCC E 170 consist mainly of magnesium carbonate, quartz (crystalline silicon dioxide), clay and mica. The IBO further states that PCC E 170 is also produced from limestone. In this production process, the limestone is calcinated at temperatures above 1,000°C to produce calcium oxide which is further slaked followed by carbonation with carbon dioxide. During this process, chemical conversion of e.g. clay to aluminates is likely to occur.

This IBO clarified that at least four member companies/groups produce GCC E 170, three produce PCC E 170 and one is producing both types. The IBO noted that other manufacturers that are not direct members of the consortium also produce E 170 but that no information on their products is available to the consortium (Documentation provided to EFSA n. 5).

The IBO declared that both GCC E 170 and PCC E 170 are used as the food additive in food for all population groups including infants below 16 weeks of age.

The IBO declared that nano calcium carbonate (engineered nanomaterial) as well as forms of calcium carbonate coated or functionalised and with chemically modified surfaces are not used as the food additive E 170 (Documentation provided to EFSA n. 2, 5, 12).

[12] https://www.efsa.europa.eu/en/consultations/call/call-technical-and-toxicological-data-calcium-carbonate-e-170-uses.

[13] As explained by the IBO: *a naturally occurring substance as such, unprocessed or processed only by manual, mechanical or gravitational means, by dissolution in water, by flotation, by extraction with water, by steam distillation or by heating solely to remove water, or which is extracted from air by any means*.

The IBO (consortium) provided data separately for GCC and PCC E 170 and therefore, whenever possible, the technical data submitted by this IBO were reported in this opinion either to GCC E 170 or PCC E 170 (Documentation provided to EFSA n. 2, 5–11).

The revisions of the existing EU specifications proposed by the Panel are provided under Section 3.4.

3.2.2. Toxic elements

The following was requested in the EFSA call for data for all population groups:

- analytical data on current levels of lead, mercury, cadmium and arsenic in commercial samples of the food additive;
- the lowest technologically achievable level for aluminium, lead, mercury, cadmium and arsenic in order to adequately define their maximum limits in the specifications.

EFSA has also received data on additional elements which are also reported here.

One IBO (Consortium) has submitted information on the toxic elements in GCC and PCC E 170, provided by five members of the consortium (Documentation provided to EFSA n. 2, 5, 9, 11).

3.2.2.1. Calcium carbonate (E 170) – GCC

Arsenic, lead, cadmium and mercury

One IBO provided information on the level of toxic elements for 69 samples of GCC E 170 coming from three member companies produced in the year 2019, analysed in four different laboratories and accompanied with certificates of analysis. A number of analytical methods were reported, mainly based on inductively coupled plasma-mass spectrometry (ICP-MS) but some using AAS and with a variety of sample preparation methods used, all of them based on acid digestion (Documentation provided to EFSA n. 2).

In these 69 samples, the level of As was reported in 37 samples in the range 0.05–0.54 mg/kg, in 15 samples as < 0.2 mg/kg, in three samples as < 0.4 mg/kg and in 14 samples As was not detected. The limit of quantification (LOQ) and limit of detection (LOD) were ranging 0.01–0.5 mg/kg and 0.0067–0.03 mg/kg, respectively.

The level of Pb analysed in 55 samples ranged from 0.03–0.4 mg/kg, for 9 samples was reported as < 0.2 mg/kg and in 5 samples was not detected. The LOQ and LOD were ranging 0.005–0.05 mg/kg and 0.0017–0.03 mg/kg, respectively.

In 28 samples, the level of Cd ranged 0.041–0.8 mg/kg, for 12 samples was reported as < 0.2 mg/kg and for 3 samples as < 0.5 mg/kg. The Cd level was not detected in 26 samples. The LOQ and LOD were ranging 0.005–0.1 mg/kg and 0.0017–0.01 mg/kg, respectively.

The Panel noted that in none of the batches the levels of toxic elements exceeded the maximum limits set in the EU specifications for Pb, Cd and As (Table 2).

In nine samples the level of Hg ranged 0.01–0.05 mg/kg, in four samples was reported as < 0.01 mg/kg and in five samples as < 0.1 mg/kg. In 51 analysed batches the level of Hg was not detected. The LOQ and LOD were ranging 0.005–0.03 mg/kg and 0.0017–0.01 mg/kg, respectively.

Aluminium

The IBO provided information on the level of Al in 33 samples of GCC E 170 coming from different member companies analysed by different laboratories. A number of analytical methods were reported, mainly based on inductively coupled plasma optical emission spectroscopy (ICP-OES) and ICP-MS but some with X-ray fluorescence (XRF) and with a variety of sample preparation methods used resulting in total-Al or extractable Al concentrations (Documentation to EFSA n. 2, 5, 9). The reported levels of Al ranged 11–420 mg/kg.

The Panel noted that the data provided were obtained with different analytical methods the results of which are not equivalent. Consequently, these data were not used in this risk assessment.

In response to a request from EFSA, the same IBO provided information on the level of total Al analysed in 20 samples of GCC E 170 coming from three member companies using HNO_3 acid digestion for all batches. The level of HCl-extractable Al was also determined in the samples using the JECFA extraction method prescribed for calcium silicate (JECFA, 2015). (Documentation to EFSA n. 11).

The analytical results for the samples coming from different manufacturers span a wide range.

These 20 samples are reported in groups coming from the different manufacturers\analytical laboratories to enable a comparison of the total-Al and HCl-extractable Al levels.

For five samples the total-Al ranged 33.6–43.5 mg/kg and HCl-extractable ranged 0.3–0.1.5 mg/kg; in three batches total-Al content ranged from 193–253 mg/kg and HCl-extractable was reported as 1 mg/kg; in 12 batches the total-Al content ranged 132–218 mg/kg and HCl-extractable was reported as < 1 mg/kg.

The Panel considered that the Al levels determined after HCl-extraction are significantly lower compared to the total-Al content. The Panel considered that, the JECFA HCl extraction method is not suitable for Al extraction from $CaCO_3$ without adaptation because the HCl concentration of 0.5 M is too low in relation to the amount of $CaCO_3$ submitted to the test (as prescribed) and so the acid is neutralised. For this reason, this method cannot be recommended for the analysis of toxic elements in calcium carbonate and these data were not used.

3.2.2.2. Calcium carbonate (E 170) – PCC

Arsenic, lead, cadmium and mercury

Occurrence data were reported for 15 samples of PCC E 170 from two member companies of the consortium and produced in the period 2015–2019, analysed in three different laboratories and accompanied by certificates of analysis. A large number of analytical methods were reported, mainly based on ICP-OES and ICP-MS but some applying atomic absorption spectroscopy (AAS) using a variety of sample preparation methods used (all of them based on acid digestion) (Documentation provided to EFSA n. 2).

For these 15 samples the level of As was reported in two samples at 0.58 mg/kg and 0.79 mg/kg, in 11 samples as < 0.5 mg/kg and in 2 samples as < 1 mg/kg. The LOQs were ranging from 0.05 mg/kg to 1 mg/kg.

The level of Pb in 10 samples ranged from 0.27 to 0.34 mg/kg, for 3 samples the Pb was reported as below the LOQ of 0.5 mg/kg and in 2 samples the Pb was reported as below the LOQ of 2 mg/kg.

The level of Cd in 13 samples was reported as < 0.1 mg/kg and for 2 samples as < 1 mg/kg, with reported LOQs of 0.1 and 1 mg/kg, respectively.

The Panel noted that the maximum limits set in the EU specifications for Pb, Cd and As were not exceeded.

The level of Hg in 10 samples was reported as below the LOQ of 0.01 mg/kg, for 2 samples below the LOQ of 0.2 mg/kg and 3 samples were not analysed for the Hg content.

Aluminium

One IBO provided information on the level of aluminium (Al) in 32 samples of PCC E 170 provided by several member companies and analysed by four different laboratories. A number of analytical methods were reported, mainly based on ICP-OES and ICP-MS but some with XRF and with a variety of sample preparation methods used resulting in total-Al or extractable Al concentrations (Documentation to EFSA n. 2, 5, 9). The reported levels of Al ranged from 100 to 720 mg/kg.

The Panel noted that the data provided were obtained with different analytical methods the results of which are not equivalent. Consequently, these data were not used in this risk assessment.

In response to a request from EFSA, the same IBO provided information on the level of Al analysed in 24 samples of PCC E 170 coming from four member companies (Documentation provided to EFSA n. 11). Total-Al content was analysed in all 24 samples of which 19 were analysed after HNO_3 acid digestion. A further 5 of 24 samples were analysed for the total-Al content directly with an XRF only. Additionally, 10 of the 19 samples analysed by total acid digestion were also analysed in parallel by the XRF method.

The level of HCl-extractable Al was additionally determined in all 24 samples using the JECFA extraction method prescribed for calcium silicate (JECFA, 2015).

The analytical results for the samples coming from different manufacturers span a wide range. These 24 samples are reported in groups coming from the different manufacturers/analytical laboratories to enable a comparison of the total-Al and HCl-extractable Al levels. For 4 samples, the total-Al was 0.3 mg/kg and HCl-extractable Al ranged 0.16–0.19 mg/kg; in 10 samples, total-Al ranged from 145–206 mg/kg and HCl-extractable Al 4.6–5.2 mg/kg; in 5 samples the total-Al content ranged 966–1,120 mg/kg and HCl-extractable Al was reported as < 20 mg/kg and in five batches analysed only with XRF the level of total-Al was reported at 100–200 mg/kg and HCl-extractable Al as < 0.1 mg/kg.

The Panel noted that similarly to the GCC E 170, the Al levels determined for PCC E 170 after HCl-extraction are significantly lower compared to the total-Al content. As described for GCC above, the JECFA HCl extraction method as prescribed is not suitable for the analysis of toxic elements in calcium carbonate and these data were not used.

Other elements

The IBO provided information on the levels of antimony (Sb) copper (Cu), chromium (Cr) barium (Ba) and zinc (Zn) in 15 samples. For 10 samples coming from a manufacturer of PCC E 170 levels were: Sb (< 0.1 mg/kg), Cu (0.22–0.37 mg/kg), Cr (0.31–0.52 mg/kg), Ba (5.5–13 mg/kg) and Zn (< 2–5.5 mg/kg). No LOQ or LOD values were provided for these elements. For five samples coming from two other manufacturers the level of the elements were Sb (< 0.1 mg/kg), Cu (< 1–< 0.5 mg/kg), Cr (< 1–< 5 mg/kg), Ba (3 batches 1.1–1.3 mg/kg) and Zn (three batches only, 0.2–1.7 mg/kg). No LOQ and LOD values were provided for these elements. (Documentation to EFSA n. 2).

The Panel noted that in none of the batches, the levels of Sb, Cu, Cr, Ba and Zn exceeded the maximum limit (< 100 mg/kg) set in the EU specifications (Table 2) for these elements singly or in combination.

Based on the lowest technologically achievable levels and analytical limitations, the IBO proposed specification limits for the five elements in E 170 separately for infants < 16 weeks of age and for all populations, but without differentiation between GCC and PCC materials, as presented in Table 3 (Documentation to EFSA n. 2, 5).

Table 3: Proposed specification limits for the toxic elements lead, mercury, cadmium, arsenic and aluminium in E 170 submitted by the interested business operator (Documentation provided to EFSA n. 2, 5)

Age group	Lead	Mercury	Cadmium	Arsenic	Aluminium (total)
All populations	3 mg/kg	0.5 mg/kg	1 mg/kg	2 mg/kg	700 mg/kg
Infants below 16 weeks of age	3 mg/kg	0.5 mg/kg	1 mg/kg	2 mg/kg	500 mg/kg

The IBO (documentation submitted to EFSA n. 2) stated that the impurities in calcium carbonate are of geogenic origin and represent the natural background. Their content can only be controlled to a certain extent by applying selective mining techniques. The IBO further stated that the proposed limits for impurities as listed in Table 3 already take into account the selective mining procedures. According to the IBO, decontamination processes at industrial scale are not available for toxic elements in calcium carbonate.

For Al, the IBO provided a proposal for the maximum limit based on the total content of Al in E 170. According to the IBO there is no agreed methodology for the measurement of aluminium in E 170 (Documentation to EFSA n. 2, 5). The submitted data show that the results of the analysis of aluminium content is highly dependent on the digestion method and under these circumstances, an approac,h considering total aluminium levels is proposed. The IBO acknowledged that 'the maximum limit values proposed for aluminium are higher than other limit values for aluminium established in Regulation (EC) No 1333/2008 as these consider soluble values. The term "total" shall thus be included in the entry to clarify the difference'.

The IBO further stated that in GCC E 170, aluminium is a structural element of both clay and mica and aluminium remains unaltered in the crystalline structure. Magnesium carbonate and quartz do not contain aluminium. In case of PCC E 170, chemical conversion of e.g. clay to aluminates is likely to occur during the production process. The IBO further explained that this phenomenon will lead to a different solubility behaviour of aluminium compared to the initial clays which will bring an increased solubility of bound aluminium in the presence of, e.g. hydrochloric acid. The IBO states therefore that it is preferred to consider the total amount of aluminium in E 170 and not only the acid soluble fraction, as the digestion method will highly influence the results of analysis (Documentation to EFSA n. 2).

3.2.3. Fate and reaction products in food

The following was requested in the EFSA call for data for the uses of calcium carbonate (E 170) in special formulae used for infants below 16 weeks of age under special medical conditions (FC 13.1.5.1):

- the fate and the reaction products of calcium carbonate (E 170) in the formula ready to use.
- particular specification requirements for identity and the purity of calcium carbonate (E 170) (e.g. with respect to lead, aluminium and other toxic elements). This includes data on physical characterisation regarding the particle size as requested in part A.1 (of the call for data) in the food additive and the formulae as consumed.

As already noted by the ANS Panel at the time of the re-evaluation of E 170, calcium carbonate can be anticipated to be unstable in acidic foods (EFSA ANS Panel, 2011). According to the IBO (Documentation provided to EFSA no. 3), calcium carbonate (E 170) is highly stable under the conditions these food products would be exposed to. However, it cannot be ruled out that in the product matrix, especially in a liquid form, there would be dissociation of calcium carbonate into the free calcium ion and free carbonate ion. Additionally, it cannot be ruled out that upon dissociation, calcium and/or carbonate could interact with other ions present to form salts, complexes, chelates, aggregates, etc. (e.g. a portion of calcium carbonate dissociates, the resulting calcium ion reacts with other ions, such as phosphate, to become calcium phosphate).

The IBO stated that calcium carbonate when used as a food additive in food for special medical purpose (FSMP) for infants below 16 weeks of age, meet the current identity and purity specifications laid down in Regulation (EU) No 231/2012 for E 170.

3.2.4. Particle size

The following was requested in the EFSA call for data for all population groups:

- Detailed and comprehensive proposed specifications for the characterisation of the fraction of nanoparticles present in the food additive calcium carbonate (E 170).
- Information on particle size and particle size distribution (PSD) for the food additive calcium carbonate (E 170) supported by analytical data, in line with the 'EFSA guidance on the risk assessment of the application of nanoscience and nanotechnologies in the food and feed chain: Part 1, human and animal health'. [14]

One IBO provided information on PSD of 46 batches of E 170 coming from five member companies, as determined by laser diffraction (LD) (Documentation provided to EFSA n. 2). The calculated average median size of all analysed E 170 particles ranged between 0.51 and 41.1 μm. For 16 batches, the 10th percentile was calculated and ranged between 0.32 and 3.41 μm. The Panel noted that LD analysis is not considered a proper method to investigate the presence of nanosized particle as it does not provide information on the size of the constituent particles as required by the EFSA Guidance on Particle-TR (EFSA Scientific Committee, 2021a) and is prone to errors for polydisperse materials (Rauscher et al., 2019; Mech et al., 2020a,b).

Following a request from EFSA for additional information, the same IBO provided representative scanning electron microscopy (SEM) images on batches of GCC E 170 and of PCC E 170 (Documentation provided to EFSA n. 5). Information on particle size and PSD (supported by analytical data) or quantitative measurements were not provided.

The IBO stated that the SEM images show that small particles, including nanoparticles, may be present in both GCC and PCC E 170 products. According to the IBO, free nanoparticles are only rarely observed and appear to be an exception according to the SEM or TEM images. Most of the small particles, including nanoparticles, are part of larger aggregates and/or agglomerates with a diameter of several micrometres. (Documentation provided to EFSA n. 5).

The Panel considered that, based on the data provided, the presence of small particles including nanoparticles in the GCC, and PCC calcium carbonate used as a food additive (E 170) cannot be excluded.

In the response to the EFSA call the same IBO (consortium) did not provide the requested proposal for specifications in relation to the particle size (i.e. 'Detailed and comprehensive proposed specifications for the characterisation of the fraction of nanoparticles present in the food additive calcium carbonate (E 170)'). The IBO stated that 'they do not support the inclusion of specifications on size, particle size distribution or nanoparticles in E 170 calcium carbonate' based on the information regarding '(i) the absence of toxicological concerns for bulk and nano calcium carbonate (based on literature review), (ii) the technical limitations to quantify nano calcium carbonate in bulk products, (iii) the daily exposure to nano calcium carbonate particles from other sources than E 170, (iv) the need to maintain flexibility in the food chain and in other legislation'. Furthermore, the IBO stated that 'calcium carbonate particles (nano or not) will fully dissociate into its corresponding ions in acidic conditions similar to the gastric fluid' (Documentation provided to EFSA n. 2).

[14] The call for data referred to the 'EFSA guidance on the risk assessment of the application of nanoscience and nanotechnologies in the food and feed chain: Part 1, human and animal health' (EFSA Scientific Committee, 2018) which has been updated and complemented in 2021 by the 'Guidance on technical requirements for regulated food and feed product applications to establish the presence of small particles including nanoparticles' (EFSA Scientific Committee, 2021b).

3.2.5. Dissolution rate

In response to the EFSA additional request to determine if the particulate form of calcium carbonate (E 170) is solubilised under conditions simulating gastrointestinal digestion, one IBO provided information on the dissolution rate of GCC and PCC E 170 at pH 3 (simulating the stomach pH of the population above 16 weeks of age (EFSA Guidance on Particle-TR)) and at pH 6 (simulating the stomach pH of infants below 16 weeks of age, Nguyen et al., 2015; EFSA Scientific Committee, 2017, 2021a). For both GCC E 170 and PCC E 170, at least two independent experiments were performed at each pH and the methods were described in detail. According to the IBO, for all dissolution tests performed, at pH 3 and 6 for both PCC and GCC E 170, the concentrations tested correspond to the worst-case exposure to this food additive (Documentation provided to EFSA n. 5, 6, 7, 8, 10).

Specifically, the IBO reported that the concentration of E 170 tested (1,858 mg/L) at pH 6 was calculated to represent infant stomach conditions considering the maximum content of calcium in infant formulae and follow-on formulae (140 mg/100 kcal established in the Regulation (EU) No 2016/127) and assuming an energy intake from an infant formula of 531 kcal/day following EFSA (EFSA, NDA Panel, 2013), which resulted in 743 mg of calcium consumption per day. The IBO considered that 50% of the calcium present in the formula originates from E 170 and from this, calculated a daily intake of the food additive E 170 (i.e. 929 mg/day) which was further multiplied by a factor of 2 for an additional safety margin resulting in 1,858 mg of calcium carbonate consumption per day. The volume of gastric simulant recommended for infants and children in the EFSA Guidance on Particle-TR to dissolve the daily ingested amount of the tested substance for the dissolution tests is 1 L (Documentation provided to EFSA n. 8, 10).

The Panel noted that the IBO did not consider the maximum content of calcium at 250 mg/100 kcal established in the Regulation (EU) No 2016/128 for the FSMP (FC 13.1.5.1). However, the Panel noted that the amount of E 170 tested (corresponding to 1,858 mg/day) in the dissolution rate test at pH 6 (infant case) is over three times higher than the infant (< 16 weeks of age) daily exposure from the consumption of FSMP, calculated to be 528 mg/day (i.e. 110 mg/kg bw per day, for 95th percentile in the scenario using the highest value of the reported typical use levels (Table 5), multiplied by the infants default bw of 4.8 kg). The Panel considers that the concentration tested for the infant case is a realistic representation of the maximum daily amount ingested by consumers of FSMPs.

The considerations above by the Panel with respect to the exposure, do not necessarily cover the currently permitted uses of calcium carbonate (E 170) at *QS*, since exposure estimates cannot be calculated in that case.

3.2.5.1. Calcium carbonate (E 170) – GCC

Measurements of the dissolution rate were performed at room temperature at pH 3. A concentration of 12,500 mg of calcium carbonate/L was tested, corresponding to 5,000 mg of calcium/L. The concentration of dissolved calcium was determined at five time points (0, 5, 10, 30 and 60 min) by ICP-MS following ultrafiltration using a 10 kDa membrane filter. After 30 min, the solubilised fraction of GCC E 170 was in the range 93–103% and no plateau was observed.

The dissolution rate test at pH 6 (infant case) was performed at room temperature, with prior sonication (35 kHz, room temperature, 1 min) to disaggregate/deagglomerate the sample. In the test 1,858 mg of calcium carbonate/L was used, corresponding to 743 mg/L of calcium, with measurement at five time points (0, 5, 10, 30 and 60 min) and the level of dissolved calcium was determined by ICP-MS following ultrafiltration using a 10 kDa membrane filter. After 30 min, the solubilised fraction of GCC E 170 was 90% and no plateau was observed (Documentation provided to EFSA n. 8).

3.2.5.2. Calcium carbonate (E 170) – PCC

Measurements of the dissolution rate were performed at 37°C at pH 3. A concentration 12,500 mg of calcium carbonate/L was tested, corresponding to 5,000 mg/L of calcium, at five time points (0, 5, 10, 15 and 30 min) and the level of dissolved calcium was determined by titration with EDTA following ultrafiltration using a 100 kDa membrane filter.[15] After 30 min, the solubilised fraction of PCC E 170 was in the range 93–103% and no plateau was observed (Documentation provided to EFSA n. 7).

[15] The Panel noted that the size of the membrane filter used for the ultrafiltration does not meet the requirements of the current Guidance on technical requirements for regulated food and feed product applications to establish the presence of small particles including nanoparticles (EFSA Scientific Committee, 2021). However, these data were submitted to EFSA before the publication of this Guidance.

The dissolution rate test was also performed at room temperature at pH 6 (infant case) with prior sonication (35 kHz, room temperature, 1 min) to disaggregate/deagglomerate the sample. In the test 1,858 mg of calcium carbonate /L was used, corresponding to the 743 mg/L of calcium, and the level of dissolved calcium was determined at five time points (0, 30, 60, 90 and 120 min) by ICP-MS following ultrafiltration using a 3–10 kDa membrane filter. After 30 min, the solubilised fraction of PCC E 170 was 92–93% (Documentation provided to EFSA n. 10).

The Panel noted that some plateau was observed in the reported dissolution rate study at pH 6 for PCC E 170. However, the Panel noted that in the calculations the IBO did not consider the removal of the portion of calcium carbonate from the flask (dissolved and in suspension) for the analysis at each timepoint. This led to a miscalculation (underestimation) of the fraction of material dissolved, causing the appearance of a plateau. Using the raw data provided by the IBO, the Panel recalculated the dissolution rate of the PCC E 170 in this experiment and at 30 min the solubilised fraction of PCC E 170 was in the range 97.2–98.2% with no plateau observed (see Appendix D).

The Panel considers that the results of the tests at pH 3, simulating the stomach conditions of the population above 16 weeks of age and at pH 6, which mimics the buffered gastric pH of infants below 16 weeks of age, show that after 30 min for both GCC and PCC E 170 rapid dissolution is achieved, i.e. it exceeds the threshold value of 88% indicated in the EFSA Guidance on Particle-TR (EFSA Scientific Committee, 2021a) to achieve full solubilisation in the stomach at the concentration tested.

3.3. Exposure assessment

3.3.1. Authorised uses and use levels for calcium carbonate (E 170)

According to Regulation (EC) No 1333/2008, calcium carbonate (E 170) is included in Group I food additives (authorised as *QS*) and Group II food colours authorised as *QS*. In this opinion, these levels are termed maximum permitted levels (MPLs).

Calcium carbonate (E 170) is currently authorised in 119 food categories, as presented in Table 4.

Table 4: MPLs of calcium carbonate (E 170) in foods according to Regulation (EC) No 1333/2008

Food category number	Food category name	Restrictions/ exceptions	E-number	MPL (mg/L or mg/kg as appropriate)
01.3	Unflavoured fermented milk products, heat-treated after fermentation		Group I	QS
01.4	Flavoured fermented milk products including heat-treated products		Group I	QS
01.4	Flavoured fermented milk products including heat-treated products		Group II	QS
01.5	Dehydrated milk as defined by Directive 2001/114/EC	Except unflavoured products	Group II	QS
01.6.3	Other creams		Group I	QS
01.6.3	Other creams	Only flavoured creams	Group II	QS
01.7.1	Unripened cheese excluding products falling in category 16	Except mozzarella	Group I	QS
01.7.1	Unripened cheese excluding products falling in category 16	Only flavoured unripened cheese	Group II	QS
01.7.2	Ripened cheese		E 170	QS
01.7.3	Edible cheese rind		Group II	QS
01.7.4	Whey cheese		Group II	QS
01.7.5	Processed cheese		Group I	QS
01.7.5	Processed cheese	Only flavoured processed cheese	Group II	QS
01.7.6	Cheese products (excluding products falling in category 16)		Group I	QS
01.7.6	Cheese products (excluding products falling in category 16)	Only ripened products	E 170	QS

Food category number	Food category name	Restrictions/ exceptions	E-number	MPL (mg/L or mg/kg as appropriate)
01.7.6	Cheese products (excluding products falling in category 16)	Only flavoured unripened products	Group II	QS
01.8	Dairy analogues, including beverage whiteners		Group I	QS
01.8	Dairy analogues, including beverage whiteners		Group II	QS
01.9	Edible caseinates		E 170	QS
02.2.2	Other fat and oil emulsions including spreads as defined by Council Regulation (EC) No 1234/2007 and		Group I	QS
02.3	Vegetable oil pan spray		Group I	QS
03	Edible ices		Group I	QS
03	Edible ices		Group II	QS
04.2.1	Dried fruit and vegetables		Group I	QS
04.2.2	Fruit and vegetables in vinegar, oil or brine		Group I	QS
04.2.4.1	Fruit and vegetable preparations excluding compote		Group I	QS
04.2.4.1	Fruit and vegetable preparations excluding compote	Only *mostarda di frutta*	Group II	QS
04.2.5.3	Other similar fruit or vegetable spreads	Except *crème de pruneaux*	Group II	QS
04.2.5.4	Nut butters and nut spreads		Group I	QS
04.2.6	Processed potato products		Group I	QS
05.1	Cocoa and Chocolate products as covered by Directive 2000/36/EC	E 170, E 500–504, E 524–528 and E 530: 7% on dry matter, without fat, expressed as potassium carbonates	E 170	70 000
05.1	Cocoa and Chocolate products as covered by Directive 2000/36/EC	Only energy-reduced or with no added sugar	Group I	QS
05.2	Other confectionery including breath refreshening microsweets		Group I	QS
05.2	Other confectionery including breath refreshening microsweets		Group II	QS
05.3	Chewing gum		Group I	QS
05.3	Chewing gum		Group II	QS
05.4	Decorations, coatings and fillings, except fruit based fillings covered by category 4.2.4		Group I	QS
05.4	Decorations, coatings and fillings, except fruit based fillings covered by category 4.2.4		Group II	QS
06.2.2	Starches		Group I	QS
06.3	Breakfast cereals		Group I	QS
06.3	Breakfast cereals	Only breakfast cereals other than extruded, puffed and/or fruit flavoured breakfast cereals	Group II	QS

Food category number	Food category name	Restrictions/ exceptions	E-number	MPL (mg/L or mg/kg as appropriate)
06.4.2	Dry pasta	Only gluten free and/ or pasta intended for hypoproteic diets in accordance with Directive 2009/39/EC	Group I	QS
06.4.4	Potato Gnocchi	Except fresh refrigerated potato gnocchi	Group I	QS
06.4.5	Fillings of stuffed pasta (ravioli and similar)		Group I	QS
06.5	Noodles		Group I	QS
06.5	Noodles		Group II	QS
06.6	Batters		Group I	QS
06.6	Batters		Group II	QS
06.7	Pre-cooked or processed cereals		Group I	QS
06.7	Pre-cooked or processed cereals		Group II	QS
07.1	Bread and rolls	Except products in 7.1.1 and 7.1.2	Group I	QS
07.2	Fine bakery wares		Group I	QS
07.2	Fine bakery wares		Group II	QS
08.3.1	Non-heat-treated meat products		Group I	QS
08.3.2	Heat–treated meat products	Except *foie gras, foie gras entier, blocs de foie gras, Libamáj, libamáj egészben, libamáj tömbben*	Group I	QS
08.3.3	Casings and coatings and decorations for meat		Group I	QS
08.3.3	Casings and coatings and decorations for meat	Except edible external coating of pasturmas	Group II	QS
09.2	Processed fish and fishery products including molluscs and crustaceans		Group I	QS
09.2	Processed fish and fishery products including molluscs and crustaceans	Only fish paste and crustacean paste	E 170	QS
09.2	Processed fish and fishery products including molluscs and crustaceans	Only surimi and similar products and salmon substitutes based on *Theragra chalcogramma*, *Pollachius virens* and *Clupea harengus*	Group II	QS
09.3	Fish roe	Only processed fish roe	Group I	QS
09.3	Fish roe	Except Sturgeons' eggs (Caviar)	Group II	QS
10.2	Processed eggs and egg products		Group I	QS
11.2	Other sugars and syrups		Group I	QS
12.1.1	Salt		E 170	QS
12.1.2	Salt substitutes		Group I	QS
12.2.2	Seasonings and condiments		Group I	QS
12.2.2	Seasonings and condiments	Only seasonings, for example curry powder, tandoori	Group II	QS

Food category number	Food category name	Restrictions/ exceptions	E-number	MPL (mg/L or mg/kg as appropriate)
12.3	Vinegars		Group I	QS
12.4	Mustard		Group I	QS
12.4	Mustard		Group II	QS
12.5	Soups and broths		Group I	QS
12.5	Soups and broths		Group II	QS
12.6	Sauces		Group I	QS
12.6	Sauces	Excluding tomato-based sauces	Group II	QS
12.7	Salads and savoury based sandwich spreads		Group I	QS
12.7	Salads and savoury based sandwich spreads		Group II	QS
12.8	Yeast and yeast products		Group I	QS
12.9	Protein products, excluding products covered in category 1.8		Group I	QS
12.9	Protein products, excluding products covered in category 1.8		Group II	QS
13.1.3	Processed cereal-based foods and baby foods for infants and young children as defined by Directive 2006/125/EC	Only processed cereal based foods and baby foods, only for pH adjustment	E 170	QS
13.1.5.1	Dietary foods for infants for special medical purposes and special formulae for infants		E 170	QS
13.2	Dietary foods for special medical purposes defined in Directive 1999/21/EC (excluding products from		Group I	QS
13.2	Dietary foods for special medical purposes defined in Directive 1999/21/EC (excluding products from		Group II	QS
13.3	Dietary foods for weight control diets intended to replace total daily food intake or an individual		Group I	QS
13.3	Dietary foods for weight control diets intended to replace total daily food intake or an individual		Group II	QS
13.4	Foods suitable for people intolerant to gluten as defined by Regulation (EC) No 41/2009	Including dry pasta	Group I	QS
13.4	Foods suitable for people intolerant to gluten as defined by Regulation (EC) No 41/2009		Group II	QS
14.1.2	Fruit juices as defined by Directive 2001/112/EC and vegetable juices	Only vegetable juices	Group I	QS
14.1.2	Fruit juices as defined by Directive 2001/112/EC and vegetable juices	Only grape juice	E 170	QS
14.1.3	Fruit nectars as defined by Directive 2001/112/EC and vegetable nectars and similar products	Only vegetable nectars	Group I	QS
14.1.4	Flavoured drinks		Group I	QS
14.1.4	Flavoured drinks	Excluding chocolate milk and malt products	Group II	QS

Food category number	Food category name	Restrictions/ exceptions	E-number	MPL (mg/L or mg/kg as appropriate)
14.1.5.2	Other	Excluding unflavoured leaf tea; including flavoured instant coffee	Group I	QS
14.2.3	Cider and perry		Group I	QS
14.2.3	Cider and perry	Excluding *cidre bouché*	Group II	QS
14.2.4	Fruit wine and made wine		Group I	QS
14.2.4	Fruit wine and made wine	Excluding *wino owocowe markowe*	Group II	QS
14.2.5	Mead		Group I	QS
14.2.5	Mead		Group II	QS
14.2.6	Spirit drinks as defined in Regulation (EC) No 110/2008	Except whisky or whiskey;	Group I	QS
14.2.6	Spirit drinks as defined in Regulation (EC) No 110/2008	Except: spirit drinks as defined in Article 5(1) and sales denominations listed in Annex II, paragraphs 1–14 of Regulation 110/2008 and spirits (preceded by the name of the fruit) obtained by maceration and distillation, Geist (with the name of the fruit or the raw material used), London Gin, Sambuca, Maraschino, Marrasquino or Maraskino and Mistrà	Group II	QS
14.2.7.1	Aromatised wines		Group I	QS
14.2.7.2	Aromatised wine-based drinks		Group I	QS
14.2.7.3	Aromatised wine-product cocktails		Group I	QS
14.2.7.3	Aromatised wine-product cocktails		Group II	QS
14.2.8	Other alcoholic drinks including mixtures of alcoholic drinks with non-alcoholic drinks and spirit		Group I	QS
14.2.8	Other alcoholic drinks including mixtures of alcoholic drinks with non-alcoholic drinks and spirit		Group II	QS
15.1	Potato-, cereal-, flour- or starch-based snacks		Group I	QS
15.1	Potato-, cereal-, flour- or starch-based snacks		Group II	QS
15.2	Processed nuts		Group I	QS
15.2	Processed nuts		Group II	QS
16	Desserts excluding products covered in category 1, 3 and 4		Group I	QS
16	Desserts excluding products covered in category 1, 3 and 4		Group II	QS

Food category number	Food category name	Restrictions/ exceptions	E-number	MPL (mg/L or mg/kg as appropriate)
17.1	Food supplements supplied in a solid form, excluding food supplements for infants and young children		Group I	QS
17.1	Food supplements supplied in a solid form excluding food supplements for infants and young children		Group II	QS
17.2	Food supplements supplied in a liquid form, excluding food supplements for infants and young children		Group I	QS
17.2	Food supplements supplied in a liquid form excluding food supplements for infants and young children	Only food supplements in syrup form	Group II	QS
18	Processed foods not covered by categories 1 to 17, excluding foods for infants and young children		Group I	QS

MPL: Maximum permitted level; QS: *quantum satis*.

According to Annex III, Part 1, calcium carbonate (E 170) is authorised as a carrier in food additives.

In addition, according to Annex III, Part 3, calcium carbonate (E 170) is authorised at QS as food additives (including carriers) in food enzymes.

Finally, according to Annex III, Part 5, calcium carbonate (E 170) is authorised as a food additive in nutrients except nutrients intended to be used in foods for infants and young children (1–3 years of age).

3.3.2. Authorised uses as a nutrient source and fortifier and regulatory limits for calcium

Calcium carbonate is listed in Regulation (EU) No 609/2013[16] among the sources of calcium permitted for use in food intended for infants and young children (infant formulae, follow-on formulae, processed cereal-based food and baby food), in FSMPs and in total diet replacement for weight control. Calcium carbonate is also listed among the mineral substances permitted for use in food supplements according to Directive 2002/46/EC[17] and may be added to foods according to Regulation (EC) No 1925/2006[18] for fortification.

The current regulatory limits for calcium are established in Commission delegated Regulation (EU) 2016/127[19], applicable to in infant and follow-on formula, and in Commission delegated Regulation (EU) 2016/128[20] for FSMPs. They range from a minimum content of 50 mg calcium/100 kcal to a maximum of 140 mg calcium/100 kcal for infant formula and follow-on formula. For FSMPs, there are two set of limits for infants and children:

[16] Regulation (EU) No 609/2013 of the European Parliament and of the Council of 12 June 2013 on food intended for infants and young children, food for special medical purposes, and total diet replacement for weight control and repealing Council Directive 92/52/EEC, Commission Directives 96/8/EC, 1999/21/EC, 2006/125/EC and 2006/141/EC, Directive 2009/39/EC of the European Parliament and of the Council and Commission Regulations (EC) No 41/2009 and (EC) No 953/2009 Text with EEA relevance. OJ L 181, 29.6.2013, pp. 35–56.

[17] Directive 2002/46/EC of the European Parliament and of the Council of 10 June 2002 on the approximation of the laws of the Member States relating to food supplements (Text with EEA relevance). OJ L 183, 12.7.2002, pp. 51–57.

[18] Regulation (EC) No 1925/2006 of the European Parliament and of the Council of 20 December 2006 on the addition of vitamins and minerals and of certain other substances to foods. OJ L 404, 30.12.2006, pp. 26–38.

[19] Commission Delegated Regulation (EU) 2016/127 of 25 September 2015 supplementing Regulation (EU) No 609/2013 of the European Parliament and of the Council as regards the specific compositional and information requirements for infant formula and follow-on formula and as regards requirements on information relating to infant and young child feeding (Text with EEA relevance). OJ L 25, 2.2.2016, pp. 1–29.

[20] Commission Delegated Regulation (EU) 2016/128 of 25 September 2015 supplementing Regulation (EU) No 609/2013 of the European Parliament and of the Council as regards the specific compositional and information requirements for food for special medical purposes (Text with EEA relevance). OJ L 25, 2.2.2016, pp. 30–43.

- for FSMPs developed to satisfy the nutritional requirements of infants: a minimum content of calcium of 50 mg/100 kcal and a maximum content of calcium of 250 mg/100 kcal;
- for FSMPs other than that developed to satisfy the nutritional requirements of infants: a minimum content of calcium of 35 mg/100 kcal and a maximum content of calcium of 175 mg/100 kcal for infants (and respectively 50 and 250 mg/100 kcal for children of 1–10 years of age).

3.3.3. Exposure data

Some food additives are authorised in the EU in infant formulae as defined by Commission Regulation 2016/127/EC (FC 13.1.1) and in dietary foods for infants for special medical purposes and special formulae for infants (FC 13.1.5.1) at a specific MPL. However, a food additive may be used at a lower level than the MPL. Therefore, actual use levels are required for performing a more realistic exposure assessment especially for those food additives authorised at *QS*.

In the framework of Commission Regulation (EU) No 257/2010 regarding the re-evaluation of approved food additives, EFSA issued a public call[21] for technical and toxicological data on calcium carbonate (E 170) as a food additive for uses in foods for all population groups including infants below 16 weeks of age. It is noted that in the public call information on the use levels of E 170 in FCs other than FC 13.1.5.1 was not requested. In response to this public call, information on the actual use levels of calcium carbonate (E 170) in special foods for infants below 16 weeks of age was made available to EFSA by industry. No analytical data on the concentration of calcium carbonate (E 170) in foods were made available by the Member States. Therefore, for the general population, the Panel used the use levels provided to EFSA in response to the call for data published at the time of the re-evaluation of calcium carbonate (E 170)[10] to estimate the exposure in the present assessment (see Section 3.3.3).

3.3.3.1. Reported use levels as a food additive

For the food category 13.1.5.1, two IBOs provided EFSA with 9 use levels of calcium carbonate (E 170) (Documentation provided to EFSA n. 1, 3). According to these IBOs, typical levels of calcium carbonate (E 170) are on average of 353 mg/L; the highest value of typical levels reported is 424 mg/L in FSMPs (FC 13.1.5.1) for infants below 16 weeks of age. The Panel noted that maximum levels were not provided although E 170 is authorised at QS. Therefore, the assessment is limited to the highest value of the reported typical levels.

One IBO (Documentation provided to EFSA n. 1) has reported the use levels of calcium carbonate (E 170), as well as analytical data on the concentration of calcium carbonate in infant FSMP (FC 13.1.5.1.) for nine samples of the formulation. The E 170 added to the final product ranged from 32.4 to 42.2 mg/100 mL. The total calcium measured ranged from 98 to 163 mg/100 mL (117–132 mg/100 kcal) and the amount of calcium from the addition of E 170 to the formulae ranged from 13 to 17 mg/100 mL. The percentage of calcium in the infant FSMP (FC 13.1.5.1) coming from the use of the food additive ranged from 9% to 13% (Documentation provided to EFSA n. 1, 3).

The Panel noted that one IBO provided percentage of calcium coming from calcium carbonate in infant formula, however, these were not considered further in the exposure assessment since calcium carbonate as a food additive (E 170) is authorised only in FC 13.1.5.1.

For the general population, one IBO provided use levels for FC 17.1 only, for the period 2001–2019 (Documentation provided to EFSA n. 13), see Annex A. Considering that the reporting dates of the use levels available at the time of the re-evaluation are within this timeframe, the Panel considered both the data sets as a whole.[22] For the remaining FC, the Panel used the reported use levels considered in the re-evaluation of calcium carbonate (EFSA ANS Panel, 2011) covering 23 food categories out of the 119 authorised.

[21] Call for technical and toxicological data on calcium carbonate (E 170) for uses as a food additive in foods for all population groups including infants below 16 weeks of age. Available from: https://www.efsa.europa.eu/en/consultations/call/call-technical-and-toxicological-data-calcium-carbonate-e-170-uses.

[22] It is noted that the maximum use level reported in EFSA ANS Panel (2011) was 500,000 mg/kg for the use as food additive (FC 17.1) while the maximum reported use level in the 2019 submission (Documentation provided to EFSA n. 13) was 362,000 mg/kg for the use as nutrient. Considering that in the Mintel database few use levels equal or higher than 500,000 were found, the dietary exposure for the scenario consumer only of food supplements was estimated considering a maximum use level of 500,000 mg/kg.

3.3.3.2. Summarised data extracted from Mintel's Global New Products Database

Mintel's GNPD is an online database which monitors new introductions of packaged goods in the market worldwide. It contains information of over 4.1 million food and beverage products of which more than 1,300,000 are or have been available on the European food market. Mintel started covering EU's food markets in 1996, currently having 24 out of its 27 member countries, and Norway is also presented in Mintel's GNPD.[23]

For the purpose of this Scientific Opinion, Mintel's GNPD[24] was used for checking the labelling of food and beverage products and food supplements for calcium carbonate (E 170) within the EU's food market as the database contains the compulsory ingredient information on the label.

According to Mintel's GNPD, calcium carbonate was labelled on 174 products of 'Baby formula (0–6 months)' between January 2018 and April 2023, which represent 50% of the total number of food products belonging to this subcategory present in Mintel's GNPD. It is noted that calcium carbonate (E 170) is not authorised as an additive in FC 13.1.1, therefore, this labelling may be due to its use as a calcium source.

In the category of baby foods (including fruit products, desserts and yoghurts, growing up milk 1–4 years, biscuits and rusks, cereals, formula, etc.), 603 other products were found in Mintel's GNPD as labelled with calcium carbonate (E 170).

Considering all foods on the EU market, 6,643 products (including special formulae and other baby foods) were labelled with calcium carbonate and/or E 170 between January 2018 and April 2023 according to Mintel GNPD. The percentages of products containing calcium carbonate among all products of the same category ranged from less than 0.1% in many food subcategories to 51% in Mintel's GNPD food subcategory 'Growing Up Milk (1–4 years)'. The average percentage of foods labelled to contain calcium carbonate and/or E 170 was 1.9%.

Annex B lists the percentage of the food products labelled with calcium carbonate (E 170) out of the total number of food products per food subcategory according to Mintel's GNPD food classification.

3.3.4. Dietary exposure estimates

3.3.4.1. Dietary exposure to calcium carbonate (E 170) for infants below 16 weeks

Exposure to calcium carbonate (E 170) from its uses as a food additive in FSMP formulae (FC 13.1.5.1) for infants below 16 weeks was estimated. This scenario is based on the recommended consumption levels from SC Guidance (EFSA, 2017). This guidance 'recommends values of 200 and 260 mL formula[25]/kg bw per day as conservative mean and high level consumption values to be used for performing the risk assessments of substances which do not accumulate in the body present in food intended for infants below 16 weeks of age'. These recommended consumption levels correspond to 14- to 27-day-old infants consumption. No regulatory maximum level exposure assessment scenario was performed as no numerical MPL are set for special infant formulae (FC 13.1.5.1).

Table 5 summarises the estimated exposure to calcium carbonate (E 170) from its use as a food additive in FC 13.1.5.1 for infants below 16 weeks of age.

Table 5: Dietary exposure to calcium carbonate (E 170) in foods for infants below 16 weeks of age considering the consumption of special infant formulae (FC 13.1.5.1) according to Annex II to Regulation (EC) No 1333/2008 (in mg/kg bw per day)

	Infants (< 16 weeks of age)
Refined estimated exposure assessment scenario	
Scenario using the highest value of the reported typical use levels (424 mg/L)	
• Mean consumption (200 mL/kg bw per day)	85
• High-level consumption (95th percentile, 260 mL/kg bw per day)	110
Scenario using the mean value of the reported typical use levels (353 mg/L)	
• Mean consumption (200 mL/kg bw per day)	71
• High-level consumption (95th percentile, 260 mL/kg bw per day)	92

bw: body weight.

[23] Missing Cyprus, Luxembourg and Malta.
[24] http://www.gnpd.com/sinatra/home/ accessed on 3/4/2023.
[25] Editorial.

The maximum occurrence scenario was used in the assessment, the mean occurrence scenario is also reported and indicates that there are products on the market giving lower exposure levels.

3.3.4.2. Updated dietary exposure assessment for the general population

To address the uncertainties from the re-evaluation (EFSA ANS Panel, 2011) linked to the potential intake of aluminium resulting from the dietary exposure to calcium carbonate (E 170), an update of the exposure assessment to E 170 for the general population was performed. The occurrence data used in the current exposure assessment are the ones available and used in the ANS Panel opinion on the re-evaluation (EFSA ANS Panel, 2011) and the one submitted by one IBO in 2019 (Documentation provided to EFSA n. 13) and cover the use of calcium carbonate as a food additive (E 170) (Section 3.3.1) and as a source of calcium (Section 3.3.2). These data can be seen in Annex C. Concerning the consumption data, the EFSA Comprehensive database (November 2022 release) was used for the current assessment.

Both exposure estimates were calculated, and the total is also presented in the current opinion (Table 6).

Table 6: Dietary exposure to calcium carbonate for the general population from its use as a food additive according to Annex II to Regulation (EC) No 1333/2008, as a calcium source and from both (food additive and calcium source combined), in mg/kg bw per day

	Infants (12 weeks–11 months)	Toddlers (12–35 months)	Children (3–9 years)	Adolescents (10–17 years)	Adults (18–64 years)	The elderly (≥ 65 years)
From the use as a food additive: refined estimated exposure assessment scenario						
Brand-loyal scenario						
• Mean	0.6–24	15–49	8.5–40	4–21	5–13	5–11
• 95th percentile	13–68	28–108	17–77	9–44	12–29	11–24
Non-brand-loyal scenario						
• Mean	0.6–19	15–38	7–29	2–17	5–11	5–11
• 95th percentile	13–68	28–81	15–64	4–36	11–23	9–24
From the use as a source of calcium: refined estimated exposure assessment scenario						
• Mean	12–59	3–58	4–23	2–12	0.7–18	0.4–24
• 95th percentile	36–246	21–214	21–60	10–39	4–68	2–75
From the use as both a food additive and a source of calcium: refined estimated combined exposure assessment scenario[(a)]						
• Mean	16–73	27–92	21–47	6–27	8–27	6–35
• 95th percentile	51–311	65–281	50–94	17–60	18–89	14–96

bw: body weight.
(a): This scenario used the use levels considered for the non-brand loyal scenario for the use of E 170 as a food additive.

When considering the use of calcium carbonate (E 170) as a food additive, from the refined estimated exposure scenario, in the *brand-loyal scenario*, mean exposure ranged from 0.6 mg/kg bw per day in infants to 49 mg/kg bw per day in toddlers. The high exposure (p95) ranged from 9 mg/kg bw per day in adolescents to 108 mg/kg bw per day in toddlers. In the non-brand loyal scenario, mean exposure ranged from 0.6 mg/kg bw per day in infants to 38 mg/kg bw per day in toddlers. The high exposure (p95) ranged from 4 mg/kg bw per day in adolescents to 81 mg/kg bw per day in toddlers.

Considering use levels from the use of calcium carbonate as a source of calcium, mean exposure to calcium carbonate ranged from 0.4 mg/kg bw per day for the elderly to 59 mg/kg bw per day in infants. The 95th percentile of exposure ranged from 2 mg/kg bw per day for the elderly to 246 mg/kg bw per day in infants.

Considering both uses of calcium carbonate, as a food additive (E 170) and as a source of calcium, mean exposure ranged from 6 mg/kg bw per day for the elderly to 92 mg/kg bw per day in toddlers.

The 95th percentile of exposure ranged from 14 mg/kg bw per day for the elderly to 311 mg/kg bw per day in infants.

For consumers' only of food supplements, mean exposure to calcium carbonate as a food additive (E 170), as a source of calcium and considering the consumption of food supplements, ranged from 9 mg/kg bw per day for the elderly to 167 mg/kg bw per day in children. The high exposure (p95) ranged from 51 mg/kg bw per day in the elderly to 458 mg/kg bw per day in adolescents.

For infants' and toddlers' consumers only of FSMP (FC 13.1.5.1), mean exposure to calcium carbonate as a food additive (E 170) and as a source of calcium ranged from 21 mg/kg bw per day for both infants and toddlers to 88 mg/kg bw per day in toddlers. The high exposure (p95) ranged from 51 mg/kg bw per day in infants to 313 mg/kg bw per day also in infants.

3.3.5. Uncertainty analysis

In accordance with the guidance provided in the EFSA opinion related to uncertainties in dietary exposure assessment (EFSA, 2007), the following sources of uncertainty have been considered and summarised in Table 7.

Table 7: Qualitative evaluation of influence of uncertainties on the dietary exposure estimate

Sources of uncertainties	Direction[(a)]
Infants < 16 weeks of age	
Consumption data: one reference point only to estimate exposure during the period of up to 16 weeks of age	+/–
Refined exposure assessment scenarios: – exposure calculations based on the maximum level (reported use from industries) – exposure calculations based on the mean level (reported use from industries)	 + +/–
General population	
Consumption data: different methodologies/representativeness/underreporting/ misreporting/no portion size standard	+/–
Methodology used to estimate high percentiles (95th) long-term (chronic) exposure based on data from food consumption surveys covering only a few days	+
Correspondence of reported use levels to the food items in the EFSA Comprehensive Database: uncertainties to which types of food the levels refer	+/–
Uncertainty in possible national differences in use levels of food categories	+/–
Reported use levels: – use levels considered applicable to all foods within the entire food category, whereas on average only 1.9% of the foods belonging to those food categories were labelled as containing the additive – reported use levels taken from the re-evaluation of calcium carbonate for all FC except FC 17.1 (EFSA ANS Panel, 2011) whereas use levels now may be different	 + +/–
Food categories included in the exposure assessment: no occurrence data for certain food categories which were therefore not considered in the exposure estimates	–
Foods which may contain the food additive according to Annex III to Regulation (EC) No 1333/2008 not taken into account	–
Refined exposure assessment scenario: – exposure calculations based on the maximum (brand-loyal scenario) – exposure calculations based on the mean levels (brand-loyal scenario and non-brand-loyal scenario)	 + +/–

(a): +: uncertainty with potential to cause overestimation of exposure; –: uncertainty with potential to cause underestimation of exposure.

Calcium carbonate (E 170) is authorised in many food categories including foods for infants (FCs 13.1.3 Processed cereal-based foods and baby foods for infants and young children and 13.1.5.1 Dietary foods for infants for special medical purposes and special formulae for infants) according to Annex II to Regulation (EC) No 1333/2008.

Based on the assumption that carers of children would be brand-loyal to an infant formula for special medical purposes (FC 13.1.5.1), the exposure assessment scenario (Table 5) would in general result in an average reliable estimation of exposure for infants below 16 weeks of age.

In all but one food category, calcium carbonate (E 170) is authorised at *QS*; therefore, the exposure estimates are based on reported use levels provided to EFSA. These data were not available for all the food categories in which calcium carbonate (E 170) is authorised and only some of these food categories could be considered in the current exposure assessment. However, according to Mintel (Annex B), the main foods in which calcium carbonate (E 170) is labelled are taken into account. In addition, some food categories in which calcium carbonate (E 170) is authorised, actually do not contain calcium carbonate (E 170) (cf. Mintel, Annex B); this is the case for the food categories of dairy products (FC 1, except cheeses), of fruits and vegetables (FC 4) and of alcoholic beverages (FC 14.2). For other food categories in which calcium carbonate (E 170) is authorised but for which no data were available, the percentage of foods labelled with calcium carbonate (E 170) is low (e.g. edible ices (FC 3) and desserts (FC 16), the percentage of foods labelled with calcium carbonate (E 170) ranges between 1.3% and 5.2%).

The percentage of foods per sub-category labelled to contain calcium carbonate (E 170) ranged between < 0.1% up to 51% with an average of 1.9%, whereas in the assessment it was assumed that 100% of the foods belonging to an authorised food category contained the additive.

It has to be mentioned that the reported use levels considered in the current exposure assessment are the ones requested in a call for data published in 2006 and used in the previous EFSA ANS opinion (EFSA ANS Panel, 2011). More updated data were received only for FC 17.1 (Documentation provided to EFSA n. 13). It may be that the current use levels are different.

Overall, the uncertainties identified for the general population's exposure assessment resulted in an overestimation of the exposure to calcium carbonate (E 170) from its use as a food additive according to Annex II for the refined exposure assessment scenario.

3.3.6. Intake of calcium from calcium carbonate (food additive E 170, fortification, supplement)

In 2011, in the re-evaluation of calcium carbonate (E 170), the ANS Panel estimated the intake of calcium from the use of calcium carbonate using different scenarios.

In the current opinion, based on the exposure estimates (Table 6), the calcium intake from the use of calcium carbonate (E 170) as a food additive was estimated at the mean between 0.2 mg/kg bw per day (infants) to 20 mg/kg bw per day (toddlers). At the 95th percentile, calcium intakes ranged from 4 mg/kg bw per day (adolescents) to 43 mg/kg bw per day (toddlers). Calcium intakes from the use of calcium carbonate as a food additive and as a source of calcium (fortification) were estimated at the mean between 2 mg/kg bw per day (the elderly) to 37 mg/kg bw per day (toddlers). At the 95th percentile, calcium intakes ranged from 6 mg/kg bw per day (the elderly) to 125 mg/kg bw per day (infants). Calcium intakes from the use of calcium carbonate (E 170) as a food additive, source of calcium (fortification) and from the consumption of food supplements were estimated for the population of food supplements consumers at the mean between 3 mg/kg bw per day (the elderly) to 67 mg/kg bw per day (children). At the 95th percentile, calcium intakes ranged for this group from 20 mg/kg bw per day (the elderly) to 183 mg/kg bw per day (adolescents).

The intake of calcium expressed as mg/day is reported in Tables 8 and 9.

Table 8: Intake of calcium per person (mg/day) for infants, toddlers (1–3 years) and other children (3–9 years), from: a) uses of calcium carbonate (E 170) as a food additive; b) uses of calcium carbonate as a source of calcium in foods; c) the sum of food additive (E 170) use and sources of calcium and; d) use of calcium carbonate as a source of calcium in food supplements (consumers only scenario)

	Infants (12 weeks–11 months)				Toddlers (12–35 months)				Children (3–9 years)			
	Mean		P95		Mean		P95		Mean		P95	
	Min	Max	Min	Max	Min	Max	Min	Max	Min	Max	Min	Max
a) From E 170 (BL scenario)	2	88	48	245	72	238	137	521	81	380	163	726
b) As a source of calcium	45	211	131	885	16	280	100	1,034	35	214	200	566
c) As both an additive and a source of calcium	56	264	183	1,121	129	443	315	1,355	203	450	475	896
d) For consumers' only of food supplements (number of consumer)	–	–	–	–	–	–	–	–	461 (n = 381)	1,568 (n = 20)	945 (n = 381)	3,336 (n = 139)

Table 9: Intake of calcium per person (mg/day) for adolescents, adults, the elderly from: a) uses of calcium carbonate (E 170) as a food additive; b) uses of calcium carbonate as a source of calcium in foods; c) the sum of food additive (E 170) use and sources of calcium and; d) use of calcium carbonate as a source of calcium in food supplements (consumers only scenario)

	Adolescents (10–17 years)				Adults (18–64 years)				The elderly (≥ 65 years)			
	Mean		p95		Mean		p95		Mean		p95	
	Min	Max	Min	Max	Min	Max	Min	Max	Min	Max	Min	Max
a) From E 170 (BL scenario)	81	456	193	934	161	393	373	870	148	346	322	730
b) As a source of calcium	48	255	214	822	21	535	115	2,056	11	726	66	2,292
c) As both an additive and a source of calcium	132	574	360	1,280	238	824	545	2,680	181	1,058	425	2,935
d) For consumers' only of food supplements (number of consumer)	421 (n = 110)	3,202 (n = 80)	1,289 (n = 110)	9,762 (n = 80)	432 (n = 21)	2,432 (n = 66)	1,738 (n = 246)	10,553 (n = 66)	309 (n = 10)	3,530 (n = 6)	1,569 (n = 143)	7,184 (n = 87)

n: number of consumers for the exposure scenario of consumers' only of food supplements.

3.3.7. Intake of calcium from all sources (food additives, fortification, supplements and natural sources)

The NDA Panel issued an opinion on the dietary reference value (DRV) for calcium (EFSA NDA, 2015) where calcium intake was estimated considering consumption of foods either fortified or not (i.e. without food supplements). Based on the EFSA Comprehensive Database available at the time, calcium intake was estimated for 13 dietary surveys (including UK), for the population from infants to the elderly. Nutrient composition data for calcium were derived from the EFSA Nutrient Composition Database (Roe et al., 2013) with data from seven countries (including UK). Average calcium intake ranged between 307 and 584 mg/day in infants (aged between 1 and 11 months, four surveys), between 533 and 838 mg/day in children aged 1 to < 3 years (five surveys), between 589 and 986 mg/day in children aged 3 to < 10 years (seven surveys), between 675 and 1,273 mg/day in children aged 10 to < 18 years (six surveys) and between 690 and 1,122 mg/day in adults (≥ 18 years) (eight surveys). High level (p95) calcium intake ranged between 658 and 832 mg/day in infants (aged between 1 and 11 months, three surveys), between 915 and 1,310 (for UK) mg/day in children aged 1 to < 3 years (four surveys), between 978 and 1,624 mg/day in children aged 3 to < 10 years (seven surveys), between 1,136 and 2,258 mg/day in children aged 10 to < 18 years (five surveys) and between 1,151 and 2,188 mg/day in adults (≥ 18 years) (eight surveys).

Calcium intake was also more recently estimated by different dietary surveys across EU countries. In Ireland, mean intake for children (5–12 years) was estimated at 791 mg/day (p95 = 1,224 mg/day) (Kehoe et al., 2023); mean intake for adolescents (13–18 years) was estimated at 812 mg/day (p75 = 1,003 mg/day) (Cashman et al., 2022), while for the elderly (+65 years), mean calcium intake was estimated at 906 mg/day excluding supplements and 984 mg/day including the supplements (O'Connell et al., 2021).

In Italian children (median age of 8.3 years old), median calcium intake is estimated at 460 mg/day (Q1–Q3 = [353–642] (D'Auria et al., 2022).

In Poland, calcium intake for adults (between 40 and 75 years old) was estimated at the mean at 783 mg/day (median = 688 mg/day, Q1–Q3 = [491–929]) (Augustyniak and Galas, 2022).

A study on pregnant women in the Netherlands estimated their mean calcium intake at 950 mg/day (Willemse et al., 2023).

In France, the INCA 3 study (ANSES, 2017) estimated the calcium intake for the child population (0–10 years old) at 830 mg/day at the mean (median = 815 mg/day), for the adolescents (11–17 years old) at 929 mg/day at the mean (median = 857 mg/day) and for the adults (18–79 years old) at 929 mg/day at the mean (median = 864 mg/day) (ANSES, 2017).

3.4. Proposed revision to existing EU specifications for calcium carbonate (E 170)

The potential exposure to impurities from the use of calcium carbonate as a food additive (E 170) and as a nutrient source of calcium can be calculated by assuming that the impurity is present in calcium carbonate up to a certain limit value, and then by calculation *pro-rata* to the estimates of exposure to the food additive itself.

The Panel noted that the IBO provided information on the level of impurities for the calcium carbonate (E 170) used as a food additive. Considering that calcium carbonate may also be used in the manufacture of foods as a source of calcium for nutritional purposes and that the same purity criteria established for the use as a food additive would apply also to the use as a source of calcium, the Panel has assumed that the data provided by the IBO on impurities in E 170 may apply equally to calcium carbonate when used as a source of calcium.

In the current opinion, the dietary exposure for the general population, for infants below 16 weeks of age, and for infants' (from 12 weeks to 1 year of age) and toddlers' consumers only of FSMP was estimated (see Section 3.3.4, Tables 5 and 6). For infants below 16 weeks of age, the refined exposure estimates based on the highest value and mean of the reported typical use levels of E 170 reported by industry (Table 5) were considered. The mean and 95th percentile exposure estimates were 85 and 110 mg/kg bw per day using the highest value of the reported typical use level, and 71 and 92 mg/kg bw per day for the mean reported typical use level. For infants' and toddlers' consumers only of FSMP (FC 13.1.5.1), the dietary exposure to calcium carbonate (E 170) were 88 and 313 mg/kg bw per day, respectively, at the highest mean and 95th percentile, using the highest value of the typical use levels reported by industry.

With regard to the dietary exposure to calcium carbonate for the general population, the Panel considered the highest mean and 95th percentile, which were calculated in three exposure scenarios:

i) calcium carbonate used as a food additive (E 170) only (highest mean and 95th percentile: 49 and 108 mg/kg bw per day for toddlers, refined brand loyal scenario).
ii) calcium carbonate used as a food additive (E 170) and as a source of calcium from fortified food (highest mean and 95th percentile: 92 and 312 mg/kg bw per day for toddlers and infants, respectively).
iii) calcium carbonate used as a food additive (E 170) and as a source of calcium for consumers only of food supplements (highest mean and 95th percentile: 167 and 458 mg/kg bw per day for children and for adolescents, respectively).

Considering that:

- currently calcium carbonate (E 170) as a food additive is allowed at *QS* in FSMP (FC 13.1.5.1).
- calcium carbonate is authorised in Regulation (EU) No 609/2013[16] among the potential sources of calcium permitted for use in food intended for infants and young children (infant formulae, follow-on formulae, processed cereal-based food and baby food), in FSMPs, and in total diet replacement for weight control.
- the current regulatory limits for calcium range from a minimum content of 50 mg calcium/100 kcal to maximum of 140 mg calcium/100 kcal for infant formula and follow-on formula (Commission delegated regulation (EU) 2016/127[19]). For the FSMP the content of calcium ranges from a minimum of 50 mg/100 kcal to 250 mg calcium/100 (Commission delegated Regulation (EU) 2016/128[20]).

the Panel used two additional exposure scenarios to perform the risk assessment to toxic elements from the use of this food additive:

iv) calcium carbonate used in FSMP at the allowed maximum calcium level and at the highest consumption value of 260 mL formula/kg bw per day as recommended in the EFSA guidance (EFSA Scientific Committee, 2017) and the highest energy requirement 70 kcal/100 mL of the formula as set in the regulation EU 128/2016.
v) calcium carbonate used in infant formula at the allowed maximum calcium level and at the highest consumption value of 260 mL formula/kg bw per day as recommended in the EFSA guidance (EFSA Scientific Committee, 2017) and the highest energy requirement 70 kcal/100 mL of the formula as set in the Regulation EU 127/2016.

The level of the impurity in calcium carbonate combined with the estimated intakes of calcium carbonate as calculated by the Panel could result in an exposure which can be compared with the following reference points (RPs) or health-based guidance values (HBGV) for the undesirable impurities potentially present in this food additive (see Table 10).

Table 10: Reference points/health-based guidance values for impurities potentially present in calcium carbonate used as a food additive (E 170) and as a nutrient source of calcium

Impurity HBGV/RP	Basis/reference
Lead (Pb)/0.5 μg/kg bw per day ($BMDL_{01}$)	The reference point is based on a study demonstrating perturbation of intellectual development in children with the critical response size of 1 point reduction in IQ. The EFSA CONTAM Panel mentioned that a 1 point reduction in IQ is related to a 4.5% increase in the risk of failure to graduate from high school and that a 1 point reduction in IQ in children can be associated with a decrease of later productivity of about 2%. A risk cannot be excluded if the exposure exceeds the $BMDL_{01}$ (MOE lower than 1). EFSA CONTAM Panel (2010)
Mercury (Hg)/4 μg/kg bw per week (TWI)	The HBGV was set using kidney weight changes in male rats as the pivotal effect. Based on the $BMDL_{10}$ of 0.06 mg/kg bw per day, expressed as mercury, and an uncertainty factor of 100 to account for inter and intra species differences, with conversion to a weekly basis and rounding to one significant figure, a TWI for inorganic mercury of 4 μg/kg bw per week, expressed as mercury was established. EFSA CONTAM Panel (2012)

Impurity HBGV/RP	Basis/reference
Cadmium (Cd)/2.5 μg/kg bw per week (TWI)	The derivation of the reference point is based on a meta-analysis to evaluate the dose–response relationship between selected urinary cadmium and urinary beta-2-microglobulin as the biomarker of tubular damage recognised as the most useful biomarker in relation to tubular effects. A group-based $BMDL_5$ of 4 μg Cd/g creatinine for humans was derived. A chemical specific adjustment factor of 3.9 was applied to account for human variability in urinary cadmium within each dose-subgroup in the analysis resulting in a reference point of 1.0 μg Cd per g creatinine. In order to remain below 1 μg Cd/g creatinine in urine in 95% of the population by age 50, the average daily dietary cadmium intake should not exceed 0.36 μg Cd/kg bw, corresponding to a weekly dietary intake of 2.5 μg Cd/kg bw. EFSA CONTAM Panel (2009a)
Arsenic (As)/0.3–8 μg/kg bw per day ($BMDL_{01}$)	The reference point is based on a range of benchmark dose lower confidence limit ($BMDL_{01}$) values between 0.3 and 8 μg/kg bw per day identified for cancers of the lung, skin and bladder, as well as skin lesions. In general, the MOE should be at least 10,000 if the reference point is based on carcinogenicity in animal studies. However, as the BMDL for As is derived from human studies, an interspecies extrapolation factor (i.e. 10) is not needed, i.e. a MOE of 1,000 would be sufficient. EFSA CONTAM Panel (2009b); EFSA Scientific Committee (2012)
Aluminium (Al)/1,000 μg/kg bw per week (TWI)	The HBGV is based on the combined evidence from several studies in mice, rats and dogs that used dietary administration of aluminium compounds. In these studies, the lowest no-observed-adverse-effect levels (NOAELs) for effects on neurotoxicity, testes and embryotoxicity, were reported at 30, 27 and 100, and for effects on the developing nervous system, between 10 and 42 mg aluminium/kg bw per day, respectively. Based on the combined evidence from the above-mentioned studies, the EFSA AFC Panel established a TWI of 1,000 μg Al/kg bw per week. EFSA (2008)

HBGV: health based guidance value; RP: Reference point; $BMDL_{01}$: benchmark dose (lower confidence limit); TWI: tolerable weekly intake; MOE: margin of exposure.

The risk assessment of the undesirable impurities helps to determine whether there could be a possible health concern if these impurities would be present at the maximum limit values in calcium carbonate (E 170). The assessment is performed by calculating the MOE (margin of exposure) by dividing the reference point (e.g. BMDL) by the exposure estimate, or by estimating the contribution of the use of the calcium carbonate to the HBGV (expressed as percentage of the HBGV).

3.4.1. Toxic elements

The Panel noted that the occurrence data on toxic elements submitted by the IBO for E 170 are substantially lower than the current limits in the EU specifications (Documentation provided to EFSA n. 2). The Panel considered that the maximum limits in the EU specifications for toxic elements should be established based on actual levels in the commercial food additive. If the European Commission decides to revise the current limits in the EU specifications, the estimates of toxic elements intake as presented below could be considered.

The Panel noted that the data on the levels of Pb, Cd and As provided by the IBOs vary in format, as some of the data submitted were reported as below the LOQ, and other data were reported at exact analytical values determined, with or without reporting the LOQ value.

The Panel further noted that there are no substantial differences between the levels of Pb, Cd, As, Hg and Al provided for GCC and PCC E 170. However, the level of Al strongly depends on the sample preparation method used (i.e. partial extraction or full digestion) as reported in the Section 3.2.2. Furthermore, the Panel noted that for samples from one manufacturer of PCC E 170, considerably higher total-Al content was reported than for all other GCC or PCC E 170 samples. According to the IBO (Documentation provided to EFSA n. 2) the main differences in the level of toxic elements in E 170 among various manufacturers are due to sources of the raw material used.

The IBO proposed a limit for Pb, Hg, Cd, As and Al in E 170 separately for uses in food for the general population and for food for infants < 16 weeks of age as presented in Table 2. The proposals

differ only in the limit value for Al being 500 mg/kg for infants < 16 weeks of age and 700 mg/kg for all (other) population groups. Furthermore, the IBO proposed that the maximum limit in the EU specifications for E 170 for Al should be set based on the total aluminium content in this food additive (see Section 3.2.2).

Considering the data provided by the IBO on the Al levels, the fact that Al is a part of the structure of PCC E 170 and that E 170 up to the concentration tested in the dissolution rate tests is expected to be fully dissolved under the stomach conditions (see Section 3.1.4) the Panel concurs with the IBO that the maximum limits for Al in the EU specifications for E 170 should be based on the total-Al content in E 170.

The Panel noted that the maximum limits proposed by the IBO for Pb, Hg, Cd and As are substantially higher than most of levels of these toxic elements reported by the IBO. Based on the analytical data submitted by the IBO, for the purpose of the risk assessment, the Panel calculated the 90th percentile of the upper bound level of Pb, Cd and As for GCC E 170 and PCC E 170 which were 0.3 mg/kg for each element in the case of GCC E 170 and 0.5 mg/kg for Pb and 0.3 mg/kg for Cd and As in the case of PCC E 170 and. For Hg, it was not possible to calculate the 90th percentile since for only nine batches was an exact analytical level reported, and the majority of the data were reported as below a reporting level. Therefore, the Panel chose the highest reported measured value of 0.05 mg/kg for Hg to perform the risk assessment.

The Panel noted that the limits proposed by the IBO for Al (i.e. at 500 mg/kg for infants < 16 weeks of age and 700 mg/kg for all population) would be exceeded for five batches of PCC E 170 for which Al level was in the range of 966–1,120 mg/kg. Therefore, the Panel excluded these data from further considerations. The remaining data were insufficient to calculate the 90th percentile and therefore the highest measured (253 mg/kg) value rounded to 250 mg/kg was chosen for the risk assessment.

Based on these considerations, the Panel performed the risk assessment that would result if these toxic elements were present in E 170, at (see Table 11):

i) the maximum current limit in the EU specifications for E 170,
ii) the limit as proposed by the IBO and
iii) the 90th percentile values, using the upper bound levels, calculated by the Panel based on the analytical data submitted for Pb, Cd and As, the highest measured value, i.e. 0.05 mg/kg for Hg and at 250 mg/kg for Al, after exclusion of data (five batches) which would exceed the limits proposed by the IBO (see Table 3)

Table 11: Different scenarios considered for the potential exposure to toxic elements from the use of E 170

Source of the values listed	Lead	Mercury	Cadmium	Arsenic	Aluminium all uses in food for population > 16 weeks	Aluminium food for infants < 16 weeks
Current limits in the EU specifications for E 170 (mg/kg)	3	–	1	3	–	–
Limits as proposed by IBO (mg/kg)	3	0.5	1	2	700	500
Values selected by the Panel for the risk assessment (mg/kg)	0.3	0.05	0.3	0.5	250	250

The Panel emphasised that the choice of the maximum limit values as well as other considerations, such as on multiple sources of exposure to conclude on the maximum limits for toxic elements in the specifications, is in the remit of risk management. The numbers used here are merely taken to support the risk assessment of these toxic elements as presented below.

The outcome of the risk assessment for these three scenarios is illustrated in Table 12 (infants < 16 weeks of age) and Table 13 (all population groups).

Table 12: Risk assessment for toxic elements potentially present in the E 170 used as a food additive in the food for infants < 16 weeks of age

Exposure to E 170 (mg/kg bw per day)	(i) Based on the current EU specifications limits for toxic elements in E 170 for use in food				
	MOE for Pb at 3 mg/kg	% of the TWI for Hg –	% of the TWI for Cd at 1 mg/kg	MOE for As at 3 mg/kg	% of the TWI for Al –
71[(a)]	2.35	–	19.9%	1.41–37.6	–
92[(b)]	1.81	–	25.8%	1.09–29.0	–
85[(c)]	1.96	–	23.8%	1.18–31.4	–
110[(d)]	1.52	–	30.8%	0.91–24.2	–
634[(e)]	0.26	–	177.6%	0.6–4.2	–
1,136[(f)]	0.15		318.1%	0.08–2.3	
Exposure to E 170 (mg/kg bw per day)	**(ii) Based on maximum limits as proposed by the interested business operator (Documentation provided to EFSA n. 2, 5, 9, 11)**				
	MOE for Pb at 3 mg/kg	**% of the TWI for Hg at 0.5 mg/kg**	**% of the TWI for Cd at 1 mg/kg**	**MOE for As at 2 mg/kg**	**% of the TWI for Al at 500 mg/kg for infants < 16 weeks of age**
71[(a)]	2.35	6.2%	19.9%	2.11–56.3	24.9%
92[(b)]	1.81	8.1%	25.8%	1.63–43.5	32.2%
85[(c)]	1.96	7.4%	23.8%	1.76–47.1	29.8%
110[(d)]	1.52	9.6%	30.8%	1.36–36.4	38.5%
634[(e)]	0.26	55.5%	177.6%	0.24–6.3	222%
1,136[(f)]	0.15	99.4%	318.1%	0.13–3.5	398%
Exposure to E 170 (mg/kg bw per day)	**(iii) Based on the 90th percentile of upper bound for Pb, Cd and As, for Hg and Al at the highest measured value (Documentation provided to EFSA n. 2, 5, 9, 11)**				
	MOE for Pb at 0.3 mg/kg	**% of the TWI for Hg at 0.05 mg/kg**	**% of the TWI for Cd at 0.3 mg/kg**	**MOE for As at 0.5 mg/kg**	**% of the TWI for Al at 250 mg/kg**
71[(a)]	23.47	0.6%	6%	8.45–225.4	12.4%
92[(b)]	18.12	0.8%	7.7%	6.52–173.9	16.1%
85[(c)]	19.61	0.7%	7.1%	7.06–188.2	14.9%
110[(d)]	15.15	1%	9.2%	5.45–145.5	19.3%
634[(e)]	2.6	5.5%	53.3%	0.95–25.2	111%
1,136[(f)]	1.47	9.9%	95.4%	0.53–14.1	199%

(a): Mean exposure level for infants below 16 weeks of age (Refined estimated exposure assessment scenario using the highest value of the use level reported by industry (424 mg/kg) in infant formula FC 13.1.5.1)).

(b): 95th percentile exposure level for infants below 16 weeks of age (Refined estimated exposure assessment scenario using highest value of the reported typical use levels (424 mg/kg) in infant formula (FC 13.1.5.1)).

(c): Mean exposure level for the infants below 16 weeks of age (Refined estimated exposure assessment scenario using the mean value of the reported typical use levels (353 mg/kg) in infant FSMP (FC 13.1.5.1)).

(d): 95th percentile exposure level for the population below 16 weeks of age (Refined estimated exposure assessment scenario using the mean value of the reported typical use levels (353 mg/kg) in infant FSMP (FC 13.1.5.1)).

(e): The estimated exposure level for the infants < 16 weeks of age considering that the E 170 was used at the maximum calcium level i.e. at 140 mg/100 kcal as set in the regulation EU 127/2016 in the infant formula, and at the highest consumption value of 260 mL formula/kg bw per day as recommended in the EFSA guidance (EFSA Scientific Committee, 2017).

(f): The estimated exposure level for the infants < 16 weeks of age considering that the E 170 was used at the maximum calcium level i.e. at 250 mg/100 kcal as set in the regulation EU 128/2016 in the FSMP infant formula, and at the highest consumption value of 260 mL formula/kg bw per day as recommended in the EFSA guidance (EFSA Scientific Committee, 2017).

Table 13: Risk assessment for toxic elements potentially present in the E 170 used as a food additive and source of calcium in food and food supplements for all population groups and infants > 16 weeks of age to 1 year and toddlers, consumers of FSMP (FC. 13.1.5.1.) only

Exposure to E 170 (mg/kg bw per day)	(i) Based on the current EU specifications limits for toxic elements in E 170 for use in food for all age groups				
	MOE for Pb at 3 mg/kg	% of the TWI for Hg –	% of the TWI for Cd at 1 mg/kg	MOE for As at 3 mg/kg	% of the TWI for Al –
88[a]	1.89	–	24.6%	1.14–30.3	–
313[b]	0.53	–	87.6%	0.32–8.5	–
49[c]	3.40	–	13.7%	2.04–54.4	–
108.1[d]	1.54	–	30.3%	0.92–24.7	–
91.9[e]	1.81	–	25.7%	1.09–29	–
311.5[f]	0.54	–	87.2%	0.32–8.6	–
167[g]	1.00		46.8%	0.60–16	
458[h]	0.36		128.2%	0.22–5.8	
Exposure to E 170 (mg/kg bw per day)	**(ii) Based on limits as proposed by the interested business operator (Documentation provided to EFSA n. 2, 5, 9, 11)**				
	MOE for Pb at 3 mg/kg	**% of the TWI for Hg at 0.5 mg/kg**	**% of the TWI for Cd at 1 mg/kg**	**MOE for As at 2 mg/kg**	**% of the TWI for Al at 700 mg/kg for all population**
88[a]	1.89	7.7%	24.6%	1.7–45.5	43.1%
313[b]	0.53	27.4	87.6%	0.479–12.8	153.4%
49[c]	3.40	4.3%	13.7%	3.06–81.6	24%
108.1[d]	1.54	9.5%	30.3%	1.39–37.0	53%
91.9[e]	1.81	8.0%	25.7%	1.63–43.5	45.0%
311.5[f]	0.54	27.3%	87.2%	0.48–12.8	152.6%
167[g]	1.00	14.6%	46.8%	0.89–24	81.8%
458[h]	0.36	40.1%	128.2%	0.33–8.7	224.4%
Exposure to E 170 (mg/kg bw per day)	**(iii) Based on the 90th percentile of upper bound for Pb, Cd and As, for Hg and Al at the highest measured value (Documentation provided to EFSA n. 2, 5, 9, 11)**				
	MOE for Pb at 0.3 mg/kg	**% of the TWI for Hg at 0.05 mg/kg**	**% of the TWI for Cd at 0.3 mg/kg**	**MOE for As at 0.5 mg/kg**	**% of the TWI for Al at 250 mg/kg**
88[a]	19	0.8%	7.4%	6.82–181.8	15.4%
313[b]	5.3	2.7%	26.3%	1.92–51.1	54.8%
49[c]	34.01	0.4%	4.1%	12.24–326.5	8.6%
108[d]	15.42	0.9%	9.1%	5.50–148	18.9%
91.9[e]	18.14	0.8%	7.7%	6.53–174.1	16.1%
311.5[f]	5.35	2.7%	26.2%	1.93–51.4	54.5%
167[g]	9.98	1.46	14.0%	3.6–95.8	29.2%
458[h]	3.64	4.0%	38.5%	1.3–34.9	80.2%

(a): Highest exposure level for the infants above 16 weeks age and toddlers (Refined estimated exposure assessment scenario using highest value of the reported typical use levels (424 mg/kg) in infant FSMP (FC 13.1.5.1) – infants above 16 weeks to 1 year, – mean).

(b): Highest exposure level for the infants above 16 weeks age and toddlers (Refined estimated exposure assessment scenario using highest value of the reported typical use levels (424 mg/kg) in infant FSMP (FC 13.1.5.1) – infants above 16 weeks to 1 year -95th percentile).

(c): Highest exposure level for the general population (Refined Brand-Loyal Scenario -Toddlers – mean (Refined brand loyal estimated exposure assessment scenario) E 170 used as a food additive only).

(d): Highest exposure level for the general population (Refined Brand-Loyal Scenario -Toddlers – 95th percentile, E 170 used as a food additive only).

(e): Highest exposure level for the general population (Refined non brand-loyal scenario -Toddlers – mean E 170 used as a food additive and a source of calcium in fortified food).
(f): Highest exposure level for the general population (Refined non brand-loyal scenario -Infants – 95th percentile, E 170 used as a food additive and a source of calcium in fortified food).
(g): Highest exposure level for consumers' only of food supplements (Refined Brand-Loyal Scenario – Children – mean, E 170 used as a food additive, a source of calcium and in food supplement).
(h): Highest exposure level for consumers' only of food supplements (Refined Brand-Loyal Scenario -Adolescent – 95th percentile, E 170 used as a food additive, a source of calcium and in food supplement).

The resulting figures show, in scenarios (i) and (ii) as described above, that the exposure to toxic elements Pb, Cd, Hg, As and Al from the consumption of E 170 could be substantial and would give rise to concern. For some population groups, the exposure to Al from the use of calcium carbonate exceeds substantially the TWI in the case that Al would be present at the limit proposed by the IBO and when considering the scenario (iii) the exposure to Al could be a substantial percentage of TWI.

Furthermore, the Panel noted that the highest reported measured value for Al of 1,120 mg/kg is considerably higher than the limit proposed by the IBO of 500 mg/kg for infants < 16 weeks and of 700 mg/kg for all population groups, which would lead to a significantly higher exceedance of the TWI.

Taking into account the calculations performed by the Panel (Tables 12 and 13) and the fact that the food additive is not the only potential dietary source of toxic elements, the Panel recommended to lower the maximum limits for Pb, Cd, As in E 170 and to introduce maximum limits for Hg and Al.

Furthermore, the Panel noted that maximum levels for lead and cadmium in infant formula are set by Commission Regulation (EU) 2023/915[26]; therefore, the Panel calculated the impact of the level of the toxic elements: lead and cadmium in the food additive, on the final product and compared that with the legal limits for these elements in the final formula for the infants below 16 weeks of age (see Appendix B). Considering the results of these estimations and the fact that the food additive is not the only potential source of toxic elements in the infant formula the Panel emphasises the need to reduce the specification limit values for lead and cadmium in Regulation (EU) no 231/2012.

3.4.2. Additional revisions

The Panel noted that the IBO did not provide data on the PSD of the E 170 or a proposal for the specifications in relation to the particle size. Dissolution tests considering both the infant and the adult stomach conditions and daily exposure to E 170 (3.2.5) demonstrated that the consumer will not be exposed to a fraction of small particles including nanoparticles up to the concentrations tested by the IBO Based on the data provided the Panel was of the view that there would be no need to introduce in the EU specifications for E 170 any parameter in relation to the particle size.

Based on the information submitted by IBO, the Panel considered that a modified definition of the food additive should be included to indicate that: calcium carbonate used as E 170 is not an engineered nanomaterial and is not coated or functionalised or with chemically modified surfaces (Documentation submitted to EFSA n. 5 and 12).

Based on the data provided (See Section 3.2.1) the Panel is of the view that the definition of E 170 should include the source material of the calcium ions i.e.: limestone.

The Panel also considered that the CAS numbers 1317-65-3 corresponding to limestone and 471-34-1 corresponding to PCC should be included in the existing EU specifications for E 170.

3.4.3. Summary of the proposed revision to the EU specifications

Overall, based on the analytical data provided by the IBO in response to the EFSA call for data along with the considerations above, the Panel recommends the following revisions of the existing EU specifications for calcium carbonate E 170 as listed in Table 14.

[26] Commission Regulation (EU) 2023/915 of 25 April 2023 on maximum levels for certain contaminants in food and repealing Regulation (EC) No 1881/2006 (Text with EEA relevance) C/2023/35. OJ L 119, 5.5.2023, pp. 103–157.

Table 14: Proposal for a revised version of the existing EU Specifications for calcium carbonate E 170

	Commission Regulation (EU) No 231/2012	**Comment/justification for revision**
Definition	Calcium carbonate is the product obtained from ground limestone or by the precipitation of calcium ions with carbonate ions	To be included that: – E 170 calcium is not an engineered nanomaterial and is not coated or functionalised or with chemically modified surfaces. – the source of calcium ions used for the precipitation of calcium carbonate shall be limestone.
Colour Index No	See Table 1	
EINECS	See Table 1	
CAS number	–	To introduce Limestone: CAS Number 1317-65-3 Precipitated calcium carbonate: CAS number 471-34-1
Chemical name	See Table 1	
Chemical formula	See Table 1	Unchanged
Molecular weight	See Table 1	Unchanged
Assay	See Table 1	Unchanged
Description	See Table 1	
Identification		
Solubility	See Table 1	Unchanged
Purity		
Loss on drying	See Table 1	Unchanged
Acids insoluble substances	See Table 1	Unchanged
Magnesium and Alkali salts	See Table 1	Unchanged
Free Alkali	–	Unchanged
Fluoride	See Table 1	Unchanged
Antimony (as Sb)	See Table 1	Unchanged
Copper (as Cu)		Unchanged
Chromium (as Cr)		Unchanged
Zinc (as Zn)		Unchanged
Barium (as Ba)		Unchanged
Arsenic	Not more than 3 mg/kg	Maximum limit to be lowered on the basis of the information provided by IBO and on the considerations of the Panel
Lead	Not more than 3 mg/kg	Maximum limit to be lowered on the basis of the information provided by IBO and on the considerations of the Panel
Cadmium	Not more than 1 mg/kg	Maximum limit to be lowered on the basis of the information provided by IBO and on the considerations of the Panel
Mercury	–	Introduce the maximum limit on the basis of the information provided and on the considerations of the Panel
Aluminium	–	Introduce the maximum limit on the basis of the information provided and on the considerations of the Panel[(a)]

(a): As in detail explained in the Discussion Section (Section 3.5) it is recommended to consider specifying the analytical method used to determine the analytical content of total Al.

3.5. Biological and toxicological data

3.5.1. Previous evaluation by ANS Panel (2011)

A summary of the main conclusions for the biological and toxicological data from the assessment of the ANS Panel during the re-evaluation of E 170 (EFSA ANS Panel, 2011) is presented below.

New information and assessments related to the specific age group below 16 weeks of age are reported in Section 3.5.2.

Absorption, distribution, metabolism, excretion

Calcium carbonate dissociates into its constituent ions in the acid milieu of the stomach. Some of the calcium is absorbed, via active transport or passive diffusion, the bulk (89–90%) of unabsorbed calcium is complexed to bile acids, free fatty acids and oxalic acid and excreted with the faeces (Heaney, 2002). As reported by EFSA, absorption of calcium from calcium carbonate in rats and humans is comparable to that from calcium citrate malate, average absorption of calcium from calcium carbonate over a range of studies being in the range of 20–40% (EFSA, 2007*). As reported by SCF (*2003*), after intestinal absorption, calcium and carbonate/bicarbonate ions can enter normal metabolic pathways and body pools. The majority of absorbed calcium is stored in the skeleton. Excess calcium is excreted with water via kidneys (and also via faeces and skin) and excess carbonate is excreted as carbon dioxide via respiration (SCF,* 2003*).*

Toxicological studies

A number of short term studies (generally less than 90 days) have been carried out with calcium carbonate in rats and mice, to investigate the effects of high-calcium diets on calcium levels in the body (Puerro-Vicente et al., 1993) and on homeostasis of other minerals (Takasugi et al., 2005). Effects of high calcium on membrane biochemistry in the colon (Awad et al, 1990) or effects on apoptosis and cell proliferation in the colon (Penman et al., 2000) have also been investigated. These studies have also assessed the toxicity of high levels of calcium carbonate in the diet, as manifest by effects on growth and food consumption, and have overall not demonstrated any evidence of toxicity attributable to calcium carbonate. Similarly, a 31-week study in cats and kittens, comparing the effects of high calcium carbonate and high calcium chloride diets revealed changes in homeostasis of calcium and other minerals in the body, but no overt toxicity (Pastoor et al., 1994). The [ANS] Panel considered that the investigations carried out in these studies were of limited value in assessing the safety of calcium carbonate. The only notable treatment-related effect seen in a 91-day feeding study designed to compare the effects of calcium carbonate to those of calcium citrate malate in rats at dietary calcium levels equivalent to 250 or 500 mg calcium/kg bw/day was nephrocalcinosis, seen in both males and (more marked) in females (EFSA, 2007*). These dietary doses correspond to approximately 625 or 1,250 mg calcium carbonate/kg bw/day. The Panel considered however that the nephrocalcinosis finding in rats is not relevant for human safety assessment because the rat is a species known to be particularly sensitive to mineralisation of the renal tubule epithelium due to dietary alteration of the calcium and phosphorus homeostasis (Ritskes-Hoitinga et al.,* 1989, 1991, 1992*). Results from a 91-day toxicity study in Beagle dogs designed to compare the effects of calcium carbonate to those of calcium citrate malate at equivalent calcium levels in the diet as in the rat study reported above (providing intakes of approximately 250 and 500 mg calcium/kg bw/day) did not report any signs of nephrocalcinosis or other evidence of toxicity (EFSA,* 2007*).*

Nephrocalcinosis was also not observed in a recent combined repeat dose oral toxicity/ reproduction/developmental toxicity screening study with nanoform calcium carbonate (having a particle size of 60–100 nm when examined by SEM), carried out in Wistar rats at dose levels of up to 1,000 mg/kg bw/day (Harlan Laboratories, 2010a). The only changes seen in this study, in which dosing was continued for up to 48 days, were slight but statistically significant haematological and biochemical effects in males receiving 1,000 mg/kg bw/day, and significant reductions in plasma phosphate levels in all male treated groups. The [ANS] Panel considered that these changes were non-adverse and agreed with the NOAEL of 1,000 mg/kg bw/day identified by the authors of the study, the highest dose tested. No evidence of toxicity was reported in a study in which mice were administered calcium carbonate (described by the authors as nano calcium carbonate) by oral gavage at dose levels up to 1,300 mg/kg bw/day for 28 days (Huang et al., 2009*). The [ANS] Panel noted however that only limited investigations were carried out in this study. Calcium carbonate (with a particle size of 60–*

100 nm when examined by SEM) has given negative results in a range of in vitro genotoxicity assays. No data are available on the chronic toxicity or carcinogenicity of calcium carbonate. The [ANS] Panel considered however that it is unlikely that calcium carbonate has carcinogenic potential, given that both calcium and carbonate are natural constituents of the body and normal metabolites of man, animals and plants and have a long history of safe use as a source of calcium supplementation for humans.

Several reproductive and developmental toxicity studies in rats and mice have been carried out with calcium carbonate. In rats fed diets containing calcium carbonate at levels up to approximately 1,500 mg/kg bw/day, no dose-related changes indicative of developmental toxicity were reported (Shackelford et al., 1993). The Panel considered that a NOAEL of 1,500 mg/kg bw/day could be identified for reproductive effects of calcium carbonate in this study. However, there were dose-related increases of the femoral calcium content and decreases in tissue phosphorus, magnesium, iron and copper in both dams and fetuses (Shackelford et al., 1994). The Panel also noted the results of a recent OECD guideline-compliant combined repeat dose oral toxicity/reproduction/developmental toxicity screening study carried out with calcium carbonate (having a particle size of 60–100 nm when examined by SEM) in Wistar rats at dose levels up to 1,000 mg/kg bw/day in which no effects on reproduction, including developmental toxicity, were reported (Harlan Laboratories, 2010a). Other studies have shown evidence of fetotoxicity of calcium (as calcium carbonate) when administered during pregnancy at levels in the diet equivalent to 3,750 mg/kg bw/day calcium carbonate, together with additional calcium intake from calcium lactate in drinking water (Fairney and Weir, 1970; Liebgott et al., 1989). In the study of Richards and Greig in mice reported in 1952, diets with a calcium carbonate content of 1.1% (1,650 mg calcium carbonate/kg bw/day) resulted in a decreased number and total weight of litters and in cardiac hypertrophy and thymic atrophy in the offspring when killed at age 21 days. Overall, the Panel noted that in rodents high doses of calcium carbonate (> 1,500 mg/kg bw/day) causing hypercalcaemia during gestation can result in adverse effects on reproduction, fetotoxicity and elemental imbalances in the offspring. However a recent repeat dose oral toxicity/reproduction study provided a NOAEL of 1,000 mg/kg bw/day, the highest dose tested, for developmental toxicity and the Panel considered overall that there is no concern for the reproductive effects of calcium carbonate at intakes below 1,500 mg/kg bw/day.

Allergenicity

No data are available indicating that calcium carbonate has allergenic properties or can invoke sensitivity or intolerance reactions in exposed individuals.

Human data

*The [ANS] Panel noted that hypercalcaemia and alkalosis can occur in humans taking calcium carbonate with large amounts of milk or cream for the treatment of peptic ulcer (milk-alkali syndrome), often associated with renal dysfunction, metastatic calcification and other symptoms. Similar changes have been reported in individuals taking large amounts of calcium carbonate and other calcium-containing antacids or large amounts of calcium food supplements. The SCF (*2003*) reported that one third of the cases had consumed both alkali and calcium (between 2.0 and 16.5 g/day of supplementary calcium), while one third developed symptoms as a result of high calcium carbonate intakes alone (between 2 to 10.8 g additional calcium per day from several months to 30 years). The [ANS] Panel additionally noted that while the meta-analysis carried out by Bolland and co-workers (Bolland et al.,* 2010*,* 2011*), showing an increased risk of myocardial infarction in individuals given regular calcium supplementation in the management of osteoporosis, was a very large and robust study, the trends reported were very modest, and are not supported by the findings in a similar study carried out by Lewis et al. (*2011*). The [ANS] Panel also noted that the trends in cardiovascular risks following calcium supplementation contrasted with those found with dietary calcium, and that the authors considered that a plausible mode of action could be identified to explain these differences, based on serum levels of calcium following dietary intake and supplementation (Bolland et al.,* 2010*,* 2011*)*.

3.5.2. Data submitted

The following was requested in the EFSA call for data:

Within the frame of the EFSA Guidance of the Scientific Committee on the risk assessment of substances present in food intended for infants below 16 weeks of age the following information on

the toxicological properties of calcium carbonate (E 170) and its adverse effects relevant for its use in special formulae used for infants below 16 weeks of age under special medical conditions (FC 13.1.5.1):

- post-marketing surveillance reports on undesired and adverse reactions indicating the ages and other relevant data of the exposed infants and young children and the use level of calcium carbonate (E 170) in the marketed products
- published and unpublished case reports (e.g. available nutrivigilance data) on undesired and adverse effects, associated with the oral administration of calcium carbonate in any form to infants and young children

Data to address the above requests were provided by two IBOs which are summarised in the following sections.

3.5.2.1. Toxicological data

One IBO submitted an overview of the toxicological studies provided in the REACH registration dossier on calcium carbonate (bulk and nano forms) and the relevant study reports/publications (Documentation provided to EFSA n. 2, 5). The toxicological studies provided did not investigate endpoints of relevance for the safety assessment for infants below 16 weeks of age nor were performed in an animal model relevant for that population (i.e. piglet). Hence, the submitted information does not contribute to the assessment of calcium carbonate as a food additive for use in food for infants and young children.

Regarding the toxicological studies relevant for assessment of the safety of calcium carbonate (E 170) in the population above 16 weeks of age, the Panel noted that, with the exception of a 90-day rat study, summarised for completeness below, all the other toxicological studies were already available and assessed in the re-evaluation of calcium carbonate (E 170; EFSA ANS Panel, 2011).

Subchronic oral toxicity study

Sung et al. (2015) report on a 90-day oral toxicity study in Sprague–Dawley rats according to OECD TG 408 (OECD, 1998) and GLP principles of the Ministry of Food and Drug Safety of South Korea.[27] Based on results of a 14-day study, doses of 0, 250, 500 and 1,000 mg/kg bw per day of nano calcium carbonate (50–300 nm by Energy-Filtering transmission electron Microscopy (ET-TEM); supplied by the Ministry of Food and Drug Safety of South Korea; dispersed in distilled water) were applied to 10 male and 10 female rats per group. The Panel noted that the study was performed in 2015 and, therefore, before the publication of the 'EFSA Guidance on risk assessment of nanomaterials to be applied in the food and feed chain: human and animal health' (EFSA Scientific Committee, 2021b). However, based on the dissolution rate studies in this assessment (see Section 3.2.5), the Panel considered that dissolution of nano calcium carbonate would have occurred in the stomachs of the rats in this study. The Panel noted that the current assessment is not on nano calcium carbonate (engineered nanomaterial) (see also Section 1.1.3) but included the above study, applying a conventional risk assessment approach (EFSA ANS Panel, 2012; EFSA Scientific Committee, 2017, 2021a), as it was done in the re-evaluation (EFSA ANS Panel, 2011). No mortalities and no changes in bw or food consumption were observed. No treatment-related toxicologically relevant changes were reported in ophthalmoscopy, haematology, clinical chemistry, necropsy or histopathology. Statistically significant increases in blood calcium levels were minor and only in high-dose females but not in males. Slight decreases in white blood cell, lymphocyte and monocyte counts were observed only in mid dose females. Changes in testes, epididymis, cysts in kidneys and increased thymus weight in males were also not dose related. The Panel agrees with the study authors that a NOAEL of 1,000 mg/kg bw per day, corresponding to the highest dose tested, could be identified from this study.

3.5.2.2. Clinical studies

The IBOs submitted six publications retrieved from the open literature (De Portela et al., 1983; Alon et al., 1986; Clark et al., 1989; Borschel et al., 2013; Borschel et al., 2014; Marriage et al., 2015). For three of them, also the full study report was provided (Documentation provided to EFSA n. 3, 4). Two

[27] Laboratory practices were done according to Ministry of Food and Drug Safety (MFDS) Notification No. 2013-40, 'Principles of Good Laboratory Practice' (5th revision, Apr 2013). The study was approved by the IACUC of the Korea Conformity Laboratory.

of the studies have been performed in infants and children with chronic renal failure (Alon et al., 1986; Clark et al., 1989), one study in infants recovering from undernutrition (De Portela et al., 1983). The population of the three studies consists of sick patients; therefore, the results are not applicable to the population of infants and young children for whom risks are assessed in this opinion. In the three remaining publications (Borschel et al., 2013; Borschel et al., 2014; Marriage et al., 2015) the content of calcium carbonate as food an additive was not given and, therefore, the exposure could not be assessed by the Panel. Even the full study report provided for the study of Marriage et al. (2015) does not give this information. In addition, the investigated endpoints did not include potential adverse outcomes related to calcium carbonate, e.g. hypercalcaemia which seems to be an earlier sign of excessive calcium intake with renal stones and a higher cardiovascular risk (Tankeu et al., 2017; Chiodini and Bolland, 2018).

The Panel considered that the information in the studies is not useful for the assessment of the safety of calcium carbonate (E 170) as a food additive in food for infants and young children.

3.5.2.3. Post-marketing surveillance data

Post-marketing data were submitted from one IBO (Documentation provided to EFSA n. 1). The post-marketing safety report covered the time period from 01 June 2017 to 31 May 2019. In this period, 4,605 reports were sent to the IBO in total while the product placed on the market as sold corresponding to more than 105,000,000 patient treatment days. There were no serious adverse events among those reported. The reactions were unspecific (flatulence, diarrhoea, softer stools,) and a causal relationship to the ingestion of the product could not be demonstrated.

No reports were found by the IBO in the literature and the IBO did not perform clinical studies from which adverse reactions could have emerged.

3.6. Discussion

The current assessment deals with the risk assessment of calcium carbonate (E 170) when used in food for infants below 16 weeks of age in the food category (FC) 13.1.5.1 (Dietary foods for infants for special medical purposes and special formulae for infants). It also addresses, as a follow-up, the issues and the uncertainties that were identified by the ANS Panel at the time of the re-evaluation of calcium carbonate (E 170) (EFSA ANS Panel, 2011), including the potential exposure to aluminium resulting from its presence as an impurity in calcium carbonate (E 170) for all population groups (including infants < 16 weeks).

In response to a public call issued by EFSA in 2018 in support of the present assessment, data from IBOs were made available to EFSA for Dietary foods for infants for special medical purposes and special formulae for infants (FC 13.1.5.1). Exposure to calcium carbonate (E 170) as a food additive from infant formulae (FC 13.1.5.1) was estimated for infants below 16 weeks of age, using the highest value and the mean of the reported typical use level. Using the highest value of the reported typical use level, calcium carbonate (E 170) exposure ranged between 85 mg/kg bw per day (mean consumption) and 110 mg/kg bw per day (at the high-level consumption). Using the mean value of the reported typical use level, calcium carbonate (E 170) exposure ranged between 71 mg/kg bw per day (mean consumption) and 92 mg/kg bw per day (at the high-level consumption) (Table 5).

For the general population (from infants > 16 weeks of age to the elderly), mean dietary exposure to calcium carbonate (E 170) ranged from 0.6 mg/kg bw per day for infants to 37.7 mg/kg bw per day for toddlers; at the 95th percentile, dietary exposure to calcium carbonate (E 170) ranged from 4.2 mg/kg bw per day for adolescents to 80.9 mg/kg bw per day for toddlers. Exposure to calcium carbonate as a source of calcium ranged at the mean from 0.4 mg/kg bw per day for the elderly to 58.6 mg/kg bw per day for infants; at the 95th percentile, it ranged from 2.2 mg/kg bw per day from the elderly to 245.7 mg/kg bw per day for infants.

Considering both uses of calcium carbonate as a food additive (E 170) and as a source of calcium, mean exposure would range from 5.9 mg/kg bw per day for the elderly to 91.9 mg/kg bw per day for toddlers, while exposure at the 95th percentile would range from 13.9 mg/kg bw per day for the elderly to the 311.5 mg/kg bw per day for infants.

Based on these estimates, the mean intake of calcium from the use of calcium carbonate as a food additive (E 170) and as a source of calcium is estimated to be from 56 mg/day for infants up to 1,058 mg/day for the elderly. At the 95th percentile, intake of calcium ranged from 183 mg/day for infants to 2,935 mg/day for the elderly. In addition, for the consumers of food supplements (and considering also their whole diet), mean intake of calcium ranged from 271 mg/day to 3,530 mg/day

for the elderly. At the 95th percentile, intake of calcium ranged from 945 mg/day for children to 10,553 mg/day for adults.

Analytical data on toxic elements were provided by one IBO for levels of Pb, Cd, As, Hg and Al in the calcium carbonate GCC and PCC used as a food additive E 170. The Panel noted that the occurrence data submitted by the IBOs for Pb, Cd, As in E 170 are substantially lower than the current limits in the EU specifications. The Panel further observed that there are no substantial differences between the levels of Pb, Cd, As, Hg and Al provided for GCC and PCC E 170. However, the Panel further noted that the level of Al strongly depends on the sample preparation method used (i.e. partial extraction or full digestion) as reported in the Section 3.2.2.

One IBO proposed a maximum limit for Pb, Hg, Cd, As and Al in E 170 separately for uses in food for the general population and for food for infants < 16 weeks of age as presented in Table 2. The proposals differ only in the levels of Al being 500 mg/kg for infants < 16 weeks of age and 700 mg/kg for all population groups. The IBO proposed that the maximum limit in the EU specifications for E 170 for Al should be set based on the total aluminium content in this food additive (see Section 3.2.2).

Considering the data provided by the IBO on the Al levels, the fact that Al is a part of the structure of calcium carbonate PCC and that E 170 up to the concentration tested in the dissolution rate tests is expected to be fully dissolved under the stomach conditions (see Section 3.1.4) the Panel concurs with the IBO that the maximum limits for Al in the EU specifications for E 170 should be based on the total-Al content in E 170.

The impurities found in GCC E 170 consist mainly of magnesium carbonate, quartz, clay and mica. Aluminium is a structural element of both clay and mica. The IBOs did not provide a database that was extensive enough to be able to conclude on the possible agreement or differences in the level of total-Al obtained using different methodologies. In particular no information was available for comparison purposes using XRF method applied to GCC E 170 samples and hydrofluoric acid (HF) digestion was not applied to any sample, neither GCC nor PCC E 170. XRF measures all Al present in a sample. HF-digestion will digest fully both the $CaCO_3$ matrix as well as any mineral inclusions in GCC. Additionally, HF-digestion may not be suitable for $CaCO_3$ because of the possibility of the CaF_2 precipitation during sample preparation. HNO_3-digestion will digest fully the $CaCO_3$ but not most of the mineral inclusions. Since the HNO_3-digestion is assumed to give similar results to in vivo digestion by HCl (as reflected in the dissolution rate tests) and it is the approach preferred by most analytical laboratories, the Panel considers the method using HNO_3-acid digestion (with or without HCl) of the FA samples the most appropriate method for total Al determination in E 170.

The Panel performed the risk assessment that would result if Pb, Hg, Cd, As and Al were present in E 170 at (i) the maximum current limit in the EU specification; (ii) limits proposed by the IBO (iii) at the 90th percentile values, using the upper bound levels, calculated by the Panel based on the analytical data submitted for Pb, Cd and As, the highest measured value for Hg i.e. 0.05 mg/kg and for Al rounded to 250 mg/kg.

Considering that calcium carbonate may also be used in the manufacture of foods as a source of calcium for nutritional purposes and that the same purity criteria established for the use as a food additive could apply also to the use as a source of calcium, the Panel has assumed that the data provided by the IBO on impurities in E 170 may apply equally to calcium carbonate when used as a source of calcium.

For infants below 16 weeks of age, the Panel considered the highest mean and 95th percentile of the refined exposure estimates based on the maximum and mean use levels of E 170 reported by the IBOs (Table 5). For the infants from 16 weeks to 1 year of age and toddlers consumers only of FSMP, the dietary exposure to calcium carbonate (E 170) at the highest mean and 95th percentile estimates were considered.

As currently calcium carbonate (E 170) as a food additive is allowed at *QS* in FSMP (FC 13.1.5.1) and considering that calcium carbonate may also be used for nutritional purposes as a source of calcium in infant formula and FSMP and that it needs to meet the specifications of E 170, the Panel considered two additional dietary exposure estimates to E 170 for infants < 16 weeks of age: if calcium carbonate was used in infant formula and FSMP at the allowed maximum calcium level as set in the respective Regulations EU No 2016/127 and EU 2016/128, and at the highest consumption value of 260 mL formula/kg bw per day as recommended in the EFSA guidance (EFSA Scientific Committee, 2017) considering the highest energy requirement of 70 kcal/100 mL (EU 2016/128). The Panel noted that the same assumption was considered by the IBO to calculate the concentration to be tested in the dissolution rate test. However, the illustrative calculations described above would result in an

overestimation, noting that calcium carbonate might not be the only source of calcium in infant formula and FSMPs.

With regard to the dietary exposure to calcium carbonate for the general population, the Panel considered the highest mean and 95th percentile which was calculated in three scenarios:

i) calcium carbonate used as a food additive E 170 only (highest mean and 95th percentile 49.3 and 108.1 mg/kg bw per day for toddlers).
ii) calcium carbonate used as a food additive (E 170) and a source of calcium from fortified food (highest mean and 95th percentile 91.9 and 311.5 mg/kg bw per day for toddlers and infants, respectively).
iii) calcium carbonate used as a food additive (E 170) and a source of calcium for consumers only of food supplements (highest mean and 95th percentile 167 for elderly and 458 mg/kg bw per day for adolescents).

The resulting figures (see Tables 12 and 13) show, that at the current EU Specifications limits and at the limits proposed by the IBO, the exposure to toxic elements Pb, Cd, Hg, As and Al from the consumption of E 170 could be substantial and would give rise to concern. For some of the population groups the exposure to Al from the use of the calcium carbonate exceeds substantially (up to circa 4-fold) the TWI in the case that Al would be present at the limit proposed by the IBO. Furthermore, the Panel noted that at the highest measured value for Al of 1,120 mg/kg reported by the IBO, the TWI would be greatly exceeded (up to 890%).

The Panel noted that already in 2008, the AFC Panel (EFSA, 2008) concluded that the TWI of 1 mg/kg bw per week for Al is likely to be exceeded in a significant part of the European population. The AFC Panel considered that the major route of exposure to aluminium compounds for the general population was through food, both as a consequence of the natural occurrence of aluminium in food and the use of aluminium compounds in food processing, including food additives. Considering this and the outcome of the current risk assessment for aluminium present in E 170 (as above) and the fact that there are other dietary sources of aluminium, the Panel is of the opinion that limiting the content of aluminium in foods should be considered.

The Panel noted that the maximum limits in the EU specifications for toxic elements should be established based on actual levels in the commercial food additive. Therefore, the Panel recommended that the maximum limits should be lowered for Pb, Cd and As and that maximum limits for Hg and Al should be introduced on the basis of the information provided by the IBO and on the considerations of the Panel (see Table 14).

Additionally, the Panel calculated the impact of the potential level of the toxic elements lead and cadmium in the food additive (i.e. up to the specifications limit values) on the final product and compared that with the legal limits for these elements in the final formula for infants below 16 weeks of age set by Commission Regulation (EU) 2023/915 (see Appendix B). Considering the results of these estimations and the fact that the food additive is not the only potential source of toxic elements in the infant formula the Panel emphasises the need to reduce the specification limit values for lead and cadmium in Regulation (EU) No 231/2012.

Regarding particle size the Panel considered that, based on the data provided, the presence of small particles including nanoparticles in the pristine GCC and PCC calcium carbonate used as a food additive (E 170) cannot be excluded.

One IBO further provided dissolution rate tests results for GCC and PCC E 170, performed at pH 3 and pH 6 mimicking the stomach conditions of adults and infants, respectively. Based on that data the Panel concluded that the dissolution rate tests, performed according to the protocol of the EFSA Guidance on Particle-TR indicate that calcium carbonate when used as a E 170 is expected to be fully dissolved in the stomach at the concentration tested. The Panel noted that the concentration tested in the dissolution rate test for the general population is a fair representation of the reported use levels of E 170 used as a food additive as reported at the time of the re-evaluation by the ANS Panel (EFSA ANS Panel, 2011). The Panel considers that the concentration tested for the infant case is a realistic representation of the maximum content of calcium in infant formula and FSMPs. The Panel considered that there is no concern with regard to the exposure to small particles, including nanoparticles, present in E 170 when used as a food additive up to the concentrations tested (see Section 3.2.5) and that the previous risk assessment completed by the ANS Panel in 2011 does not need to be complemented with nano specific considerations. Consequently, also with respect to the evaluation of the safety in infants below 16 weeks of age, this is considered to be adequately covered by the applicable guidance of the EFSA SC (EFSA Scientific Committee, 2017).

In view of the additional information submitted by IBOs on the form of calcium carbonate (E 170) used as a food additive, the Panel considers that the definition of the food additive E 170 should be revised in the current EU specifications for calcium carbonate (E 170) (Commission Regulation (EU) No 231/2012) indicating that: calcium carbonate (E 170) has no surface treatments or coatings and is not an intentionally engineered nanomaterial.

Based on the similarity of the data provided on the levels of toxic elements and the dissolution rates tests for GCC and PCC E 170 and the fact that these two forms can be used interchangeably, the Panel does not see the need to introduce separate technical specifications for GCC and PCC E 170.

An overview of the toxicological studies provided in the REACH registration dossier together with the relevant study reports/publications was provided by one IBO. Within those studies, the only study not considered in the ANS Panel opinion on the re-evaluation (EFSA ANS Panel, 2011) was a 90-day oral toxicity study with nano calcium carbonate in Sprague–Dawley rats. Based on the absence of toxicologically relevant effects, the Panel agreed with the study authors that a NOAEL of 1,000 mg/kg bw per day, corresponding to the highest dose tested, could be identified from this study. The Panel noted that the toxicological studies provided had not investigated endpoints of relevance for infants below 16 weeks of age and that none of the studies was performed according to the call for data in a relevant animal model (i.e. piglet). Hence, the submitted information does not contribute to the assessment of calcium carbonate as a food additive for use in food for infants below 16 weeks of age.

Results from six clinical studies were provided by one IBO. Three trials were performed in infants and children with underlying health conditions (chronic renal failure, recovering from undernutrition) and were, therefore, considered not relevant for the current assessment. In the three remaining publications the content of calcium carbonate as a food additive was not given and, therefore, the exposure could not be assessed by the Panel. Of note, the provided clinical trials did not address endpoints related potential adverse effects of calcium carbonate e.g. hypercalcaemia. Hence, the information in these studies was considered not useful for the assessment of the safety of calcium carbonate (E 170) as a food additive in food for infants and young children.

In the context of the re-evaluation of calcium carbonate, the ANS Panel agreed with the group ADI 'not specified' assigned by the SCF to a group of carbonates including calcium carbonate, when considering the use of calcium carbonate as a food additive. The Panel noted that, after adoption of the conceptual framework in 2014 (EFSA ANS Panel, 2014), the conclusion 'ADI not specified' was no longer considered fit for purpose, and changed this to 'No safety concern at the reported uses and uses levels'. Calcium carbonate could be considered to be of low intrinsic toxicity. However, the presence of toxicologically relevant impurities/residuals in E 170 could still raise concerns. In particular, for aluminium, the Panel noted that the exposure would exhaust a substantial percentage of the TWI or even largely exceed it (see Section 3.4.1). Aluminium is virtually unavoidably present in E 170, since the food additive is produced from natural rock in which aluminium is ubiquitously present. The Panel therefore considered that in addition to introducing limits in the EU specifications for aluminium in E 170, a further reduction in aluminium intake through E 170 can be achieved only by reducing the exposure to the food additive E 170.

The ANS Panel also noted that the estimated exposures to calcium from all sources, including the use of calcium carbonate as a food additive, taken together with intakes of calcium from supplements and from food fortification are below 2,500 mg/day.

The Panel considered that the safety assessment of calcium carbonate in the population below 16 weeks of age could be based on the comparison between the content of calcium in IF and FSMPs against the maximum content of calcium in infant formulae and follow-on formulae (140 mg/100 kcal established in the Regulation (EU) No 2016/127) and the maximum content of calcium at 250 mg/100 kcal established in the Regulation (EU) No 2016/128 for the FSMP (FC 13.1.5.1). Regulatory limits for calcium are established for infant formulae and infant FSMPs in Commission delegated regulation (EU) 2016/127 and 2016/128, respectively. Regarding the levels of calcium in FSMP, the Panel noted that the IBOs provided nine example formulations with levels for calcium ranging from 115 to 132 mg/100 kcal which complies with the maximum limit of 250 mg/100 kcal of Commission delegated regulation (EU) 2016/128 (see Appendix C).

The Panel considered the calcium content in the infant formula at minimum level of 50 mg calcium/100 kcal and the maximum level of 140 mg calcium/100 kcal from Commission delegated Regulation (EU) 2016/127 and converted them to mg calcium/mL. The Panel noted that the levels of calcium in the infant formulae provided by the IBOs (n = 6; range 49–56 mg/100 mL) are below the 'converted' maximum amount of calcium (84–98 mg/100 mL). The Panel noted that calcium carbonate is not

authorised in infant formulae as a food additive (FC 13.1.1), however, it is allowed for other uses as explained in Section 3.3.2.

The Panel compared the intake of calcium from calcium carbonate with the UL of 2,500 mg/day applicable to the population above 17 years old. The Panel noted that the intake of calcium from calcium carbonate is below this limit for the adult population for the scenario considering the use of calcium carbonate 'as food additive' or 'source of calcium'. When the exposure scenario considering both uses 'as an additive and as a source of calcium' (Scenario C in Table 9) is taken into account the UL is exceeded for the 'adults' and 'elderly and very elderly' population (95th percentile). The UL is also exceeded for the scenario 'consumers only of food supplements' (scenario d in Table 9) both in the adults (95th percentile) and in the elderly and very elderly population (95th percentile and mean).

Concerning the population below 17 years old, the Panel noted that EFSA NDA Panel (2012) states that: '*although available data do not allow the setting of a UL for infants, children or adolescents, no risk has been identified with the highest current levels of calcium intake in these age groups* (EFSA NDA Panel, 2012)'.

The present estimates in the exposure scenario which takes into account consumers only of food supplements is higher than the calcium intake at P95, reported in the NDA opinion (2012). However, the results are hard to compare because in the dietary assessment studies which the NDA Panel has used, the exposures were assessed for the whole population and not for the group of consumers only of food supplement separately, as in this opinion, which explains the lower exposure levels in the NDA opinion 2012.

The Panel noted that the exposure to calcium in the scenario which takes into account consumers only of food supplements (all age groups above 3 years) is greatly exceeding the UL and may be of concern given the known adverse effects of high-dose calcium supplementation (gastrointestinal side effects, kidney stones, cardiovascular effects) (Tankeu et al., 2017; Chiodini and Bolland, 2018).

The Panel noted that the high exposures associated with the use of food supplements are not because of the exposure from the food additive which is only 10–20% of the overall exposure. Therefore, the Panel considered that the exposure to calcium from calcium carbonate as a food additive (E 170) does not raise concerns.

4. Conclusions

In this follow-up from the previous re-evaluation of the food additive calcium carbonate (E 170), the Panel concluded that there is no need for a numerical ADI for calcium carbonate and that, in principle, there are no safety concern with respect to the exposure to calcium carbonate *per se* at the currently reported uses and use levels in all age groups of the population, including infants below 16 weeks of age. With respect to the calcium intake resulting from the use of E 170 in food for the general population and infants < 16 weeks of age, the Panel concluded that it contributes only to a small part to the overall calcium dietary exposure. However, the unavoidable presence of aluminium in E 170 is of concern and should be addressed, in the first instance, by the introduction of a limit in the purity criteria of the EU specifications for E 170 but also by the reduction of the intake of this toxic element resulting from the dietary exposure to E 170. In addition, the Panel concluded that the technical data provided by the IBO support further amendments of the specifications for E 170 laid down in Commission Regulation (EU) No 231/2012, as presented by the recommendations made in Table 14.

5. Documentation as provided to EFSA

1) Abbott Nutrition, 2019. Submission of data in response to the call for technical and toxicological data on calcium carbonate (E 170) for uses as a food additive in foods for all population groups including infants below 16 weeks of age. Submitted on 22 October 2019.
2) Calcium Carbonate Association (CCA) Europe, 2019. Submission of data in response to the call for technical and toxicological data on calcium carbonate (E 170) for uses as a food additive in foods for all population groups including infants below 16 weeks of age. Submitted on 15 October 2019.
3) Specialised Nutrition Europe, 2019. Submission of data in response to the call for technical and toxicological data on calcium carbonate (E 170) for uses as a food additive in foods for all population groups including infants below 16 weeks of age. Submitted on 14 October 2019.
4) Specialised Nutrition Europe, 2019. Clarification on the data submitted in response to the call for technical and toxicological data on calcium carbonate (E 170) for uses as a food

additive in foods for all population groups including infants below 16 weeks of age. Submitted on 11 May 2020.

5) Calcium Carbonate Association (CCA) Europe, 2020. Response to the additional information request following the call for technical and toxicological data on calcium carbonate (E 170) for uses as a food additive in foods for all population groups including infants below 16 weeks of age. Submitted on 25 September 2020.
6) Calcium Carbonate Association (CCA) Europe, 2020. Response to the additional information request following the call for technical and toxicological data on calcium carbonate (E 170) for uses as a food additive in foods for all population groups including infants below 16 weeks of age. Submitted on 2 December 2020.
7) Calcium Carbonate Association (CCA) Europe, 2021. Response to the additional information request following the call for technical and toxicological data on calcium carbonate (E 170) for uses as a food additive in foods for all population groups including infants below 16 weeks of age. Submitted on 12 August 2021.
8) Calcium Carbonate Association (CCA) Europe, 2022. Response to the additional information request following the call for technical and toxicological data on calcium carbonate (E 170) for uses as a food additive in foods for all population groups including infants below 16 weeks of age. Submitted on 18 March 2022.
9) Calcium Carbonate Association (CCA) Europe, 2022. Response to the additional information request following the call for technical and toxicological data on calcium carbonate (E 170) for uses as a food additive in foods for all population groups including infants below 16 weeks of age. Submitted on 6 May 2022.
10) Calcium Carbonate Association (CCA) Europe, 2022. Response to the additional information request following the call for technical and toxicological data on calcium carbonate (E 170) for uses as a food additive in foods for all population groups including infants below 16 weeks of age. Submitted on 16 August 2022.
11) Calcium Carbonate Association (CCA) Europe, 2023. Response to the additional information request following the call for technical and toxicological data on calcium carbonate (E 170) for uses as a food additive in foods for all population groups including infants below 16 weeks of age. Submitted on 19 January 2023.
12) Calcium Carbonate Association (CCA) Europe, 2023. Response to a clarification request (personal communication via email) following the call for technical and toxicological data on calcium carbonate (E 170) for uses as a food additive in foods for all population groups including infants below 16 weeks of age. Submitted on 15 of June 2023.
13) Synadiet, 2019. Submission of data in response to the call for technical and toxicological data on calcium carbonate (E 170) for uses as a food additive in foods for all population groups including infants below 16 weeks of age. Submitted on 4 November 2019.

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Abbreviations

ADI	acceptable daily intake
ADME	absorption, distribution, metabolism, excretion
AIs	adequate intake
ANS Panel EFSA	Panel on Food Additives and Nutrient Sources added to Food
ARs	average requirements
bw	body weight
CAS	Chemical Abstract Service
DRV	dietary reference value
EDTA	ethylenediaminetetraacetic acid
ET-TEM	energy-filtering transmission electron microscopy
FAF	Panel on Food Additives and Flavourings
FAO/WHO	Food and Drug Organization/World Health Organization
FC	food category
FSMPs	food for special medical purposes
GCC	ground calcium carbonate
HF	hydrofluoric acid
IBO	interested business operator
ICP-MS	inductively coupled plasma-mass spectrometry
ICP-OES	Inductively coupled plasma optical emission spectroscopy
JECFA	Joint FAO/WHO Expert Committee on Food Additives
LD	laser diffraction
LOAEL	lowest-observed-adverse-effect level
LOD	limit of detection
LOQ	limit of quantification
Mintel GNPD	Mintel's Global New Products Database
MOE	margin of exposure
NDA Panel	EFSA Panel on Nutrition, Novel Foods and Food Allergens
NOAEL	no-observed-adverse-effect level
NOEL	no-observed-effect level
OECD	Organisation for Economic Co-operation and Development
PCC	precipitated calcium carbonate
PRIs	population reference intakes
PSD	particle size distribution
QS	*quantum satis*
SC	Scientific Committee of EFSA
SCF	Scientific Committee on Food
SEM	scanning electron microscopy
TEM	transmission electron microscopes
TG	test guideline
TWI	tolerable weekly intake
UL	tolerable upper intake level
WG	Working Group
XRF	X-ray fluorescence

Appendix A – Data requested in the call for data (Call for technical and toxicological data on calcium carbonate (E 170) for uses as a food additive in foods for all population groups including infants below 16 weeks of age[28]

Kind of data	Data requested in the call for data	Responses from interested parties	Comment
A. Information regarding the follow-up of the conclusions and the recommendations of the EFSA ANS Panel opinion on the safety of calcium carbonate (E 170) as food additive			
1. Technical data	The characterisation of all the different commercial preparations of the food additive calcium carbonate (E 170) from five non- consecutive batches of each preparation, in relation to: • analytical data on current levels of lead, mercury, cadmium and arsenic in commercial samples of the food additive; • the lowest technologically achievable level for aluminium, lead, mercury, cadmium and arsenic in order to adequately define their maximum limits in the specifications; • Because of their potential importance in toxicokinetics and toxicological effects, particle size and particle size distribution should be included in the EU specifications for the food additive calcium carbonate (E 170) in Commission Regulation (EU) No 231/2012. Detailed and comprehensive proposed specifications for the characterisation of the fraction of nanoparticles present in the food additive calcium carbonate (E 170) should be submitted. Information on particle size and particle size distribution for the food additive calcium carbonate (E 170) supported by analytical data, in line with the 'EFSA guidance on the risk assessment of the application of nanoscience and nanotechnologies in the food and feed chain: Part 1, human and animal health', is requested. This should allow the establishment of parameters in the EU specifications for calcium carbonate (E 170) that fully characterise the material used as a food additive. The analyses should be performed with appropriate analytical methods. EFSA seeks specific data on the methods of analysis used. These include but are not limited to e.g. the principle of the method, the scope of the method (i.e. the range of sample types that the method is used for), the concentration units used to express the analytical result(s), validation of the method (in particular limit of detection (LOD) and (LOQ).	Provided	Assessed, see Conclusions section

[28] Available from: https://www.efsa.europa.eu/en/consultations/call/181010-4 and responses from interested parties.

Kind of data	Data requested in the call for data	Responses from interested parties	Comment
2. Literature searches	Literature searches relevant for the safety evaluation of calcium carbonate (E 170) for all uses in foods for all population groups from 5/7/2011 up to the date of the data submission, should be conducted as described in the Guidance for submission for food additive evaluations (Section 5.3 [of the same Guidance])	Provided	Assessed, no further follow-up
B. Information required for the risk assessment of calcium carbonate (E 170) as food additive for use in foods for infants below 16 weeks of age			
1. Technical data	For the uses of calcium carbonate (E 170) in the infant formulae for use in special formulae used for infants below 16 weeks of age under special medical conditions (FC 13.1.5.1), EFSA seeks information on: • the levels of use of calcium carbonate (E 170), as well as analytical data on the concentration of calcium carbonate in these formulae, • the fate and the reaction products of calcium carbonate (E 170) in the formula ready to use, • particular specification requirements for identity and the purity of calcium carbonate (E 170) (e.g. with respect to lead, aluminium and other toxic elements). This includes data on physical characterisation regarding the particle size as requested in part A.1 in the food additive and the formulae as consumed.	Provided	Assessed, see Conclusions section
2. Toxicological data	Within the frame of the EFSA Guidance of the Scientific Committee on the risk assessment of substances present in food intended for infants below 16 weeks of age the following information on the toxicological properties of calcium carbonate (E 170) and its adverse effects relevant for its use in special formulae used for infants below 16 weeks of age under special medical conditions (FC 13.1.5.1): • post-marketing surveillance reports on undesired and adverse reactions indicating the ages and other relevant data of the exposed infants and young children and the use level of calcium carbonate (E 170) in the marketed products; • published and unpublished case reports (e.g. available nutrivigilance data) on undesired and adverse effects, associated with the oral administration of calcium carbonate in any form to infants and young children.	Provided	Assessed, no further follow-up.
3. Literature searches	Literature searches should be conducted relevant for the safety evaluation of calcium carbonate (E 170) when used in foods for infants below 16 weeks of age, as described in the Guidance for submission for food additive evaluations (Section 5.3 [of the same Guidance])	Provided	Assessed, no further follow-up

Appendix B – Estimation of the fraction of the concentration of toxic elements in calcium carbonate (E 170) with respect to the regulatory maximum levels in the final food product for which the additive is used

The Panel estimated the fraction (%) of the levels of the toxic elements lead and cadmium in E 170 with respect to the regulatory maximum levels in the final product (formulae) as sold as laid down in Commission Regulation (EU) 2023/915 considering:

- The current specification for lead in E 170 according to Regulation (EU) No 231/2012, 3 mg/kg.
- The current specification for cadmium in E 170 according to Regulation (EU) No 231/2012, 1 mg/kg.
- The limits for lead and cadmium in E 170 products, 3 and 1 mg/kg, respectively, as proposed by one IBO (Documentation provided to EFSA n. 2), see also Section 3.2.2.
- The highest value of the typical use levels of E 170 in the final food of 424 mg/L and the mean value of the reported typical use levels of 353 mg/L reported by industry for the uses in FSMP (FC 13.1.5.1), see Section 3.3.4.1.
- The maximum levels (ML) for lead (0.01 mg/kg) and cadmium (0.005 mg/kg) in liquid formulae for infants as laid down in Commission Reg. (EU) 2023/915.
- The regulatory maximum limits for calcium in infants FSMPs from Commission delegated Regulation (EU) 2016/128 of 250 mg calcium/100 Kcal.

The results of the calculations can be found in Tables B.1 and B.2.

Table B.1: Estimation of the fraction of the levels of lead in E 170 with respect to the regulatory maximum levels in the final product (liquid formulae for infants below 16 weeks of age)

Specification for toxic elements Status	Lead (mg/kg)	Use level of food additive in final product (mg/L)	Concentration of toxic element in final product (mg/L)	Maximum level in Commission Reg. (EU) 2023/915 (mg/kg)	Fraction of toxic element from FA on ML of final product (%)
Current EU specification	3	424	0.0013	0.010	12.7
Current EU specification	3	353	0.0011	0.010	10.6
Current EU specification	3	1,750[(a)]	0.0053	0.010	52.5
Proposal IBO	3	424	0.0013	0.010	12.7
Proposal IBO	3	353	0.0011	0.010	10.6
Proposal IBO	3	1,750[(a)]	0.0053	0.010	52.5

(a): Calcium carbonate used in FSMP at the allowed maximum calcium level 250 mg/100 kcal and the highest energy requirement 70 kcal/100 ml of the formula as set in the regulation EU 128/2016.

Table B.2: Estimation of the fraction of the levels of cadmium in E 170 with respect to the regulatory maximum levels in the final product (liquid formulae for infants below 16 weeks of age)

Specification for toxic elements Status	Cadmium (mg/kg)	Use level of food additive in final product (mg/L)	Concentration of toxic element in final product (mg/L)	Maximum level in Commission Reg. (EU) 2023/915 (mg/kg)	Fraction of toxic element from FA on ML of final product (%)
Current EU specification	1	424	0.00042	0.005	8.5
Current EU specification	1	353	0.00035	0.005	7.1
Current EU specification	1	1,750[(a)]	0.002	0.005	35.0
Proposal IBO	1	424	0.00042	0.005	8.5

Specification for toxic elements Status	Cadmium (mg/kg)	Use level of food additive in final product (mg/L)	Concentration of toxic element in final product (mg/L)	Maximum level in Commission Reg. (EU) 2023/915 (mg/kg)	Fraction of toxic element from FA on ML of final product (%)
Proposal IBO	1	353	0.00035	0.005	7.1
Proposal IBO	1	1,750[(a)]	0.002	0.005	35.0

(a): Calcium carbonate used in FSMP at the allowed maximum calcium level and the highest energy requirement 70 kcal/100 ml of the formula as set in the regulation EU 128/2016.

Considering the results of the above estimations and the fact that the food additive is not the only potential source of toxic elements, the Panel emphasises the need to reduce the specification limit values for lead and cadmium in E 170, in Regulation (EU) no 231/2012.

Appendix C – Comparison of the content of calcium in IF and FSMPs as provided by the IBOs (Documentation provided to EFSA n. 1, 4) against the regulatory, maximum amount

IF/FSMP	Content of calcium as provided by the IBO		Maximum content[b],[c]	
	mg calcium/100 kcal	mg calcium/100 mL	mg calcium/100 kcal[a]	mg calcium/100 mL
IF	–	51	140	84-98[a]
IF	–	59	140	84-98[a]
IF	–	51	140	84-98[a]
IF	–	56	140	84-98[a]
IF	–	55	140	84-98[a]
IF	–	49	140	84-98[a]
FSMP	122	99	250	–
FSMP	117	144	250	–
FSMP	127	103	250	–
FSMP	132	163	250	–
FSMP	125	102	250	–
FSMP	129	160	250	–
FSMP	117	116	250	–
FSMP	121	98	250	–
FSMP	115	143	250	–

IF: infant formula; FSMP: food for special medical purpose; IBO: interested business operator.
(a): The maximum level of 140 mg calcium/100 kcal from Commission delegated Regulation (EU) 2016/127 was converted to mg calcium/mL considering an energy requirement of 60 or 70 kcal/100 mL from the same Regulation.
(b): Commission delegated Regulation (EU) 2016/127.
(c): Commission delegated Regulation (EU) 2016/128.

Appendix D – Rate of dissolution at pH 6 of PCC (precipitated calcium carbonate, E 170)

In the dissolution test report provided by the IBO for PCC E 170 tested at pH 6 (infant case) (Documentation provided to EFSA n. 10), the report concluded that the powder dissolved quickly and that the criterium for degradation/dissolution as specified by the EFSA Guidance i.e. at least 88% dissolution within 30 min, was clearly fulfilled in both experiments.

In the dissolution rate curves presented by the IBO, the Panel noted that, although dissolution exceeded 88% by the 30 min timepoint as required, there was the appearance of a plateau in the dissolution profiles. The final concentration of calcium did not reach the expected value calculated by the IBO, taking into account the mass of PCC used in the experiments and the volume of the dissolution medium.

The TR-Nano Guidance document states that '*The material is considered to degrade/dissolve quickly (i.e. to have a high degradation/ dissolution rate with a half-life of 10 min or less) if the degradation rate profile shows a clear decrease in the presence of particles over time (no plateau) and 12% or less of the material (mass-based) – compared with the concentration at the beginning of the test – remains as particles after 30 min*'.

The presence of a plateau may indicate that a fraction of the particulate material is recalcitrant, is slower to dissolve/degrade, and so may be persistent.

In considering the test report in full, and especially the experimental design and the calculation of the dissolution profiles from the raw data provided, the Panel noted that the dissolution profiles had not been calculated correctly.

The tests were conducted according to the TR guidance. The test item was dispersed at room temperature in water containing 85 mmol/L $NaHCO_3$ and 40 mmol/L NaCl and the pH was then adjusted to the target value using HCl. In these tests, the concentration of HCl required to achieve a pH of 6 is very low in comparison to the amount of PCC E 170 calcium carbonate submitted to the test. The HCl is rapidly consumed in the acid–base reaction (calcium carbonate reacts with dilute acid with effervescence of CO_2) and the pH would swing from slightly acidic to basic. The TR Guidance anticipates such a situation and states that the pH may have to be re-adjusted during the procedure, depending on the test item. Accordingly, therefore, as the test item dissolved/reacted, the pH of the stirred system was maintained at pH 6 by the continuous replenishment of HCl using an automatic titrator dosing system adding 1 M HCl with feedback control from a pH electrode/m.

The Panel noted that in the test report, the consequence of this replenishment of HCl in affecting the total volume of the stirred system had been correctly taken into account in calculating the amount of dissolved calcium (in mmoles) using the total volume of dissolution medium and the concentration determined by ICP-MS. However, the reporting laboratory did not take into account that at each sampling timepoint an aliquot of dissolved/suspended material was removed for the ICP-MS analysis for dissolved calcium. So e.g. just prior to taking the 30-min sample, four aliquots had already been taken (1 mL to measure the initial concentration of total calcium in the dispersed sample and then 2 mL each for the 0, 5 and 10-min timepoints). Since these aliquots were taken from a total volume of ca. 200 mL this meant that e.g. only 96.6% of the initial charge of test item was in the flask at the time of sampling for the 30-min timepoint. It was this error that was responsible for the plateau, with dissolution seeming to stop short of 100%.

Using the raw data provided by the IBO, the Panel recalculated the dissolution rate of the PCC E 170 in this experiment and the outcome is presented in Figure D.1. At 30 min the solubilised fraction of PCC E 170 was 97.2% and 98.2% for the duplicate experiments and no plateau was observed. At 60 min the solubilisation is considered by the Panel to be complete at 100% of the expected value, taking into account the experimental measurement uncertainty.

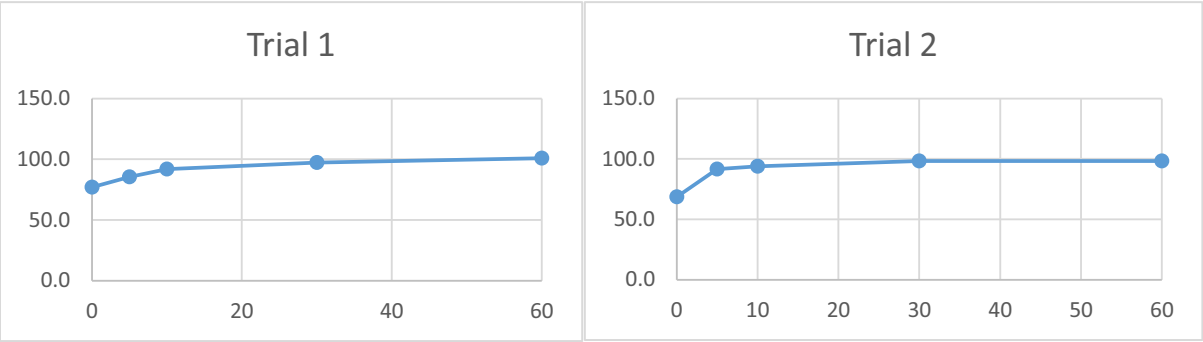

Figure D.1: Dissolution profiles for PCC E 170 at pH 6 (infant case) as recalculated by the Panel. x-axis: sampling point in minutes. y-axis: percentage of the test item that is dissolved/ degraded. Trial 1 and Trial 2 represent the duplicate experiments.

Annex A – Summary of reported use levels (mg/kg or mg/L as appropriate) of calcium carbonate (E 170) provided by industry

Annex B – Number and percentage of food products labelled with calcium carbonate (E 170) out of the total number of food products present in the Mintel GNPD per food subcategory between 2018 and 2023

Annex C – Concentration levels of calcium carbonate (E 170) used in the exposure assessment scenarios (mg/kg or mL/kg as appropriate)

Annex D – Summary of total estimated exposure of food additive (E 170) from their use as food additives for the maximum level exposure scenario and the refined exposure assessment scenarios per population group and survey: mean and 95th percentile (mg/kg bw per day)

Annex E – Main food categories contributing to exposure to food additive (E 170) using the maximum level exposure assessment scenario and the refined exposure assessment scenarios (> 5% to the total mean exposure)

Annex A–E can be found in the online version of this output (in the 'Supporting information' section).