SCIENTIFIC OPINION

EFSA Journal

ADOPTED: 26 January 2022

doi: 10.2903/j.efsa.2022.7135

Safety assessment of the substance nano precipitated calcium carbonate for use in plastic food contact materials

EFSA Panel on Food Contact Materials, Enzymes and Processing Aids (CEP), Claude Lambré, José Manuel Barat Baviera, Claudia Bolognesi, Andrew Chesson, Pier Sandro Cocconcelli, Riccardo Crebelli, David Michael Gott, Konrad Grob, Evgenia Lampi, Marcel Mengelers, Alicja Mortensen, Inger-Lise Steffensen, Christina Tlustos, Henk Van Loveren, Laurence Vernis, Holger Zorn, Laurence Castle, Emma Di Consiglio, Roland Franz, Nicole Hellwig, Maria Rosaria Milana, Stefan Merkel, Eric Barthélémy, Daniele Comandella, Ellen Van Haver and Gilles Rivière

Abstract

The EFSA Panel on Food Contact Materials, Enzymes and Processing Aids (CEP) assessed the safety of the substance 'nano precipitated calcium carbonate', FCM substance No. 1087, the particles size of which is in the range of [redacted], with a median of [redacted]. The substance is intended to be used as a filler in all plastics at up to 5% w/w for contact with acidic food and at up to 40% w/w for contact with all other types of food. Articles made with the substance are intended for long-term storage at room temperature or below. The particulate form of the calcium carbonate dissolved rapidly under simulated gastric conditions and, therefore, in accordance with the EFSA Guidance on Particle – Technical Requirements (2021), an assessment of the particles in nanoform is not required and a conventional risk assessment is sufficient. Calcium carbonate, not in nanoform, is authorised for use in plastic FCM without specific migration limit (FCM No. 21) and for use as a food additive (E 170). Migration, from low-density polyethylene (LDPE) containing 40% of the substance, was below 0.03 mg/kg in isooctane and 95% ethanol, and 5.4 mg/kg in 10% ethanol. For LDPE containing 5% of the substance, corresponding to the maximum intended amount for contact with acidic foods, the migration was 17 mg/kg. Therefore, the CEP Panel concluded that the substance nano precipitated calcium carbonate is not of safety concern for consumers when used as a filler in all types of polymer for all types of food, except for infant food formulae. The Panel noted, however, that for acidic foods, the overall migration limit may be exceeded.

Keywords: calcium carbonate, nano, filler, food contact materials, safety assessment, FCM No. 1087

Requestor: Belgian Federal Public Service - Public Health, Food Chain Safety and Environment

Question number: EFSA-Q-2019-00232

Correspondence: fip@efsa.europa.eu

Panel members: José Manuel Barat Baviera, Claudia Bolognesi, Andrew Chesson, Pier Sandro Cocconcelli, Riccardo Crebelli, David Michael Gott, Konrad Grob, Claude Lambré, Evgenia Lampi, Marcel Mengelers, Alicja Mortensen, Gilles Rivière, Vittorio Silano (until 21 December 2020 †), Inger-Lise Steffensen, Christina Tlustos, Henk Van Loveren, Laurence Vernis and Holger Zorn.

Competing interests: R. Franz declared that Fraunhofer institute at which he is employed provides advisory services to private business operators active in the sector on food contact materials. In line with EFSA's Policy on Independence (http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/policy_independence.pdf) and the Decision of the Executive Director on Competing Interest Management (http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/competing_interest_management_17.pdf), a waiver was granted to R. Franz regarding his participation to the EFSA's Working Group on Food Contact Materials (FCM WG) in accordance with Article 21 of the Decision of the Executive Director on Competing Interest Management. Pursuant to Article 21(6) of the above-mentioned Decision, the involvement of R. Franz is authorised as a member in the FCM WG, allowing him to take part in the discussions and in the drafting phase of the scientific output, but he is not allowed to be, or act as, a chairman, a vice-chairman or rapporteur of the working group.

Note: The full opinion will be published in accordance with Article 10(6) of Regulation (EC) No 1935/2004 once the decision on confidentiality, in line with Article 20(3) of the Regulation, will be received from the European Commission. The following information have been provided under confidentiality and they are redacted awaiting the decision of the Commission: the manufacturing details, the identities and levels of impurities and some of the information on the particle and agglomerate sizes.

Declarations of interest: The declarations of interest of all scientific experts active in EFSA's work are available at https://ess.efsa.europa.eu/doi/doiweb/doisearch.

Suggested citation: EFSA CEP Panel (EFSA Panel on Food Contact Materials, Enzymes and Processing Aids), Lambré C, Barat Baviera JM, Bolognesi C, Chesson A, Cocconcelli PS, Crebelli R, Gott DM, Grob K, Lampi E, Mengelers M, Mortensen A, Steffensen I-L, Tlustos C, Van Loveren H, Vernis L, Zorn H, Castle L, Di Consiglio E, Franz R, Hellwig N, Milana MR, Merkel S, Barthélémy E, Comandella D, Van Haver E and Rivière G, 2022. Scientific Opinion on the safety assessment of the substance nano precipitated calcium carbonate for use in plastic food contact materials. EFSA Journal 2022;20(2): 7135, 8 pp. https://doi.org/10.2903/j.efsa.2022.7135

ISSN: 1831-4732

The EFSA Journal is a publication of the European Food Safety Authority, a European agency funded by the European Union.

Table of contents

1. Introduction

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

Before a substance is authorised to be used in food contact materials (FCM) and is included in a positive list, EFSA's opinion on its safety is required. This procedure has been established in Articles 8, 9 and 10 of Regulation (EC) No 1935/2004[1] of the European Parliament and of the Council of 27 October 2004 on materials and articles intended to come into contact with food.

According to this procedure, the industry submits applications to the Member States' competent authorities which transmit the applications to the European Food Safety Authority (EFSA) for their evaluation.

In this case, EFSA received an application from the federal public service of the Health, Food Chain Safety and Environment, Belgium, requesting the evaluation of the substance nano precipitated calcium carbonate (PCC), included in the CAS number 471-34-1 and with the FCM substance No. 1087. The dossier was submitted on behalf of the Calcium Carbonate Association Europe (CCA Aisbl).

According to Regulation (EC) No 1935/2004 of the European Parliament and of the Council on materials and articles intended to come into contact with food, EFSA is asked to carry out an assessment of the risks related to the intended use of the substance and to deliver a scientific opinion.

2. Data and methodologies

2.1. Data

The applicant has submitted a dossier in support of its application for the authorisation of the substance nano precipitated calcium carbonate to be used in plastic food contact materials.

Additional information was provided by the applicant during the assessment process in response to the request from EFSA sent on 30 January 2020, with addendum sent on 4 May 2021 (see Documentation provided to EFSA).

Data submitted and used for the evaluation are:

Non-toxicological data and information

- Chemical identity
- Description of manufacturing process of substance/FCM
- Physical and chemical properties, including solubility and dissolution rate tests
- Intended uses
- Existing authorisation(s)
- Migration of the substance from low-density polyethylene (LDPE)
- Surface analysis of a LDPE substance composite before and after migration testing

Toxicological data

- Bacterial gene mutation test (with nano PCC)
- *In vitro* mammalian cell gene mutation test (with nano PCC)
- *In vitro* mammalian chromosome aberration test (with nano PCC)
- Biokinetic study (bulk or nano PCC)
- 90-day oral toxicity study in rats (with nano PCC)
- Review of the toxicological studies on calcium carbonate (bulk or nano PCC) and on the fatty acids

2.2. Methodologies

The assessment was conducted in line with the principles laid down in Regulation (EC) No 1935/2004 on materials and articles intended to come into contact with food. This Regulation underlines that applicants may consult the Guidelines of the Scientific Committee on Food (SCF) for the presentation of an application for safety assessment of a substance to be used in FCM prior to its authorisation (EC, 2001), including the corresponding data requirements. The dossier that the applicant submitted for evaluation was in line with the SCF guidelines (European Commission, 2001).

[1] Regulation (EC) No 1935/2004 of the European parliament and of the council of 27 October 2004 on materials and articles intended to come into contact with food and repealing Directives 80/590/EEC and 89/109/EEC. OJ L 338, 13.11.2004, p. 4–17.

The methodology is based on the characterisation of the substance that is/are the subject of the request for safety assessment prior to authorisation, its impurities and reaction and degradation products, the evaluation of the exposure to those substances through migration and the definition of minimum sets of toxicity data required for safety assessment.

To establish the safety from ingestion of migrating substances, the toxicological data indicating the potential hazard and the likely human exposure data need to be combined. Exposure is estimated from studies on migration into food or food simulants and considering that a person may consume daily up to 1 kg of food in contact with the relevant FCM.

As a general rule, the greater the exposure through migration, the more toxicological data is required for the safety assessment of a substance. Currently there are three tiers with different thresholds triggering the need for more toxicological information as follows:

a) In case of high migration (i.e. 5–60 mg/kg food), an extensive data set is needed.
b) In case of migration between 0.05 and 5 mg/kg food, a reduced data set may suffice.
c) In case of low migration (i.e. < 0.05 mg/kg food), only a limited data set is needed.

More detailed information on the required data is available in the SCF guidelines (European Commission, 2001).

The assessment was conducted in line with the principles described in the EFSA Guidance on transparency in the scientific aspects of risk assessment (EFSA, 2009) and considering the relevant guidance from the EFSA Scientific Committee, such as the Guidance on 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). The update of the Guidance on risk assessment of nanomaterials to be applied in the food and feed chain: human and animal health and the Guidance on technical requirements for regulated food and feed product applications to establish the presence of small particles including nanoparticles (EFSA Scientific Committee, 2021a,b) were not published at the moment of the submission of the data by the applicant. They were considered during the assessment, but not for rejecting data compliant with the version from 2018 and not with the versions from 2021.

3. Assessment

According to the applicant, the substance nano precipitated calcium carbonate (nano PCC) is intended to be used as a filler in all types of polymers to impart strength and rigidity to the polymer, at concentrations up to 5% w/w for contact with acidic food and up to 40% w/w for contact with all other types of food. Articles made with the substance are intended for long-term storage (longer than 6 months) between −10°C and +30°C.

The substance was not evaluated by SCF and EFSA in the past. However, the bulk calcium carbonate (not in nanoform) is authorised by the Regulation (EU) 10/2011 without specific migration limit (FCM No. 21, calcium salts of carbonic acid). Calcium carbonate is also authorised as food additive (E 170) and was re-evaluated by the ANS Panel in 2011 (EFSA ANS Panel, 2011). In its evaluation, the ANS Panel agreed with the group ADI 'not specified' assigned by SCF to a group of carbonates, including calcium carbonate, when considering the use of calcium carbonate as a food additive. Calcium carbonate is currently under re-evaluation as part of the programme for the re-evaluation of approved food additives, including for infants below 16 weeks of age, the details of which are described in Annex II of the Regulation EU 257/2010[2].

3.1. Non-toxicological data

3.1.1. Identity of the substance[3]

The substance is a white powder in the form of nanoparticles [redacted].

[2] Annex II of Commission Regulation (EU) No 257/2010 of 25 March 2010 setting up a programme 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.

[3] Technical dossier/2subm211019/Appendix B/section 1; Technical dossier/2subm211019/Technical Annexes/Annexes 1, 2, 3, 4.1, 4.2.

The formula weight of $CaCO_3$ is 100 Da. Energy-dispersive X-ray (EDX) spectrometry was used in order to confirm the identity of the substance by showing the presence of calcium, carbon and oxygen. According to the applicant, the purity of nano PCC is between 96.5% to 100% (typically 97.5%). The main impurities are [redacted].

The total surface area of the particles was measured using the Brunauer, Emmett and Teller (BET) method and resulted in a mass-specific surface area (MSSA) of 15–30 m^2/g. The volume-specific surface area (VSSA) was 40.5–81 m^2/cm^3, calculated based on the density of calcite (2.7 g/cm^3). The calcium carbonate nanoparticles are not porous, but they form agglomerates that have some porosity.

The primary particle size determined by transmission electron microscopy (TEM) was in the range [redacted], with a quasi-spherical shape. The median (± SD) particle size was [redacted]. The median hydrodynamic size of the agglomerates measured by dynamic light scattering (DLS) was [redacted].

3.1.2. Physical and chemical properties of the substance[4]

Bulk calcium carbonate decomposes at temperatures above 825°C.

To determine whether the particulate form of $CaCO_3$ is solubilised under conditions simulating gastrointestinal digestion, the solubilisation of the substance was tested at 37°C, both at pH 3 and 7, based on an ultrafiltration test using a filter of 100 kDa pore size. Measurements of the dissolution rate were performed with 100 mg/L of the substance, corresponding to 40 mg/L of calcium, at five time points (0, 30, 60, 90 and 120 min). After 30 min, the solubilised fraction was in the range 95%–98% at pH = 3 and in the range 46%–79% at pH = 7.

If solubility is pH dependent and the dissolution rate criterion[5] is not respected at pH = 7, it is sufficient to demonstrate that the dissolution rate at pH = 3 (pH condition simulating the stomach) ensures full dissolution (EFSA Guidance on technical requirements for nanomaterials, EFSA Scientific Committee, 2021b). Therefore, for infants older than 16 weeks, children and adults, the dissolution is rapid enough to achieve full solubilisation in the stomach.

However, the solubility tests at pH 5–6, which mimic the buffered gastric pH of infants below 16 weeks of age (Nguyen et al., 2015; EFSA Scientific Committee, 2017, 2021a), were not provided.

3.1.3. Characterisation and quantification of the substance after incorporation in FCM[6]

The external surface of LDPE samples containing the substance was analysed by scanning electron microscopy (backscattered SEM, SEM-EDX and semi-quantitative SEM-EDX) before and after migration experiments lasting for 10 days at 60°C. After contact with 95% ethanol and isooctane, no significant differences were found. However, major differences, such as changes in the shape of agglomerates and the appearance of voids that indicate release of the substance from the surface were observed after the tests with 3% acetic acid and to a lesser extent with 10% ethanol. These observations are consistent with clearly measurable migration observed in 3% acetic acid and 10% ethanol (see Section 3.1.4. below).

The characterisation of the sizes of the particles and their distribution within the plastic by surface analysis of the cross-section were not properly addressed. However, given the full solubilisation at pH 3 simulating conditions of the stomach (see Section 3.1.2), no further information was requested.

3.1.4. Specific migration[7]

The specific migration of calcium, expressed as calcium carbonate, from LDPE containing the substance at 5%, 10%, 20% and 40% into 10% ethanol, 3% acetic acid, 95% ethanol and isooctane was determined by inductively coupled plasma (ICP) with optical emission spectrometry (OES) and

[4] Technical dossier/2subm211019/Appendix B/section 2; Technical dossier/2subm211019/Technical Annexes/Annexes 1, 6, 7; Technical dossier/add data Sept 21/Annexes 4a, 4c.
[5] Half-life of 10 min or less, corresponding to dissolved fraction equal to or higher than 88% (mass-based) in 30 min.
[6] Technical dossier/2subm211019/Appendix B/section 5.1; Technical dossier/2subm211019/Technical Annexes/Annex11; Technical dossier/add data Sept 21/Annex 2.
[7] Technical dossier/2subm211019/Appendix B/section 5.1; Technical dossier/2subm211019/Technical Annexes/Annexes 9, 10, 11.

mass spectrometry (MS). The conditions were 10 days at 60°C. The migration into 3% acetic acid was also tested during 64 days at 40°C. The surface to volume (S/V) ratio was 6 dm^2/kg.

For LDPE containing 40% of the substance, the migration was below 0.03 mg/kg in isooctane and 95% ethanol, 5.4 mg/kg in 10% ethanol and 2,419 mg/kg in acetic acid (out of the scope of the request). For LDPE containing 5% of the substance, corresponding to the maximum intended amount for contact with acidic foods, the migration was 17 mg/kg.

The Panel noted that in the case of acidic foods with a low buffer capacity and packaging with high S/V ratio, the pH of the food might be slightly increased, with a possible effect on the microbiological stability of foods.

3.2. Toxicological data[8]

Toxicological data and a review of toxicological studies on calcium carbonate (bulk and nano form), mainly referring to the REACH registration dossiers, were provided. However, in accordance with the EFSA Guidance on technical requirements for nanomaterials (EFSA Scientific Committee, 2021b), based on the result obtained in the dissolution rate study, an assessment of the particles in nanoform was not necessary and a conventional risk assessment was sufficient.

The bulk calcium carbonate is authorised to be used in plastics without any restriction on the basis of the SCF classification of carbonic acids, salts (PM ref. No. 42500) in the SCF list 1 with an ADI 'not specified for carbonate'. Moreover, the ANS Panel re-evaluated $CaCO_3$ (E 170) as a food additive in 2011 (EFSA ANS Panel, 2011). In its evaluation that included some of the data submitted in this application, the ANS Panel concluded that 'trace levels of adventitious nanoscale material within macroscale calcium carbonate are not of toxicological concern' and agreed with the group ADI 'not specified' assigned by the SCF to a group of carbonates including calcium carbonate used as a food additive.

The CEP Panel noted that calcium carbonate is currently under re-evaluation as part of the program for the re-evaluation of approved food additives including for infants below 16 weeks of age. The applicant did not submit dissolution/degradation rate test(s) with a design adapted for infants below 16 weeks of age as required by EFSA Scientific Committee guidance (EFSA Scientific Committee, 2017, 2021a), nor proposed specific uses for infant formulae.

4. Conclusions

Based on the above-mentioned data, the CEP Panel concluded that the substance nano precipitated calcium carbonate is not of safety concern for consumers when used as a filler in all types of polymer for all types of food, except for infant formulae.

The Panel noted that for acidic foods, the overall migration limit may be exceeded.

5. Recommendations

Calcium carbonate is currently under re-evaluation as part of the programme for the re-evaluation of approved food additives including for infants below 16 weeks of age. Depending on the conclusion of the EFSA FAF Panel, the European Commission may reconsider the restriction for use in infant formulae.

6. Documentation provided to EFSA

1) Initial dossier. March 2019. Submitted on behalf of CCA Aisbl.
2) Additional data. September 2021. Submitted on behalf of CCA Aisbl.

References

EFSA (European Food Safety Authority), 2009. Guidance of the Scientific Committee on transparency in the scientific aspects of risk assessments carried out by EFSA. Part 2: general principles. EFSA Journal 2009;7(5):1051, 22 pp. https://doi.org/10.2903/j.efsa.2009.1051

EFSA ANS Panel (EFSA Panel on Food Additives and Nutrient Sources added to Food), 2011. Scientific Opinion on re-evaluation of calcium carbonate (E 170) as a food additive. EFSA Journal 2011;9(7):2318, 73 pp. https://doi.org/10.2903/j.efsa.2011.2318

[8] Technical dossier/2subm211019/Appendix B/section 8; Technical dossier/2subm211019/Technical Annexes/Annexes 12, 13, 14, 15; Technical dossier/add data Sept 21/Annex 7.

EFSA Scientific Committee, 2017. Guidance on the risk assessment of substances present in food intended for infants below 16 weeks of age. EFSA Journal 2017;15(5):4849, 58 pp. https://doi.org/10.2903/j.efsa.2017.4849

EFSA Scientific Committee, Hardy A, Benford D, Halldorsson T, Jeger MJ, Knutsen HK, More S, Naegeli H, Noteborn H, Ockleford C, Ricci A, Rychen G, Schlatter JR, Silano V, Solecki R, Turck D, Younes M, Chaudhry Q, Cubadda F, Gott D, Oomen A, Weigel S, Karamitrou M, Schoonjans R and Mortensen A, 2018. Guidance on risk assessment of the application of nanoscience and nanotechnologies in the food and feed chain: Part 1, human and animal health. EFSA Journal 2018;16(7):5327, 95 pp. https://doi.org/10.2903/j.efsa.2018.5327

EFSA Scientific Committee, More S, Bampidis V, Benford D, Bragard C, Halldorsson T, Hernández-Jerez A, Hougaard Bennekou S, Koutsoumanis K, Lambré C, Machera K, Naegeli H, Nielsen S, Schlatter J, Schrenk D, Silano (deceased) V, Turck D, Younes M, Castenmiller J, Chaudhry Q, Cubadda F, Franz R, Gott D, Mast J, Mortensen A, Oomen AG, Weigel S, Barthelemy E, Rincon A, Tarazona J and Schoonjans R, 2021a. Guidance on risk assessment of nanomaterials to be applied in the food and feed chain: human and animal health. EFSA Journal 2021a;19(8):6768, 111 pp. https://doi.org/10.2903/j.efsa.2021.6768

EFSA Scientific Committee, More S, Bampidis V, Benford D, Bragard C, Halldorsson T, Hernández-Jerez A, Bennekou SH, Koutsoumanis K, Lambré C, Machera K, Naegeli H, Nielsen S, Schlatter J, Schrenk D, Silano (deceased) V, Turck D, Younes M, Castenmiller J, Chaudhry Q, Cubadda F, Franz R, Gott D, Mast J, Mortensen A, Oomen AG, Weigel S, Barthelemy E, Rincon A, Tarazona J and Schoonjans R, 2021b. Guidance on technical requirements for regulated food and feed product applications to establish the presence of small particles including nanoparticles. EFSA Journal 2021b;19(8):6769, 48 pp. https://doi.org/10.2903/j.efsa.2021.6769

European Commission, 2001. Guidelines of the Scientific Committee on Food for the presentation of an application for safety assessment of a substance to be used in food contact materials prior to its authorisation.

Nguyen TT, Bhandari B, Cichero J and Prakash S, 2015. Gastrointestinal digestion of dairy and soy proteins in infant formulas: an *in vitro* study. Food Research International, 76, 348–358.

Abbreviations

ADI	acceptable daily intake
ANS Panel	EFSA Panel on Food Additives and Nutrient Sources added to Food
BET	Brunauer, Emmett and Teller
CCA Aisbl	Calcium Carbonate Association Europe
CEF Panel	EFSA Panel on Food Contact Materials, Enzymes, Flavourings and Processing Aids
DLS	dynamic light scattering
EDX	energy-dispersive X-Ray
FCM	food contact materials
ICP	inductively coupled plasma
LDPE	low-density polyethylene
MS	mass spectrometry
MSSA	mass-specific surface area
OES	optical emission spectrometry
PCC	precipitated calcium carbonate
REACH	registration, evaluation, authorisation and restriction of chemicals
S/V	surface to volume
SCF	Scientific Committee on Food
SD	standard deviation
SEM	scanning electron microscopy
TEM	transmission electron microscopy
VSSA	volume-specific surface area
w/w	weight per weight