Adopted: 31 January 2024

DOI: 10.2903/j.efsa.2024.8625

efsa JOURNAL

SCIENTIFIC OPINION

Safety of feed additives consisting of microcrystalline cellulose and carboxymethyl cellulose for all animal species (International Cellulosics Association)

EFSA Panel on Additives and Products or Substances used in Animal Feed (FEEDAP) | **Vasileios Bampidis** | **Giovanna Azimonti** | **Maria de Lourdes Bastos** | **Henrik Christensen** | **Birgit Dusemund** | **Mojca Durjava** | **Maryline Kouba** | **Marta López-Alonso** | **Secundino López Puente** | **Francesca Marcon** | **Baltasar Mayo** | **Alena Pechová** | **Mariana Petkova** | **Fernando Ramos** | **Roberto Edoardo Villa** | **Ruud Woutersen** | **Montserrat Anguita** | **Jaume Galobart** | **Paola Manini** | **Maria Vittoria Vettori** | **Matteo Innocenti**

Correspondence: feedap@efsa.europa.eu

Abstract

Following a request from the European Commission, the EFSA Panel on Additives and Products or Substances used in Animal Feed (FEEDAP) was asked to deliver a scientific opinion on the safety of microcrystalline cellulose and carboxymethyl cellulose as technological feed additives for all animal species. In its previous opinions on the safety and efficacy of the products, the FEEDAP Panel could not conclude on proper identification and characterisation as required for a feed additive. The occurrence of potential toxic impurities could also not be assessed. Based on the new data provided, the feed additives microcrystalline cellulose and carboxymethyl cellulose were properly identified and characterised and were shown to meet the specifications set for their use as food additives. Therefore, the conclusions of the safety reached in the previous opinions for microcrystalline cellulose and carboxymethyl cellulose meeting the food additive specifications apply to the microcrystalline cellulose and carboxymethyl cellulose under assessment as feed additives. The additives are considered safe for all animal species, the consumer and the environment. In the absence of data, the FEEDAP Panel is not in the position to conclude on the safety for the user.

KEYWORDS

carboxymethyl cellulose, characterisation, microcrystalline cellulose, safety, technological additive

CONTENTS

1 | INTRODUCTION

1.1 | Background and terms of reference as provided by the European Commission

Regulation (EC) No 1831/2003[1] establishes the rules governing the Community authorisation of additives for use in animal nutrition and, in particular, Article 9 defines the terms of the authorisation by the Commission.

The applicant, International Cellulosics Association (ICA), is seeking a Community authorisation of microcrystalline cellulose E 460 and carboxymethyl cellulose E 466 as feed additives to be used as emulsifiers, stabilisers, thickeners, gelling agents and binders for all animal species (Table 1).

TABLE 1 Description of the substances.

Category of additive	Technological additives
Functional group of additive	Emulsifier, stabilisers, thickeners, gelling agents and binder
Description	Microcrystalline Cellulose E 460 and Carboxymethyl cellulose E 466
Target animal category	All animal species
Applicant	International Cellulosics Association (ICA)
Type of request	New opinion

On 2 July 2020, the Panel on Additives and Products or Substances used in Animal Feed of the European Food Safety Authority ('EFSA'), in its opinion on the safety and efficacy of the products, could not conclude on proper identification and characterisation as required for a feed additive. The occurrence of potential toxic impurities could also not be assessed.

During the discussions with the Member States at a meeting of the Standing Committee on Plants, Animals, Food and Feed (Animal Nutrition section), it was suggested to check for the possibility to demonstrate proper identification and characterisation as required for a feed additive. The occurrence of potential toxic impurities had also to be assessed.

The Commission gave the possibility to the applicant to submit supplementary information and data in order to complete the assessment and to allow a revision of the EFSA's opinion. The new data have been received on 30 April 2021 and the applicant has been requested to transmit them to EFSA as well.

In view of the above, the Commission asks EFSA to deliver a new opinion on microcrystalline cellulose (E 460) and carboxymethyl cellulose (E 466) as feed additives for all animal species based on the additional data submitted by the applicant, in accordance with Article 29(1)(a) of Regulation (EC) No 178/2002.[2]

1.2 | Additional information

Microcrystalline cellulose (E 460 (i)) and carboxymethyl cellulose (E 466)[3] are currently authorised as feed additives for all animal species, without a minimum and a maximum content.

EFSA issued one opinion on the safety and efficacy of microcrystalline cellulose E 460 (i) when used in feed for all animal species (EFSA FEEDAP Panel, 2020a), and one on the safety and efficacy of carboxymethyl cellulose E466 when used in feed for all animal species (EFSA FEEDAP Panel, 2020b).

The EFSA Panel on Food Additives and Nutrient Sources added to Food (ANS) adopted in 2017 an opinion on the re-evaluation of celluloses E 460(i), E 460(ii), E 461, E 462, E 463, E 464, E 465, E 466, E 468 and E 469 as food additives (EFSA ANS Panel, 2018) and the EFSA Panel on Food Additives and Flavourings (FAF) adopted in 2022 an opinion on the re-evaluation of sodium carboxy methyl cellulose (E 466) 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 FAF Panel, 2022).

2 | DATA AND METHODOLOGIES

2.1 | Data

The present assessment is based on data submitted by the applicant in the form of supplementary information[4] to previous applications of the same products.[5]

[1]Regulation (EC) No 1831/2003 of the European Parliament and of the Council of 22 September 2003 on the additives for use in animal nutrition. OJ L 268, 18.10.2003, p. 29.

[2]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, p. 1.

[3]Synonym of sodium carboxymethyl cellulose (E466).

[4]FEED dossier reference: EFSA-Q-2021-00582.

[5]FEED dossier reference: FAD-2016-0062 and FAD-2016-0064.

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

2.2 | Methodologies

The approach followed by the FEEDAP Panel to assess the safety and the efficacy of active substance (trade name of the product) is in line with the principles laid down in Regulation (EC) No 429/2008[6] and the relevant guidance documents: Guidance on the identity, characterisation and conditions of use of feed additives (EFSA FEEEDAP Panel, 2017), Guidance on technical requirements for regulated food and feed product applications to establish the presence of small particles including nanoparticles (EFSA Scientific Committee, 2021a), Guidance on risk assessment of nanomaterials to be applied in the food and feed chain: human and animal health (EFSA Scientific Committee, 2021b).

3 | ASSESSMENT

Microcrystalline cellulose and carboxymethyl cellulose (synonym of sodium carboxymethyl cellulose) are intended to be used as technological additives (functional group: emulsifiers, stabilisers, thickeners, gelling agents and binders) in feed for all animal species, with no minimum or maximum content.

In its previous opinions (EFSA FEEDAP Panel, 2020a, 2020b), the Panel was not in the position to properly identify and characterise the two additives. No analytical data to support the identification of the active substances and the batch-to-batch consistency of the additives, as well as information on dusting potential of the additives and their particle size distribution, was made available. In addition, owing to the lack of analytical data, the occurrence of potential toxic impurities in the additives could not be assessed. In the absence of a proper identification, the FEEDAP Panel limited its conclusion on safety to microcrystalline cellulose and carboxymethyl cellulose meeting food additive specifications. The Panel concluded that microcrystalline cellulose and carboxymethyl cellulose are safe for all animal species, consumers and the environment, but could not conclude on the safety for users due to the absence of data.

In order to address the limitations in the data submitted in the original application, the applicant provided new data on the characterisation of the additives and on their impurities.

3.1 | Characterisation

3.1.1 | Characterisation of microcrystalline cellulose

Microcrystalline cellulose is identified with the single Chemical Abstracts Service (CAS) number 9004-34-6 and the European Inventory of Existing Chemical Substances (EINECS) number 232-674-9. It is manufactured from wood pulp, partially depolymerised by a hydrolysation process obtained with heat and mineral acid.

Microcrystalline cellulose is in the form of white to off-white hygroscopic granules powder of fine fibres.

The feed additive microcrystalline cellulose is claimed to be manufactured to meet the specifications set for its use as a food additive,[7] i.e. microcrystalline cellulose ≥ 97% calculated as cellulose on the anhydrous basis, pH 5–7 (10% suspension in water), loss on drying ≤ 7%, water-soluble matters ≤ 0.24%, carboxyl groups ≤ 1% and sulfated ash ≤ 0.5%. The additive is further specified to contain < 10% of particles with a diameter < 5 μm. In the original application, no evidence of the identity of the active substance in the additive was provided, as well as no analyses of carboxyl groups and sulfated ash, impurities and the dusting potential of the additive; only partial information on particle size distribution was available.

In the present application, the identity of the active substance was confirmed by the analysis of six recent batches of the additive by infrared (IR) spectroscopy.[8] The analysis of the same six batches confirmed the specification for microcrystalline cellulose ≥ 97% as cellulose on anhydrous base and showed the following results: pH 6.4–6.7, loss on drying 0.7%–3.6%, water-soluble matters 0.11%–0.19%, degree of polymerisation 220–261, conductivity 25–36 μS/cm, residue on ignition 0.005%–0.023%.[9] The analysis of five additional batches of the additive[10] showed concentrations of carboxyl groups ranging from 0.066% to 0.075%, while sulfated ash ranged between 0.01% and 0.02% in additional 15 batches.[11]

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

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

[8]Technical dossier/E460i additional data/Annex 3 and Supplementary Information February 2023/Annex II.

[9]Technical dossier/E460i additional data/Annex 1.

[10]Supplementary Information February 2023/Annex III.

[11]Supplementary Information February 2023/Annex III.

Five recent batches of the additive were analysed for cadmium, lead, mercury and arsenic concentrations, showing in all batches concentrations below the respective limit of quantification (LOQ), in compliance with the specifications set for the food additive.[12]

Polychlorinated dibenzo-*p*-dioxins (PCDDs), polychlorinated dibenzofurans (PCDFs), dioxin-like polychlorinated biphenyls (DL-PCBs) and non-DL-PCBs were analysed in six batches. The calculated upper bound (UB) concentration was < 0.07 ng WHO_{2005}-TEQ/kg for the sum of PCDD/Fs, and < 0.14 ng WHO_{2005}-TEQ/kg for the sum of PCCD/Fs and DL-PCBs. The UB for the sum of non-DL-PCBs was < 0.60 µ µg/kg.[13] In addition, in six batches of the raw pulp material from which microcrystalline cellulose is derived, the calculated UB concentration ranged between 0.06 and 0.18 ng WHO_{2005}-TEQ/kg for the sum of PCDD/Fs and between 0.10 and 0.29 ng WHO_{2005}-TEQ/kg for the sum of PCDD/Fs and DL-PCBs. The UB for the sum of non-DL-PCBs ranged between 0.36 and 1.06 µg/kg.[14]

Four batches of the additive[15] and four batches of raw pulp material[16] were analysed for aflatoxins (B1, B2, G1, G2) concentration showing values below the respective LOQ. Two batches of the additive[17] were analysed for pesticides (not specified), which were not detected in any sample.

Six batches of the additive[18] were analysed for microbiological contamination by the determination of *Escherichia coli* and *Salmonella* spp. with no detection in 10 g and in 25 g, respectively. *Pseudomonas aeruginosa*, *Staphylococcus aureus* and coliforms were also absent in 10 g of each batch of the additive. Total aerobic microbial counts and total yeast and moulds counts were < 10 CFU/g.

The detected amounts of the above-described undesirable substances and the microbial impurities do not raise safety concerns.

The dusting potential of four batches of microcrystalline cellulose[19] was determined using the Stauber-Heubach method and showed values on average of 1554 mg/m^3 (range 830–3415 mg/m^3) (mg airborne dust per m^3 of air).

Five batches of the additive[20] were analysed for particle size distribution by laser diffraction. The results showed that 16.2%–63.5% of the particles had a size below 90 µm, 8.4%–37.9% of the particles was below 50 µm and 0.5%–2% of the particles was below 5 µm. However, in line with the opinion of the FAF Panel on the re-evaluation of sodium carboxy methyl cellulose (E 466) (EFSA FAF Panel, 2022), the FEEDAP Panel notes that 'currently no standardised methods are available for the polysaccharide thickening and gelling agents used as food additives, such as sodium carboxy methyl cellulose (E 466) to measure the particle size distribution by number'.

The FAF Panel further considered that: 'Based on the data on particle size distribution […] and the criteria set in the relevant EFSA Scientific Committee Guidance (EFSA Scientific Committee, 2021a), the Panel concluded that the presence of small particles, including nanoparticles, cannot be confirmed or excluded in the pristine food additive'; in addition, 'The Panel noted, however, that polysaccharide thickening, and gelling agents used as feed additives, to exert their technical function in general swell in liquid environments. This also applies to carboxymethyl cellulose. The FAF Panel considers that carboxymethyl cellulose will not be present in the gastrointestinal tract in the pristine form taking into account the capacity to absorb and swell in water, and the volume of fluid in the stomach and gastrointestinal tract'. The FEEDAP Panel considers that the above would apply also to microcrystalline cellulose used as a feed additive.

3.1.2 | Characterisation of carboxymethyl cellulose

Carboxymethyl cellulose is identified with the single CAS number 9004-32-4, and the EINECS number 618-378-6. It is the partial sodium salt of carboxymethyl ether of cellulose.

Carboxymethyl cellulose is in the form of white or slightly yellowish or greyish odourless and tasteless granules or fibrous powder. It is almost insoluble in ethanol and yields a viscous colloidal solution with water.

The feed additive carboxymethyl cellulose is claimed to be manufactured to meet the specifications set for its use as a food additive,[21] i.e. carboxymethyl cellulose ≥ 99.5% on the anhydrous basis, carboxymethyl groups > 0.2 and < 1.5%, loss on drying < 12%, sodium glycolate < 0.4%, sodium < 12.4% and pH 5–8 (1% colloidal solution.) In the original application, no evidence of the identity of the active substance in the additive was provided, as well as no analyses of impurities, dusting potential particle size distribution of the additive.

[12]Technical dossier/E460i additional data/Annex 8. Limits of quantification: cadmium < 0.02 mg/kg, lead < 0.1 mg/kg, mercury < 0.2 mg/kg and arsenic < 0.2 mg/kg.

[13]Technical dossier/Annex IV. Upper bound concentrations are calculated on the assumption that all values of the different congeners below the limit of quantification are equal to the limit of quantification. TEQ = toxic equivalency factors for dioxins, furans and dioxin-like PCBs established by WHO in 2005 (van den Berg et al., 2006).

[14]Technical dossier/ E460i additional data/Annex 6 and Annex 7.

[15]Supplementary Information February 2023/Annex IV. Limit of quantification for aflatoxins (B1, B2, G1, G2): 0.08 µg/kg.

[16]Technical dossier/ E460i additional data/Annex 7. Limit of quantification for aflatoxins (B1, B2, G1, G2): 1.0 µg/kg.

[17]Supplementary Information February 2023/Annex IV.

[18]Technical dossier/ E460i additional data/Annex 4.

[19]Supplementary Information February 2023/Annex V.

[20]Supplementary Information February 2023/Annex I.

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

In the present application, the identity of the active substance was confirmed by the analysis by IR spectroscopy of eight recent batches of the additive.[22] The analysis of 18 batches showed the following results: carboxy methylcellulose 99.5%–100%, moisture 5.1%–7.4%, sodium glycolate 0%–0.4%, degree of substitution 0.85–0.92, pH 6.7–8.3, sodium content 6.7%–9%.[23] No data on carboxymethyl groups was provided; however, the Panel notes that the compliance with this specification was already demonstrated in the previous opinion (EFSA FEEDAP Panel, 2020b). Viscosity, measured in the same samples, varied between 499 and 5750 mPa.s.

The analysis of 42 recent batches of the additive for cadmium, lead, mercury and arsenic showed, in all batches, values below the corresponding limit of detection (LOD)/LOQ with few exceptions, lead in three batches (0.05–0.09 mg/kg), cadmium (0.05 mg/kg) and arsenic (0.06 mg/kg) in one batch each.[24]

Polychlorinated dibenzo-*p*-dioxins, PCDFs, DL-PCBs and non-DL-PCBs were analysed in five batches.[25] The calculated UB concentration ranged between 0.06 and 0.14 ng WHO_{2005}-TEQ/kg for the sum of PCDD/Fs, and between 0.09 and 0.27 ng WHO_{2005}-TEQ/kg for the sum of PCCD/Fs and DL-PCBs. The UB for the sum of non-DL-PCBs ranged between 0.3 and 6 µg/kg (in the dry substance). In addition, in six batches of the raw pulp material from which carboxymethyl cellulose is derived,[26] the calculated UB ranged between 0.06 and 0.42 ng WHO_{2005}-TEQ/kg for the sum of PCDD/Fs and between 0.10 and 0.67 ng WHO_{2005}-TEQ/kg for the sum of PCDD/Fs and DL-PCBs. The UB for the sum of non-DL-PCBs ranged between 0.36 and 2.44 µg/kg.

Aflatoxins (B1, B2, G1, G2) concentrations were analysed in three batches of the additive (and one additional batch analysed in triplicate only for B1) and in two batches of the raw pulp material, showing values below the respective LOQs.[27] Seven batches[28] of the additive were analysed for pesticides (organochlorine pesticides and pyrethroids, organophosphorus pesticides, organonitrogen pesticides and others), which were not detected in any sample.

Seven batches of the additive[29] were analysed for microbiological contamination by the determination of *Escherichia coli*, *Salmonella* spp., *Pseudomonas aeruginosa*, *Staphylococcus aureus* and coliforms which were in 10 g (four samples) or in 1 g (three samples) of the additive. Total aerobic microbial counts and total yeast and moulds counts were < 10 CFU/g. In addition, seven batches from one manufacturing plant, 30 from a second one and 500 from a third one[30] were analysed for microbiological contamination by the determination of *Escherichia coli* and *Salmonella* spp. with no detection in 10 g and in 10 or 25 g, respectively. *Pseudomonas aeruginosa* and *Staphylococcus aureus* were absent in 10 g of each batch of the additive. Total aerobic microbial count was in the range from < 5 to < 100 CFU/g, total yeast and moulds count was < 10 CFU/g in seven batches. However, no certificates of analysis were provided to support these results.

The detected amounts of the above-described undesirable substances and the microbial impurities do not raise safety concerns.

The dusting potential of three batches of carboxymethyl cellulose[31] was determined using the Stauber-Heubach method and showed values on average of 12,790 mg/m^3 (range 9990–15,391 mg/m^3) (mg airborne dust per m^3 of air).

Five batches of the additive[32] were analysed for particle size distribution by laser diffraction. The results showed that 90% of the particles had a size below 217–229 µm, 50% of the particles was below 103–113 µm and 10% of the particles was below 30–35 µm. In addition, the applicant analysed the same batches with scanning electron microscopy (SEM). However, in line with the opinion of the FAF Panel on the re-evaluation of sodium carboxy methyl cellulose (E 466) (EFSA FAF Panel, 2022), the FEEDAP Panel notes that 'currently no standardised methods are available for the polysaccharide thickening and gelling agents used as food additives, such as sodium carboxy methyl cellulose (E 466) to measure the particle size distribution by number'.

The FAF Panel further considered that: 'Based on the data on particle size distribution […] and the criteria set in the relevant EFSA Scientific Committee Guidance (EFSA Scientific Committee, 2021b), the Panel concluded that the presence of small particles, including nanoparticles, cannot be confirmed or excluded in the pristine food additive'; in addition, 'The Panel noted, however, that polysaccharide thickening, and gelling agents used as feed additives, to exert their technical function in general swell in liquid environments. This also applies to carboxymethyl cellulose. The FAF Panel considers that carboxymethyl cellulose will not be present in the gastrointestinal tract in the pristine form taking into account the capacity to absorb and swell in water, and the volume of fluid in the stomach and gastrointestinal tract'. The FEEDAP Panel considers that the above would apply also to carboxymethyl cellulose used as a feed additive.

[22]Technical dossier/E466 additional data/Annex 3 and Annex 4.

[23]Technical dossier/E466 additional data/Annex 2.

[24]Technical dossier/ E466 additional data/Annex 9. Limits of detection of the different methods of analysis used for different samples: cadmium 0.0003–0.05 mg/kg, lead 0.007–0.1 mg/kg, mercury 0.0008–0.1 mg/kg and arsenic 0.005–0.05 mg/kg. Limit of quantification of the different methods of analysis used for different samples: cadmium 0.001–0.2 mg/kg, lead 0.1–1.0 mg/kg, mercury 0.0025–0.1 mg/kg and arsenic 0.015–1.0 mg/kg.

[25]Technical dossier/ E466 additional data/Annex 6 and Annex 7. Upper bound concentrations are calculated on the assumption that all values of the different congeners below the limit of quantification are equal to the limit of quantification. TEQ = toxic equivalency factors for dioxins, furans and dioxin-like PCBs established by WHO in 2005 (van den Berg et al., 2006).

[26]Technical dossier/ E466 additional data/Annex 6 and Annex 7.

[27]LoQ: 0.1 µg/kg for aflatoxins B1, B2, G1 and G2 in raw pulp material; 0.2 and 0.9 µg/kg for Aflatoxin B1, 0.5 µg/kg for aflatoxins B2, G1 and G2 in the additive.

[28]Technical dossier/ E466 additional data/Annex 11.

[29]Supplementary Information February 2023/Annex VII.

[30]Technical dossier/ E466 additional data/Annex 5.

[31]Supplementary Information February 2023/Annex VIII.

[32]Supplementary Information September 2023/Annex VI.

3.2 | Safety

In its previous opinions (EFSA FEEDAP Panel, 2020a, 2020b), the FEEDAP Panel concluded that a proper identification and characterisation of microcrystalline cellulose and carboxymethyl cellulose as feed additives was not possible. Therefore, the FEEDAP Panel could only assess the safety for microcrystalline cellulose and carboxymethyl cellulose meeting the specifications set for their use as food additives. In particular, the Panel concluded that both microcrystalline cellulose and carboxymethyl cellulose meeting the specifications set for its use as food additives (i) are considered safe for all animal species, (ii) are of no concern for consumer safety, (iii) are safe for the environment. (iv) In the absence of data, the FEEDAP Panel was not in the position to conclude on the safety for the user.

The FEEDAP Panel considers that both microcrystalline cellulose and carboxymethyl cellulose have been fully characterised in the current application and comply with the specifications set for their use as food additives. Therefore, the conclusions on the safety of microcrystalline cellulose and carboxymethyl cellulose reached in the previous opinions apply to microcrystalline cellulose and carboxymethyl cellulose as feed additives.

4 | CONCLUSIONS

Based on the data provided, the feed additives microcrystalline cellulose and carboxymethyl cellulose were properly identified and characterised, and were shown to meet the specifications set for the food additives. Therefore, the conclusions on the safety assessments reached in the previous opinions for microcrystalline cellulose and carboxymethyl cellulose meeting the food additive specifications, apply to microcrystalline cellulose and carboxymethyl cellulose as feed additives. The additives are considered safe for all animal species, the consumer and the environment. In the absence of data, the FEEDAP Panel is not in the position to conclude on the safety for the user.

ABBREVIATIONS

ANS	EFSA Scientific Panel on Additives and Nutrient Sources added to Food
CAS	Chemical Abstracts Service
CFU	colony-forming unit
DL	dioxin-like
DM	dry matter
EINECS	European Inventory of Existing Chemical Substances
FAF	EFSA Panel on Food Additives and Flavourings
FEEDAP	EFSA Scientific Panel on Additives and Products or Substances used in Animal Feed
IR	infrared
LOD	limit of detection
LOQ	limit of quantification
PCBs	polychlorinated biphenyls
PCDDs	polychlorinated dibenzo-*p*-dioxins
PCDFs	polychlorinated dibenzofurans
SEM	Scanning electron microscopy
TEQ	toxic equivalent
UB	upper bound
WHO	World Health Organization

CONFLICT OF INTEREST

If you wish to access the declaration of interests of any expert contributing to an EFSA scientific assessment, please contact interestmanagement@efsa.europa.eu.

REQUESTOR

European Commission

QUESTION NUMBER

EFSA-Q-2021-00582

PANEL MEMBERS

Vasileios Bampidis, Giovanna Azimonti, Maria de Lourdes Bastos, Henrik Christensen, Birgit Dusemund, Mojca Durjava, Maryline Kouba, Marta López-Alonso, Secundino López Puente, Francesca Marcon, Baltasar Mayo, Alena Pechová, Mariana Petkova, Fernando Ramos, Roberto Edoardo Villa, and Ruud Woutersen.

REFERENCES

EFSA ANS Panel (EFSA Panel on Food Additives and Nutrient Sources added to Food), Younes, M., Aggett, P., Aguilar, F., Crebelli, R., Di Domenico, A., Dusemund, B., Filipič, M., Jose Frutos, M., Galtier, P., Gott, D., Gundert-Remy, U., Georg Kuhnle, G., Lambré, C., Leblanc, J.-C., Lillegaard, I. T., Moldeus, P., Mortensen, A., Oskarsson, A., … Woutersen, R. A. (2018). Scientific opinion on the re-evaluation of celluloses E 460(i), E 460(ii), E 461, E 462, E 463, E 464, E 465, E 466, E 468 and E 469 as food additives. *EFSA Journal*, *16*(1), 5047. https://doi.org/10.2903/j.efsa.2018.5047

EFSA FAF Panel (EFSA Panel on Food Additives and Flavourings), Younes, M., Aquilina, G., Castle, L., Degen, G., Engel, K.-H., Fowler, P. J., Frutos Fernandez, M. J., Fürst, P., Gürtler, R., Husøy, T., Manco, M., Mennes, W., Moldeus, P., Passamonti, S., Shah, R., Waalkens-Berendsen, I., Wright, M., Dusemund, B., … Gundert-Remy, U. (2022). Opinion on the re-evaluation of sodium carboxy methyl cellulose (E 466) 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 Journal*, *20*(12), 7665. https://doi.org/10.2903/j.efsa.2022.7665

EFSA FEEDAP Panel (EFSA Panel on Additives and Products or Substances used in Animal Feed), Rychen, G., Aquilina, G., Azimonti, G., Bampidis, V., Bastos, M. L., Bories, G., Chesson, A., Cocconcelli, P. S., Flachowsky, G., Gropp, J., Kolar, B., Kouba, M., López-Alonso, M., López Puente, S., Mantovani, A., Mayo, B., Ramos, F., Saarela, M., … Innocenti, M. L. (2017). Guidance on the identity, characterisation and conditions of use of feed additives. *EFSA Journal*, *15*(10), 5023. https://doi.org/10.2903/j.efsa.2017.5023

EFSA FEEDAP Panel (EFSA Panel on Additives and Products or Substances used in Animal Feed), Bampidis, V., Azimonti, G., Bastos, M. L., Christensen, H., Dusemund, B., Kos Durjava, M., Kouba, M., López-Alonso, M., López Puente, S., Marcon, F., Mayo, B., Pechová, A., Petkova, M., Ramos, F., Sanz, Y., Villa, R. E., Woutersen, R., Bories, G., … Aquilina, G. (2020a). Scientific opinion on the safety and efficacy of sodium carboxymethyl cellulose for all animal species. *EFSA Journal*, *18*(7), 6211. https://doi.org/10.2903/j.efsa.2020.6211

EFSA FEEDAP Panel (EFSA Panel on Additives and Products or Substances used in Animal Feed), Bampidis, V., Azimonti, G., Bastos, M. L., Christensen, H., Dusemund, B., Kos Durjava, M., Kouba, M., López-Alonso, M., López Puente, S., Marcon, F., Mayo, B., Pechová, A., Petkova, M., Ramos, F., Sanz, Y., Villa, R. E., Woutersen, R., Bories, G., … Aquilina, G. (2020b). Scientific opinion on the safety and efficacy of microcrystalline cellulose for all animal species. *EFSA Journal*, *18*(7), 6209. https://doi.org/10.2903/j.efsa.2020.6209

EFSA Scientific Committee, More, S., Bampidis, V., Benford, D., Bragard, C., Halldorsson, T., Hernández-Jerez, A., Bennekou, S. H., Koutsoumanis, K., Lambré, C., Machera, K., Naegeli, H., Nielsen, S., Schlatter, J., Schrenk, D., Silano (deceased), V., Turck, D., Younes, M., Castenmiller, J., … Schoonjans, R. (2021a). Guidance on technical requirements for regulated food and feed product applications to establish the presence of small particles including nanoparticles. *EFSA Journal*, *19*(8), 6769. https://doi.org/10.2903/j.efsa.2021.6769

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, V., Turck, D., Younes, M., Castenmiller, J., … Schoonjans, R. (2021b). Guidance on risk assessment of nanomaterials to be applied in the food and feed chain: Human and animal health. *EFSA Journal*, *19*(8), 6768. https://doi.org/10.2903/j.efsa.2021.6768

Van den Berg, M., Birnbaum, L. S., Denison, M., De Vito, M., Farland, W., Feeley, M., Fiedler, H., Hakansson, H., Hanberg, A., Haws, L., Rose, M., Safe, S., Schrenk, D., Tohyama, C., Tritscher, A., Tuomisto, J., Tysklind, M., Walker, N., & Peterson, R E. (2006). The 2005 World Health Organization reevaluation of human and Mammalian toxic equivalency factors for dioxins and dioxin-like compounds. *Toxicol Sci*, *93*(2), 224–41. https://doi.org/10.1093/toxsci/kfl055

How to cite this article: EFSA FEEDAP Panel (EFSA Panel on Additives and Products or Substances used in Animal Feed), Bampidis, V., Azimonti, G., Bastos, M. L., Christensen, H., Dusemund, B., Durjava, M., Kouba, M., López-Alonso, M., López Puente, S., Marcon, F., Mayo, B., Pechová, A., Petkova, M., Ramos, F., Villa, R. E., Woutersen, R., Anguita, M., Galobart, J., … Innocenti, M. (2024). Safety of feed additives consisting of microcrystalline cellulose and carboxymethyl cellulose for all animal species (International Cellulosics Association). *EFSA Journal*, *22*(3), e8625. https://doi.org/10.2903/j.efsa.2024.8625