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SCIENTIFIC OPINION

Scientific Opinion on the safety and efficacy of calcium formate when used as a technological additive for all animal species[1]

EFSA Panel on Additives and Products or Substances used in Animal Feed (FEEDAP)[2,3]

European Food Safety Authority (EFSA), Parma, Italy

This scientific output, published on 29/04/2015, replaces the earlier version published on 18/11/2014.[4]

ABSTRACT

This opinion concerns the re-evaluation of calcium formate for use as a preservative in feed for all animal species and categories. Calcium formate is currently authorised for use as a preservative in feed for all animal species, but is not authorised as a food additive in the EU. Considering the results of the tolerance studies with chickens for fattening and cattle for fattening, and other published studies, no adverse effects on the safety for target animals are anticipated when calcium formate is used at the maximum proposed dose in feed for pigs, poultry, fish and ruminants (15 000 mg calcium formate/kg complete feed, equivalent to 10 000 mg formic acid/kg complete feed). However, no margin of safety can be established. This conclusion can be extrapolated to other animal species provided the maximum dose applied does not exceed 15 000 mg calcium formate/kg complete feed. The contribution of calcium formate to the calcium supply of animals should be considered when formulating diets. Considering that the turnover of formate is rapid, with no evidence of accumulation in body tissues, neither calcium nor formate concentrations will increase in the edible tissues of animals maintained on feed with calcium formate added and, therefore, the use of calcium formate as a feed additive in all animal species is considered safe for the consumer. Calcium formate is non-irritant to skin but causes severe adverse effects in eyes. It is likely that handling the additive could result in skin reactions and in the production of respirable dust that could present a risk to unprotected workers. The use of calcium formate in animal nutrition is safe for the environment. Data submitted do not provide convincing evidence of the efficacy of the additive when used as a preservative for compound feed or feed materials.

KEY WORDS

technological additive, preservative, calcium formate, all animal species, safety, efficacy

[1] On request from the European Commission, Question No EFSA-Q-2011-00423, adopted on 28 October 2014.

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[4] This scientific opinion is published following the adoption of the decision of the Commission on confidentiality claims submitted by the applicant, in accordance with Article 8(6) and Article 18 of Regulation (EC) No 1831/2003. No modification was required. To avoid confusion, the original version has been removed from the EFSA Journal, but is available on request, as is a version showing all the changes made.

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SUMMARY

Following a request from the European Commission, the Panel on Additives and Products or Substances used in Animal Feed (FEEDAP) was asked to deliver a scientific opinion on the application for the re-evaluation of calcium formate when used as a preservative in feed for all animal species.

Calcium formate is currently authorised for use as preservative in feed for all animal species, but is not authorised as a food additive in the EU.

Formate is a natural constituent of ruminal and intestinal contents and manure. Since animals are exposed to formate, studies of either formic acid or its salts are considered equivalent provided the substances are used on an equimolar basis.

Considering the results of the tolerance studies with chickens for fattening and cattle for fattening, and other published studies, in which calcium formate had been fed to target species at concentrations greater than that proposed by the applicant, no adverse effects on the safety for target animals are anticipated when calcium formate is used at the maximum proposed dose in feed for pigs, poultry, fish and ruminants (15 000 mg calcium formate/kg complete feed, equivalent to 10 000 mg formic acid/kg complete feed). However, no margin of safety can be established. This conclusion can be extrapolated to other animal species provided the maximum dose applied does not exceed 15 000 mg calcium formate/kg complete feed.

The contribution of calcium formate to the calcium supply of animals should be considered when formulating diets.

Considering that the turnover of formates is rapid, with no evidence of accumulation in body tissues, neither calcium nor formate concentrations will increase in the edible tissues of animals maintained on feed with calcium formate added, and no additional exposure by consumers is expected. Therefore, the use of calcium formate as a feed additive in all animal species is considered safe for the consumer.

Calcium formate is non-irritant to skin but causes severe adverse effects in eyes. It is likely that handling the additive could result in skin reactions and in the production of respirable dust that could present a risk to unprotected workers.

Methane emissions by ruminants constitute around 2 % of total greenhouse gas emissions, and only a very small proportion of ruminants globally would receive formate as an additive. Therefore, the use of calcium formate in animal nutrition is safe for the environment.

The studies in which antimicrobial inhibitory effects of calcium formate were observed in pure cultures of four different bacterial species and a study concerning the preservative effect of calcium formate in six preservation trials do not provide convincing evidence of the efficacy of the additive when used as a preservative for compound feed or feed materials.

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BACKGROUND

Regulation (EC) No 1831/2003[5] establishes the rules governing the Community authorisation of additives for use in animal nutrition. In particular, Article 4(1) of that Regulation lays down that any person seeking authorisation for a feed additive or for a new use of a feed additive shall submit an application in accordance with Article 7 and Article 10(2) of that Regulation also specifies that for existing products within the meaning of Article 10(1), an application shall be submitted in accordance with Article 7, at the latest one year before the expiry date of the authorisation given pursuant to Directive 70/524/EEC for additives with a limited authorisation period, and within a maximum of seven years after the entry into force of this Regulation for additives authorised without a time limit or pursuant to Directive 82/471/EEC.

The European Commission received a request from LANXESS[6] for re-evaluation of the product calcium formate when used as a feed additive for all animal species (category: technological additive; functional group: preservative) under the conditions mentioned in Table 1.

According to Article 7(1) of Regulation (EC) No 1831/2003, the Commission forwarded the application to the European Food Safety Authority (EFSA) as an application under Article 10(2) (re-evaluation of an authorised feed additive). EFSA received directly from the applicant the technical dossier in support of this application.[7] According to Article 8 of that Regulation, EFSA, after verifying the particulars and documents submitted by the applicant, shall undertake an assessment in order to determine whether the feed additive complies with the conditions laid down in Article 5. The particulars and documents in support of the application were considered valid by EFSA as of 16 June 2011.

Calcium formate is currently authorised under Council Directive 70/524/EEC[8] for use as preservative in feed for all animal species (E 238) and subject to re-evaluation.

The European Food Safety Authority (EFSA) issued an opinion on the safety and efficacy of formic acid as preservative in all animal species (EFSA FEEDAP Panel, 2014).

TERMS OF REFERENCE

According to Article 8 of Regulation (EC) No 1831/2003, EFSA shall determine whether the feed additive complies with the conditions laid down in Article 5. EFSA shall deliver an opinion on the safety for the target animals, the consumer, the user and the environment and the efficacy of calcium formate, when used under the conditions described in Table 1.

[5] Regulation (EC) No 1831/2003 of the European Parliament and of the Council of 22 September 2003 on additives for use in animal nutrition. OJ L 268, 18.10.2003, p. 29.
[6] LANXESS Distribution GmbH, Katzbergstr. 1, 40764, Langenfeld, Germany.
[7] EFSA Dossier reference: FAD-2010-0303.
[8] List of the authorised additives in feedingstuffs published in application of Article 9t (b) of Council Directive 70/524/EEC concerning additives in feeding-stuffs. OJ C 50, 25.02.2004, p.1.

Table 1: Description and conditions of use of the additive as proposed by the applicant

Additive	Calcium formate			
Registration number/EC No/No (if appropriate)	E 238			
Category(ies) of additive	Technological Additives			
Functional group(s) of additive	Preservative			
Description				
Composition, description	Chemical formula	Purity criteria (if appropriate)	Method of analysis (if appropriate)	
Calcium formate	**$Ca(HCOO)_2$**	**Min 99.0%**	**ongoing**	
Trade name (if appropriate)	not applicable			
Name of the holder of authorisation (if appropriate)	not applicable			
Conditions of use				
Species or category of animal	Maximum Age	Minimum content	Maximum content	Withdrawal period (if appropriate)
		mg or Units of activity or CFU/kg of complete feedingstuffs (select what applicable)		
All	not applicable		15 000	none
Other provisions and additional requirements for the labelling				
Specific conditions or restrictions for use (if appropriate)	not applicable			
Specific conditions or restrictions for handling (if appropriate)	not applicable			
Post-market monitoring (if appropriate)	not applicable			
Specific conditions for use in complementary feedingstuffs (if appropriate)	not applicable			
Maximum Residue Limit (MRL) (if appropriate)				
Marker residue	Species or category of animal	Target tissue(s) or food products	Maximum content in tissues	
not applicable				

ASSESSMENT

This opinion is based in part on data provided by an applicant involved in the production/distribution of calcium formate. It should be recognised that these data cover only a fraction of existing additives containing calcium formate.

1. Introduction

Formic acid is an intermediate in normal one-carbon metabolism in microorganisms, plants and animals, contributing to transmethylation reactions before, ultimately, being oxidised to carbon dioxide. It can be detected, in varying amounts, in plants and animals and, in some plants and insects, provides a specialised defence against predation. Background levels of formic acid in fruit, honey, wine, roasted coffee, evaporated milk and cheese range from 1 to 2 000 mg/kg, and levels between 2.7 and 87 mg/kg are reported in brandies produced from apples, pears, plums and apricots (HSDB, 2006; OECD, 2010). World-wide industrial production of formic acid is approximately 0.75 million tonnes per annum, one-third of which is used in agriculture, primarily as a silage additive for the preservation of animal feedstuffs. Calcium formate is the calcium salt of formic acid.

Although not formally authorised in the European Union (EU) for food use, formic acid is registered under the General Standards for Food Additives (GFSA) provisions of the Food and Agricultural Organization of the United Nations (FAO) as a food preservative in sauces and similar products to a maximum of 200 mg/kg and in flavoured drinks to a maximum of 100 mg/kg (Codex, 2011). The Joint FAO/World Health Organization (WHO) Expert Committee on Food Additives established an acceptable daily intake (ADI) of formic acid of 0–3 mg/kg body weight (bw) (JECFA, 1974, 1998).

Calcium formate is a feed additive currently authorised without time limit under Council Directive 70/524/EEC[9] for its use as a preservative in feed for all animal species (E 238) and is presently listed in the EU Register of Feed Additives.[10]

The application under consideration is for the re-evaluation of calcium formate as a technological additive when used as a preservative in feed for all animal species as required by Regulation (EC) No 1831/2003.[11]

2. Characterisation

2.1. Characterisation of the additive

Calcium formate (formic acid calcium salt, $Ca(HCOO)_2$, Chemical Abstracts Service (CAS) No 544-17-2, European Inventory of Existing Commercial chemical Substances (EINECS) No 208-863-7) is a colourless solid with nearly no odour and a molecular weight of 130.1 g/mol. It is the calcium salt of formic acid and occurs naturally in food. Calcium formate is soluble in water (160 g/L at 20 °C)[12] with a bulk density of 1 150 kg/m^3. The structural formula of calcium formate is shown in Figure 1.

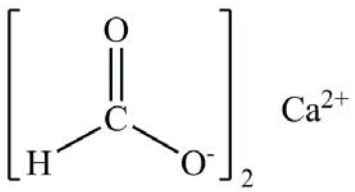

Figure 1: Structural formula of calcium formate

[9] List of the authorised additives in feedingstuffs published in application of Article 9t (b) of Council Directive 70/524/EEC concerning additives in feeding-stuffs. OJ C 50, 25.02.2004, p.1.
[10] Available online: http://ec.europa.eu/food/food/animalnutrition/feedadditives/registeradditives_en.htm
[11] Regulation (EC) No 1831/2003 of the European Parliament and of the Council of 22 September 2003 on additives for use in animal nutrition. OJ L 268, 18.10.2003, p. 29.
[12] Technical Dossier/Section II/ Sect_II_Identity.

Calcium formate is formed by chemical synthesis as a co-product during the manufacturing of trimethylolpropane (TMP). Hydrated lime is used as the source of calcium. In the presence of a basic catalyst, butyraldehyde and formaldehyde react in aqueous solution, forming an unstable intermediary product (dimethylol butyraldehyde (DIMBA)). The unstable intermediate DIMBA further reacts with formaldehyde to produce TMP and calcium formate. Calcium formate is then separated from the TMP–calcium formate solution[13], subjected to heat treatment to remove formaldehyde and then dried.

The additive is specified to contain a minimum of 99.0 % calcium formate and 68.5 % formate. This was confirmed by analysis of five batches of the additive with a mean content (w/w) of calcium formate of 99.5 % (range 99.2–99.8 %) and a mean content of formate of 68.8 % (68.6–69.1 %). The specified calcium concentration is at least 30.5 %.[14,15]

The presence of impurities is related to the manufacturing process. Analysis of five batches of calcium formate showed that concentrations of impurities (e.g. TMP, calcium carbonate, goethite, manganese oxide, silicon oxide, aluminium oxide, calcium sulphate) were below 0.1 % in all cases. Residual TMP accounted for less than 0.006 % (w/w) which is considered of no toxicological relevance.[16] Formaldehyde was below the limit of detection, which was not stated.

Analysis of five different batches of calcium formate for heavy metals and arsenic showed values below the limits of detection for arsenic, lead, cadmium (< 0.50 mg/kg) and mercury (< 0.02 mg/kg). Dioxins in these five batches were 0.09 ng WHO-PCDD/F-TEQ (polychlorinated dibenzodioxin/dibenzofuran (PCDD/F)-toxic equivalent (TEQ) concentrations) per kilogram.[17]

Particle size distribution was analysed by laser diffraction in three batches of calcium formate.[18] The results showed that approximately 60 % of the particles have a diameter of less than 100 μm, 40 % of the particles have a diameter of less than 50 μm and 6 % of the particles have a diameter of less than 10 μm.

Analysis of the dustiness of the feed additive (one batch, two replicates) was performed using a gravimetric method, determining the amount of dust of the test item which may be liberated into the air when handled, and gravimetrically collected (in mg). Specific standards by the testing laboratory were applied (0–12 mg: nearly dust-free; 12–30 mg: essentially non-dusty; >30 mg: dusty). Mean obtained gravimetric dust was 60.8 mg concluding that the test item was considered to be dusty and that calcium formate has the property to liberate dust in the air.[19]

2.2. Stability and homogeneity

2.2.1. Shelf-life

The stability of the additive (detection of formate/calcium formate) in different packaging (paper bag, glass bottles, open and closed Petri dishes) and at different storage conditions was studied over six months. Temperatures ranged from room temperature to 40 °C and relative humidity (RH) from 40 to 80 %. No loss of formate/calcium formate was detected after storage for six months in any of the different packaging and storage conditions.[20]

[13] Technical Dossier/Section II/ Annex II 2.3.1_01.
[14] Technical Dossier/Section II/Annex_II_2.1.3_08.
[15] Technical Dossier/Section II/Annex_II_2.1.4_01.
[16] Technical Dossier/Section II/Annex_II_2.1.4_02.
[17] Technical Dossier/Section II/ Annex_II_2.1.4_03-07.
[18] Supplementary information (September 2013)/Annex_6_1.
[19] Technical dossier/Section II/ Annex_II_2.2.2.1_04.
[20] Technical Dossier/Section II/Annex_II_2.4.1.2_01.

2.2.2. Stability in premixtures and feedingstuffs

A single batch of a vitamin–mineral premix for piglets was used to study the stability of the additive (130 g/kg) over a six-month period at 20 °C when stored in paper bags. No loss was detected at the end of the study.

The stability of calcium formate was assessed in three different feedingstuffs (piglet starter, diet for growing pigs and a calf milk replacer) for periods up to six months at 20 °C when stored in paper bags. The intended inclusion levels were 15 000 mg/kg for the pig feeds and 2 600 mg/kg for the milk replacer. Essentially, no loss of calcium formate was detected in the piglet and milk replacer diets after six months. Values for the pig feed showed an apparent increase in calcium formate at the end of the study. This may have resulted from the method of analysis which was based on the enzymatic detection of formate.

2.3. Homogeneity

Five samples were collected from the piglet feed and five samples from the vitamin–mineral premix used in the stability studies. Calcium formate was measured in each of the samples and the coefficient of variation (CV) calculated for each feed. Calculated CVs were 8.03 % for the vitamin–mineral premix and 4.30 % for the piglet feed.[21,22]

2.4. Conditions of use

Calcium formate is intended for use as a preservative for all feedingstuffs and premixtures in all animal species with a level of inclusion ranging between 5 000 and 15 000 mg/kg in complete feedingstuffs.[23]

2.5. Evaluation of the analytical methods by the European Union Reference Laboratory (EURL)

EFSA has verified the EURL report as it relates to the methods used for the control of the calcium formate in animal feed. The Executive Summary of the EURL report can be found in Appendix A.

3. Safety

Calcium formate dissociates in aqueous solution into the calcium cation and the formate anion. Calcium is a normal and essential food and feed constituent and it is a ubiquitous element in the environment. The contribution of calcium formate to the calcium supply of animals should be considered when formulating diets. Formate is an important constituent of intermediary one-carbon metabolism. It may be formed from endogenous and exogenous precursors via enzymatic oxidation reactions, and it is used during folic acid-dependent reactions involved in the biosynthesis of nucleotides required for the synthesis of DNA and RNA and some amino acids (e.g. serine, glycine and methionine). Formate may also be utilised in the citric acid pathway, releasing carbon dioxide and water. Formate can be produced in the body as a result of catabolism of several amino acids and their sources include diet, production by intestinal microflora and certain dietary supplements. Formate is a natural constituent of ruminal and intestinal contents and manure. Since animals are exposed to formate, studies of either formic acid or its salts are considered equivalent when the substances are used on an equimolar basis.

[21] Supplementary Information (September 2013)/Annex_II_4_1.
[22] Supplementary Information (September 2013)/Annex_II_5_1.
[23] Technical Dossier/Section II/ Sect_II_Identity.

3.1. Safety for the target species

3.1.1. Poultry

The applicant provided a tolerance study with formic acid[24] which has already been assessed by the FEEDAP Panel in a previous opinion (EFSA FEEDAP Panel, 2014). In the opinion, based on this study and on published scientific literature, the FEEDAP Panel concluded that no safety concerns were apparent in chickens for fattening at a level of 10 000 mg formic acid/kg feed, which equates to 14 600 mg calcium formate/kg feed.

This conclusion is further supported by two published studies in chickens for fattening receiving calcium formate. Pohl et al. (2012) did not observe any effect on growth of chickens of up to 49 days of supplementation of the diet with calcium formate at 15 000 mg/kg feed. Similarly, Izat et al. (1990) did not observe any adverse effects on the performance of chickens for fattening receiving diets supplemented with 14 500 mg calcium formate/kg feed.

3.1.2. Pigs

Tolerance studies carried out in pigs were not made available for the purpose of this application. Published studies in which calcium formate was supplemented at or below the maximum proposed inclusion rate found no evidence of lowered growth rate, feed intake or feed efficiency (8 500 mg/kg (Øverland et al., 2000), 18 000 mg calcium formate/kg (Eidelsburger et al., 1992), 15 000 mg calcium formate/kg (Pallauf and Hüter, 1993), 27 000 and 15 000 mg calcium formate/kg (Kirchgessner and Roth, 1989, 1990), 18 000 mg calcium formate/kg (Kirchgessner et al., 1992), 15 000 mg calcium formate/kg (Lawlor et al., 2006), 12 000 mg calcium formate/kg (Bosi et al., 2007), 18 000 mg calcium formate/kg (Torrallardona et al., 2007)), and no detrimental effects on clinical chemistry or haematology parameters when measured (15 000 mg calcium formate/kg).[25] In most studies, no detrimental effects were observed in weaned piglets receiving higher doses (18 000 mg calcium formate/kg (Eidelsburger et al., 1992), 27 000 mg calcium formate/kg (Kirchgessner and Roth, 1987), 18 000 mg calcium formate/kg (Torrallardona et al., 2007)). In one study with weaned piglets, poorer feed intake, feed conversion and weight gain were observed at a formic acid inclusion level of 24 000 mg/kg but not at 18 000 mg/kg (Eckel et al., 1992). Therefore, it can be concluded that at least 15 000 mg calcium formate/kg is well tolerated by pigs.

3.1.3. Ruminants

In its recent opinion on formic acid (EFSA FEEDAP Panel, 2014), the FEEDAP Panel noted that large quantities of formate are formed endogenously and converted into methane in the rumen and concluded that the capacity of the ruminal microbiota to metabolise formate greatly exceeds the quantities of formate added as supplemental formic acid at 10 000 mg/kg feed. No accumulation of formate would be expected.

No tolerance study was provided on cattle receiving calcium formate. However, considering the same tolerance study with formic acid in calves,[26] the FEEDAP Panel recently concluded that up to 10 000 mg formic acid/kg feed with a dry matter content of 65.3 % can be considered safe (EFSA FEEDAP Panel, 2014). The FEEDAP Panel considers that the same conclusion would apply to calcium formate at the dose of 15 000 mg calcium formate/kg complete feed.

This is further supported by studies in which calcium formate, at doses up to 15 000 mg/kg, had no detrimental effects in calves[27] (Günther, 1989) or in veal calves receiving milk replacer containing

[24] Supplementary Information (September 2013)/Annex_III_23_1
[25] Supplementary information (September 2013)/Annexes1/Annex III.1.1.
[26] Supplementary information (June 2014)/Annex_III_1.
[27] Supplementary information (September 2013)/Annexes1/Annex III.17.1.

calcium formate at 30 000 mg/kg.[28] Some adverse effects (inflammation of the abomasum) at high doses of calcium formate (4 × 170 g/animal, two days) were observed in published studies in ruminants when calcium formate was used as a source of calcium to correct calcium deficiency (Scott and van Wijk, 2000; McIntyre and Weston, 2002). The Panel notes that the quantities used in these studies are much higher than those for the proposed use as a preservative in this application.

Therefore it is concluded that calcium formate, at 15 000 mg/kg complete feed, would not present tolerance problems for calves or adult ruminants.

3.1.4. Fish

In an experiment to determine the effect of formic acid on the availability of phosphorus from a fishmeal-based diet, rainbow trout (*Oncorhynchus mykiss*) were exposed to diets containing approximately 0, 4 700 and 12 000 mg formic acid/kg complete feed for four weeks, five days a week (Vielma and Lall, 1997). No adverse effects on growth were observed.

3.1.5. Conclusion

Considering the results of the tolerance studies with chickens for fattening and cattle for fattening, and other published studies, in which formic acid or calcium formate had been fed to target species at concentrations greater than that proposed by the applicant, no adverse effects are anticipated when calcium formate is used at the maximum proposed dose in feed for pigs, poultry, fish and ruminants (15 000 mg calcium formate/kg complete feed). However, no margin of safety can be established. This conclusion can be extrapolated to other animal species provided the maximum dose applied does not exceed 15 000 mg calcium formate/kg complete feed.

The contribution of calcium formate to the calcium supply of animals should be considered when formulating diets.

3.2. Safety for the consumer

No significant increase in the presence of formate per se is expected in animal products from the use of calcium formate as feed additive, although carbon derived from formate may be incorporated into tissues as a consequence of normal anabolism. The residual unmetabolised formic acid and other minor metabolites are excreted via urine, faeces or expired air (Hanzlik et al., 2005). No calcium or formate accumulates in tissues of pigs receiving calcium formate at 15 000 mg/kg[29] or in veal calves receiving milk replacer containing calcium formate at 30 000 mg/kg.[30]

Considering that the turnover of formate is rapid, with no evidence of accumulation in body tissues, neither calcium nor formate concentrations will increase in the edible tissues of animals maintained on feed with calcium formate added and no additional exposure of consumers is expected. Therefore, the use of calcium formate as a feed additive in all animal species is considered safe for the consumer.

3.3. Safety for the user

A skin irritation test was performed following the Organisation for Economic Co-operation and Development (OECD) Guideline 404[31] (three rabbits exposed for 4 hours to 500 mg calcium formate and examined at 1, 24, 48 and 72 hours after exposure). Eye irritation was performed following OECD Guideline 405[32] (application of 100 mg calcium formate in the conjunctival sac of the right eye of three rabbits and examined after 1, 24, 48, 72 hours and from 4 to 15 days after administration).

[28] Supplementary information (September 2013)/Annexes1/Annex III.16.1.
[29] Supplementary information (September 2013)/Annexes1/Annex III.1.1.
[30] Supplementary information (September 2013)/Annexes1/Annex III.16.1.
[31] Technical Dossier/Section III/Annexes Sect. III/Annex_II_3.3.1.2.1.
[32] Technical Dossier/Section III/Annexes Sect. III/Annex_II_3.3.1.2.2.

No evidence of skin irritation was detected, but there was a strong adverse response in the eye (i.e. corneal opacity, iris irritation, conjunctival redness, conjunctival chemosis), leading to the recommended labelling of 'high risk to the eyes'. No information on skin sensitisation was available and therefore, in the absence of data, skin reactions when handling the additive cannot be excluded.

Because of the particle size distribution of calcium formate, and the high dust generation potential, it is likely that handling the additive could result in the production of respirable dust. No information on inhalation toxicity was available and, therefore, it is prudent to consider that inhalation of the additive could present a risk to unprotected workers.

Therefore, it is concluded that calcium formate is non-irritant to skin but causes severe adverse effects in the eyes. It is likely that handling the additive could result in skin reactions and the production of respirable dust that could present a risk to unprotected workers.

3.4. Safety for the environment

The use of calcium formate at the maximum proposed level as a feed additive does not exceed the recommended calcium levels in feed. Background levels of calcium are naturally high in manure and, therefore, the contribution of calcium arising from the use of the calcium formate in feed to background levels in the environment would be negligible.[33]

Formate is ubiquitous in the environment and is a natural metabolite in living organisms and a natural constituent of ruminal and intestinal contents and manure. Under aerobic conditions, it is rapidly degraded by methylotrophic bacteria to carbon dioxide or biomass. If anaerobic conditions prevail, as in the rumen and large intestine, it is converted by methanogenic archaea to methane.

In the rumen, formic acid is converted almost quantitatively to methane and carbon dioxide (Beijer, 1952; Carroll and Hungate, 1955). One mole of formate will generate 0.25 mol of methane. Calcium formate, supplied at the rate specified in the opinion, will increase methane emissions per bovine by, on average, about 5 %. Methane emissions by ruminants constitute around 2 % of total greenhouse gas emissions (Johnson and Johnson, 1995), and only a very small proportion of ruminants globally would receive formate as an additive.

Therefore, the FEEDAP Panel considers that the use of calcium formate in animal nutrition is safe for the environment.

4. Efficacy

Calcium formate has been used widely in the feed industry for decades to decrease the pH of feed, thus providing preservative effects. A fall in feed pH of about one pH unit has been reported as a result of calcium formate supplementation at the maximum inclusion rate proposed of 15 000 mg calcium formate/kg complete feed) (Lawlor et al., 2006), although much smaller differences were observed in other studies (Kirchgessner and Roth, 1990).

4.1. Preservation

The applicant provided the first set of studies in which microbial inhibitory effects of calcium formate were observed in pure cultures of four different bacterial species (*Escherichia coli*, *Pseudomonas aeruginosa*, *Staphylococcus aureus* and *Enterococcus hirae*), one fungal species (*Aspergillus niger*) and one species of yeast (*Candida albicans*). However, the relevance of these observations to feed preservation was not established.

[33] Technical Dossier/Section III/ Sect_II_Safety.

The applicant also provided a study[34] concerning the preservative effect of calcium formate in six trials made with representative feed materials (two complete feedstuffs for chickens and sows; two feed ingredients: wheat and soybean meal; and two liquid feeds for sows) after a storage period of three months (dry feed materials and compound feeds) or 48 hours (liquid feeds). The feeds were inoculated with 50 000 colony-forming units (CFU) of *E. coli*, 5 000 CFU of *Saccharomyces cerevisiae* and 5 000 CFU of *Aspergillus* spp. (not specified) per gram of feed. Moisture levels of dry feed ranged from 13 to 18 % (broiler feed: 14.4 %; sow feed: 13 %; wheat: 18.2 %; soybean meal: 17.3 %). The two liquid feeds were based on one part dry sow feed mixed with three parts water with a total moisture level of 75 and 76 %, respectively.

Calcium formate was dosed at 0, 2 100, 4 200, 8 400, 16 800 and 33 600 mg/kg feed, corresponding to 0, 1 500, 3 000, 6 000, 12 000 and 24 000 mg of pure formic acid equivalents, respectively, per kilogram of feed. Total aerobes, coliform bacteria, yeasts and moulds were followed in the feed during storage. Dry feeds were sampled for microbial counting at one week, one month and three months after inoculation (incubation temperature not specified); liquid feeds were sampled at 24 and 48 hours.

Yeast counts were too low to be estimated accurately. For the other microbial groups, only two statistically significant indications of efficacy were obtained from the 54 measurements (six feeds × three storage periods × three microbial groups), with moulds in sow dry feed and total aerobes in soybean meal, both at the end of storage. A regression analysis of the effect of the dose of calcium formate on the $\log_{10}$-transformed microbial counts across the six feeds showed a positive effect only with the mould counts.

It is concluded that these data do not provide convincing evidence of the efficacy of the additive as a preservative for compound feed or feed materials.

4.2. Effects on the quality of animal products

Calcium formate has been used as a feed additive for decades, with no adverse effects on the quality, organoleptic or nutritional characteristics of food derived from animals fed with the additive having been reported. A number of specific studies with calcium formate or related compounds have examined the impact on sensory properties of animal products without any adverse effects reported[35] (Basker and Klinger, 1979; Øverland et al., 2000).

CONCLUSIONS

No adverse effects on target animals safety are anticipated when calcium formate is used at the maximum proposed dose in feed for pigs, poultry, fish or ruminants (15 000 mg calcium formate/kg complete feed). However, no margin of safety can be established. This conclusion can be extrapolated to other animal species at a maximum dose of 15 000 mg calcium formate/kg complete feed.

Considering that the turnover of formate is rapid, with no evidence of accumulation in body tissues, neither calcium nor formate concentrations will increase in the edible tissues of animals maintained on feed with calcium formate added, and no additional exposure by consumers is expected. Therefore, the use of calcium formate as a feed additive in all animal species is considered safe for the consumer.

Calcium formate is non-irritant to skin and is not a skin sensitiser but causes severe adverse effects in the eyes. It is likely that handling the additive could result in the production of respirable dust that could present a risk to unprotected workers.

The use of calcium formate in animal nutrition is safe for the environment.

[34] Supplementary information (September 2013)/Annex_VI_1_1.
[35] Supplementary information (September 2013)/Annexes1/Annex III.1.1.

Data submitted do not provide convincing evidence of the efficacy of the additive when used as a preservative for compound feed or feed materials.

DOCUMENTATION PROVIDED TO EFSA

1. Calcium formate for all animal species and categories. November 2010. Submitted by GAB Consulting GmbH on behalf LANXESS Distribution GmbH.

2. Calcium formate for all animal species and categories. Supplementary information. September 2013. Submitted by GAB Consulting GmbH on behalf LANXESS Distribution GmbH.

3. Calcium formate for all animal species and categories. Supplementary information. June 2014. Submitted by GAB Consulting GmbH on behalf LANXESS Distribution GmbH.

4. Evaluation report of the European Union Reference Laboratory for Feed Additives on the Methods(s) of Analysis for calcium formate.

5. Comments from Member States received through the ScienceNet.

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Annex – Executive Summary of the Evaluation Report of the European Union Reference Laboratory for Feed Additives on the Method(s) of Analysis for calcium formate [1] [2]

In the current application authorisation is sought under articles 4(1)[3] and 10(2)[4] for *ammonium formate* (E295)[5], *sodium formate* (E237)[6], *calcium formate* (E238)[7] and *potassium diformate* (237a)[8] under the category of "technological additives" functional group 1(a) "preservatives" (for all) and 1(k) "silage additives" (not for *calcium formate* and *potassium diformate*) according to the classification system of Annex I of Regulation (EC) No 1831/2003.

Ammonium formate (E295) is a liquid consisting of a minimum of 35 % of ammonium formate and a maximum of 64 % of free formic acid, the rest being water. *Sodium formate* (E237) is either a solid with a minimum purity of 98 % or a liquid containing a minimum of 15 % of sodium formate and a maximum of 75 % of free formic acid, the rest being water. Authorisation is sought for the use of these two *feed additives* for all animal species and categories. Both *feed additives* are intended to be used in *premixtures, feedingstuffs, water* and *silage*. The Applicant proposes a maximum concentration (expressed as formic acid) of 5 g/L in *water*, 10 g/kg in *silage* and 20 g/kg in *feedingstuffs*.

Calcium formate (E238) is a colourless solid with a minimum purity of 98 %. Authorisation is sought for the use of the *feed additive* for all animal species and categories. The *feed additive* is intended to be used in *premixtures* and *feedingstuffs*. The Applicant proposes a maximum concentration (expressed as formic acid) of 30 g/kg in *feedingstuffs*.

Finally, *potassium diformate* (237a) is a colourless aqueous solution with a minimum of 50 % of potassium diformate in water. Authorisation is sought for the use of the *feed additive* for all animal species and categories. The *feed additive* is intended to be used in *premixtures* and *feedingstuffs*. The Applicant proposes a maximum concentration (expressed as formic acid) of 9, 18 and 12 g/kg in fish for feed, in *feedingstuffs* for weaned piglets and sows & pigs for fattening, respectively.

The following international ring-trial validated standards were submitted by the Applicants and/or identified by the EURL:

- EN ISO 6869 and EN 15510, based on atomic absorption spectrometry (AAS) and inductively coupled plasma atomic emission spectrometry (ICP-AES), respectively, for the determination of total *calcium*, *potassium* and *sodium* in the *feed additives* (*calcium formate* - E238; *potassium diformate* - 237a; *sodium formate* - E237);

- ISO 5664, based on the distillation & titration of ammonia and the Community method (R152/2009, Annex III, C) based on Kjeldahl for the determination of nitrogen and calculation the *ammonium* content in the *feed additive* from the measured nitrogen content (*ammonium formate* - E295);

- EN 15909, based on the EDTA complexometric reaction for the determination of total *calcium* in the *feed additive* (*calcium formate* - E238); and

[1] The full report is available on the EURL website: https://ec.europa.eu/jrc/sites/default/files/FinRep-FormateGroup.pdf
[2] The EURL produced a combined report for the dossier FAD-2010-0188 Potassium diformate for all animal species; dossier FAD-2010-0312 Ammonium formate, sodium formate, calcium formate for all animal species; dossier FAD-2010-0303 Calcium formate for all animal species; and dossier FAD-2009-0027 Formic acid for all animal species.
[3] FAD-2010-0312.
[4] FAD-2010-0312, FAD-2010-0303, FAD-2010-0188.
[5] FAD-2010-0312.
[6] FAD-2010-0312.
[7] FAD-2010-0312, FAD-2010-0303.
[8] FAD-2010-0188.

- EN 15909, based on reverse phase high performance liquid chromatography with UV detection (RP-HPLC-UV) at 214 nm, for the determination of total *formate* in all the *feed additives* of concern (E295, E237, 237a and E238).

The EURL recommends for official control all the above mentioned methods for the determination of *feed additives* of concern. The relevant details about the principles of analysis and the corresponding performance characteristics are provided in the report.

For the determination of *total formate* (originating from *ammonium, sodium, calcium formates* and *potassium diformate*) in *premixtures* and *feedingstuffs* the Applicant[9] proposed a single laboratory validated method based on ion-exclusion high performance liquid chromatography with UV or refractive index detection (HPLC-UV/RI). This method does not distinguish between *formic acid* and its salts. The following performance characteristics for the quantification of *total formate* (expressed as *total formic acid*), were derived from the single-laboratory validation study in *premixtures* and *feedingstuffs*: - a relative standard deviations for *repeatability* (RSDr) ranging from 1.5 to 6.5 % for the concentration ranging from 1 to 1000 g/kg; - a *recovery rate* (Rrec) ranging from 89 to 99 %; and - a limit of quantification (LOQ) of 90 mg *formic acid*/kg *feedingstuffs*. The HPLC-UV/RI method was further ring trial validated with three to five laboratories and a relative standard deviation for *reproducibility* (RSDR) ranging from 6.6 to 19.3 % was determined for *premixtures* and *feedingstuffs* containing from 4.5 to 44 g *formic acid*/kg.

Furthemore, the EURL wishes to recall the conclusions drawn in the frame of the FAD-2009-0027 "Formic acid" dossier, dated 21/05/2010:

> For the determination of *formic acid* in *feedingstuffs*, the Applicant (FAD-2009-0027) suggested a single-laboratory validated method based on ion chromatography with electrical conductivity detection (IC-ECD). Approximately 1g of sample is extracted with 80mL of water for 30 minutes and then filled up to 100 mL. After filtration through paper and membrane filters, the solution is injected into the ion chromatograph. External standard calibration is used for the quantification of the formate content. The measured formate content allows the calculation of the formic acid one. The following performance characteristics were reported: - a limit of detection (LOD) and quantification (LOQ) of 100 and 500 mg/kg feedingstuffs, respectively; - a recovery rate (R_{Rec}) close to 100%; and - a repeatability relative standard deviation (R_{SDr}) of ca. 3.5%. The validation experiments were performed with a set of different feed samples covering a formate content ranging from 3.6 to 10 g/kg. These samples were also analysed by a second independent expert laboratory and all the results were in agreement. Furthermore, the validation report included summary information related to an inter-laboratory comparison organised by VDLUFA in 2006 for the determination of organic acids in *feedingstuffs*, including formic acid, to which six laboratories participated. The following performance characteristics were reported, for sample formic acid concentrations ranging from 7.2 to 506 g/kg *feedingstuffs*: - RSD_r ranging from 4 to 10 %; and - a reproducibility relative standard deviation (RSD_R) ranging from 13 to 22 %.

Based on the performance characteristics presented, the EURL recommends for official control the ring trial validated and submitted by Applicant[10] method which is based on ion-exclusion HPLC-UV/RI to determine *total formate* (expressed as *total formic acid*) in *premixtures* and *feedingstuffs* containing *ammonium formate, sodium formate, calcium formate* or *potassium diformate*. In addition, the EURL recommends for official control the IC-ECD method submitted by the Applicant (FAD-2009-0027) for the determination of *formic acid* (and *total formate*) in *feedingstuffs*. Furthemore, the EURL considers that maximum concentration levels (5g/kg) of *sodium* and *ammonium formates* in *water* could be monitored using the two methods (HPLC-UV/RI or IC-ECD) recommended above.

[9] FAD-2010-0312.
[10] FAD-2010-0312.

None of the Applicants provided analytical method or experimental data for the quantification of *ammonium formate* and *sodium formate* in *silage*. Therefore, the EURL cannot evaluate nor recommend any method for official control to determine *ammonium formate* and *sodium formate* in *silage.*

Further testing or validation of the methods to be performed through the consortium of National Reference Laboratories as specified by Article 10 (Commission Regulation (EC) No 378/2005) is not considered necessary.

The conclusions/recommendations presented in this report for the various *formate* salts are to be combined with those presented in the FAD-2009-0027 for the *formic acid*.