

ADOPTED: 27 February 2019

doi: 10.2903/j.efsa.2019.5651

Safety and efficacy of sorbitan monolaurate as a feed additive for all animal species

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Abstract

The additive sorbitan monolaurate consists of sorbitol (and its anhydrides) esterified with fatty acids derived from coconut oil. It is intended to be used as a technological additive, functional group: emulsifier, in feedingstuffs for all animal species, at a maximum concentration of 85 mg/kg complete feed. The EFSA Panel on Additives and Products or Substances used in Animal Feed (FEEDAP) concluded that sorbitan monolaurate is safe for all animal species at the proposed maximum content of 85 mg/kg complete feed and that the use of sorbitan monolaurate in animal nutrition is not expected to pose a risk for the consumer under the proposed conditions of use. Users are unlikely to be exposed to sorbitan monolaurate via inhalation. Sorbitan monolaurate is irritant to skin and eyes and it is not considered a skin sensitiser. Owing the lack of data, the FEEDAP Panel cannot conclude on the safety of the additive for the environment. Sorbitan monolaurate is authorised for use as a food additive with the function of emulsifier. The technological effect underlying its use as a food additive could reasonably be expected to be seen when used in feed.

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Keywords: sorbitan monolaurate, technological additives, emulsifiers, safety, efficacy

Requestor: European Commission

Question number: EFSA-Q-2013-01025

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Acknowledgements: The Panel wishes to thank the following for the support provided to this scientific output: Gregoretti Lucilla and Tarres Jordi.

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Suggested citation: EFSA FEEDAP Panel (EFSA Panel on Additives and Products or Substances used in Animal Feed), Bampidis V, Azimonti G, Bastos ML, Christensen H, Dusemund B, Kouba M, Kos Durjava M, López-Alonso M, López Puente S, Marcon F, Mayo B, Pechová A, Petkova M, Ramos F, Sanz Y, Villa RE, Woutersen R, Aquilina G, Bories G, Chesson A, Nebbia C, Renshaw D, Innocenti ML and Gropp J, 2019. Scientific Opinion on the safety and efficacy of sorbitan monolaurate as a feed additive for all animal species. *EFSA Journal* 2019;17(3):5651, 15 pp. <https://doi.org/10.2903/j.efsa.2019.5651>

ISSN: 1831-4732

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1. Introduction

1.1. Background and Terms of Reference

Regulation (EC) No 1831/2003¹ establishes the rules governing the Community authorisation of additives for use in animal nutrition. In particular, 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 Kemin Europa N.V.² for re-evaluation of the authorisation of the product sorbitan monolaurate, when used as a feed additive for all animal species (category: technological additive; functional group: emulsifiers).

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). The particulars and documents in support of the application were considered valid by EFSA as of 24 April 2014.

According to Article 8 of Regulation (EC) No 1831/2003, 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. EFSA shall deliver an opinion on the safety for the target animals, consumer, user and the environment and on the efficacy of the product sorbitan monolaurate, when used under the proposed conditions of use (see Section 3.1.3).

1.2. Additional information

Sorbitan monolaurate is currently authorised as a technological additive, functional group (c) emulsifier, for all animal.

Sorbitan monolaurate (E 493) is approved as a food additive (COMMISSION REGULATION (EU) No 1129/2011)³ in a wide range of commonly consumed foods (up to 10 g/kg), including dietary food supplements (*quantum satis*).

The additive has been assessed by the Scientific Committee on Food (SCF), which established a group acceptable daily intake (ADI) of 5 mg/kg body weight (bw) per day for sorbitan monolaurate and sorbitan monooleate (European Commission (1978)). The Joint Food and Agriculture Organization of the United Nations (FAO)/World Health Organization (WHO) Expert Committee on Food Additives also assessed the additive (WHO, 1982). The Committee included sorbitan monolaurate in the group ADI of 25 mg/kg bw per day already set for the other sorbitan esters.

The EFSA Panel on Food Additives and Nutrient Sources added to Food (ANS) (EFSA ANS Panel, 2017) assessed the sorbitan esters sorbitan monostearate (E 491), sorbitan tristearate (E 492), sorbitan monolaurate (E 493), sorbitan monooleate (E 494) and sorbitan monopalmitate (E 495). The ANS Panel established a group ADI of 10 mg/kg bw per day, expressed as sorbitan, for sorbitan esters (E 491, E 492, E 493, E 494 and E 495) singly or in combination.

2. Data and methodologies

2.1. Data

The present assessment is based on data submitted by the applicant in the form of a technical dossier⁴ in support of the authorisation request for the use of sorbitan monolaurate as a feed additive.

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 and peer-reviewed scientific papers to deliver the present output.

¹ 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.

² Kemin Europa N.V. Toekomstlaan 42, 2200, Herentals Belgium.

³ Commission Regulation (EU) No 1129/2011 of 11 November 2011 amending Annex II to Regulation (EC) No 1333/2008 of the European Parliament and of the Council by establishing a Union list of food additives. OJ L 295, 12.11.2011, p. 1–177.

⁴ FEED dossier reference: FAD-2010-0333.

EFSA has verified the European Union Reference Laboratory (EURL) report as it relates to the methods used for the control of the sorbitan monolaurate in animal feed. The Executive Summary of the EURL report can be found in Annex A.⁵

2.2. Methodologies

The approach followed by the FEEDAP Panel to assess the safety and the efficacy of sorbitan monolaurate is in line with the principles laid down in Regulation (EC) No 429/2008⁶ and the relevant guidance documents:

Guidance on technological additives (EFSA FEEDAP Panel, 2012a), Technical guidance: Tolerance and efficacy studies in target animals (EFSA FEEDAP Panel, 2011), Technical Guidance for assessing the safety of feed additives for the environment (EFSA, 2008a), Guidance for the preparation of dossiers for the re-evaluation of certain additives already authorised under Directive 70/524/EEC (EFSA, 2008b), Guidance for the preparation of dossiers for additives already authorised for use in food (EFSA FEEDAP Panel, 2012b), Guidance for establishing the safety of additives for the consumer (EFSA FEEDAP Panel, 2012c) and Guidance on studies concerning the safety of use of the additive for users/workers (EFSA FEEDAP Panel, 2012d).

3. Assessment

The additive under assessment, sorbitan monolaurate, is intended to be used as a technological additive (functional group: emulsifiers) in feedingstuffs for all animal species.

3.1. Characterisation

3.1.1. Characterisation of additive

The additive sorbitan monolaurate consists of sorbitol (and its anhydrides) [REDACTED] with fatty acids derived from coconut oil. [REDACTED]

[REDACTED] The additive is a yellow/amber oily liquid, it is insoluble in water.

The typical fatty acid profile of the additive sorbitan monolaurate reflects the fatty acid composition of coconut oil and is specified to contain 40–60% lauric acid, 14–25% myristic acid, 7–15% palmitic acid, < 11% oleic acid, < 10% caprylic acid, < 10% capric acid, < 7% stearic acid, < 3% linoleic acid and < 1% caproic acid.

The predominant structure is sorbitan monolaurate, from which the additive derives its name (synonyms: sorbitan laurate, sorbitan monododecanoate; Chemical Abstract Service (CAS) number 1338-39-2 and EINECS number 215-663-3; molecular weight 346.46, density about 1,030 kg/m³). The structural formula of sorbitan monolaurate is described in Figure 1.

⁵ The full report is available on the EURL website: <https://ec.europa.eu/jrc/sites/jrcsh/files/FinRep-FAD-2010-0333%20Sorbitan%20monolaurate.pdf>

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.

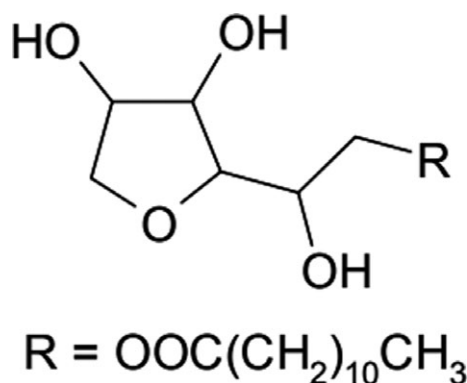


Figure 1: Structural formula of sorbitan monolaurate

The additive is manufactured to meet the specifications set by Commission Regulation (EU) No 231/2012⁷ for use as a food additive. The additive is specified to contain not less than 95% of a mixture of sorbitol, sorbitan and isosorbide esters. The analysis of five batches of the additive⁸ showed compliance with the above specifications. The additive is further specified to contain $\leq 2\%$ water and $\leq 0.5\%$ sulfated ash, and to have acid value ≤ 7 ,⁹ saponification value between ≥ 155 and ≤ 170 ,¹⁰ and hydroxyl value between ≥ 330 and ≤ 358 .¹¹ The analysis of five batches⁸ showed that also these specifications were met in all samples. The applicant proposed two additional specifications for sorbitan monolaurate as a feed additive: iodine value ≤ 10 ¹² and peroxide value ≤ 5 .¹³ The analysis of the same five batches showed compliance also with these specifications.

3.1.2. Purity

The analysed concentrations of lead (≤ 5 mg/kg), cadmium (≤ 1 mg/kg), mercury (≤ 1 mg/kg) and arsenic (≤ 3 mg/kg) in five batches of the additive⁸ were below the proposed specifications (≤ 5 , ≤ 1 , ≤ 1 and ≤ 3 mg/kg, respectively). None of them raises a safety concern.

3.1.3. Stability and homogeneity

The shelf life of the additive was studied by analysing the water content, the acid value, the saponification value and the hydroxyl value of three production batches stored in sealed containers at room temperature for 24 months.¹⁵ Essentially no changes in the analysed parameters were observed over the storage period.

No specific studies for the stability in feedingstuffs were submitted. For technological additives, stability in feedingstuffs can be demonstrated by persistence of the effect, and no demonstration of homogeneous distribution is considered necessary if the efficacy of the additive as emulsifier is demonstrated. Sorbitan monolaurate is authorised as a food additive, and the emulsifying effect seen when used in food could reasonably be expected to be seen when used in feed.

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. OJ No L 83, 22.3.2012, p. 1.

⁸ Supplementary Information August 2015/Annex_1.

⁹ Milligrams of potassium hydroxide required to neutralize the free acids in one gram of the material.

¹⁰ Milligrams of potassium hydroxide required to saponify all fatty acids contained in one gram of the material.

¹¹ Milligrams of potassium hydroxide necessary to neutralise the acetic acid which combines on acetylation of one gram of sample.

¹² Grams of iodine is consumed by 100 grams of fat.

¹³ Grams of peroxide oxygen in one kg of fat; is determined by measuring the amount of iodine which is formed by the reaction of peroxides with iodide ion.

¹⁵ Technical dossier/Section II/Annex_II_3.

3.1.4. Conditions of use

The additive is intended to be used as a emulsifier in feed materials and compound feed *quantum satis* but with a maximum content of 85 mg sorbitan monolaurate/kg complete feed.

3.2. Safety

3.2.1. Absorption, distribution, metabolism and excretion (ADME) and residues

No specific data were submitted by the applicant concerning the ADME and residues of sorbitan monolaurate in the target species. However, information is available concerning the metabolic fate of the homologous compounds sorbitan monostearate and sorbitan trioleate.

3.2.1.1. ADME

In its assessment of sorbitan-fatty acid esters the ANS Panel (EFSA ANS Panel, 2017) noted that 'there were indications from toxicokinetic studies in rats with radiolabelled sorbitan monostearate that this sorbitan ester can be either hydrolysed to its fatty acid moiety and the corresponding anhydrides of sorbitol or excreted intact in the faeces. After absorption, as indicated by radioactivity, sorbitan and isosorbide moieties, sorbitol or metabolites thereof were excreted via urine or exhaled as CO₂. The fatty acid moiety entered the endogenous metabolism of fatty acids. The Panel considered that in case intact sorbitan monostearate be absorbed it would be hydrolysed pre-systemically'. The Panel considered that these results would qualitatively apply to the homologous fatty esters of sorbitan.

The pancreas is generally assumed to be the major source of digestive lipase enzymes in fish as it is in mammals (Tocher, 2003). The same has been shown to occur in birds (Krogdahl, 1985). Consequently, the sorbitan moiety of sorbitan monolaurate is likely to be released in the digestive tract of these species and undergo a similar metabolic fate as in the rat.

3.2.1.2. Residues

One group of nine rats were fed for 28 days a diet containing 0.1% sorbitan monostearate ¹⁴C-labelled in the polyol moiety. Animals were sacrificed and the carcasses were frozen and lyophilised. Aliquots were extracted with hot chloroform and the solid extract was saponified; fatty acids were solvent extracted; the remaining phase contained the water-soluble hydrolytic products of the crude fat, including glycerol and any deposited anhydrosorbitol polyols. The analysis of the radioactivity of the different fractions indicated that 0.35% of the administered radioactivity was incorporated in the crude fat, 0.23% in the fatty acids, 0.03% in glycerol and 0.04% in unidentified residues comprising anhydrosorbitol polyols (Wick and Joseph, 1953). These results indicate that the sorbitan moiety is metabolised to a very low extent and is not expected to accumulate in the whole animal. It is reasonable to assume that no accumulation would occur in fish and bird edible tissues either.

3.2.2. Toxicological studies

The toxicology of sorbitan monolaurate has been previously evaluated by JECFA (WHO, 1974, 1982), the SCF (European Commission, 1978) and more recently by EFSA ANS Panel (EFSA, 2017) in relation to its use as a food additive. In 1978, the SCF established a group ADI for sorbitan monolaurate (E 493) and sorbitan monooleate (E 494), singly or in combination, of 5 mg/kg bw per day, calculated as sorbitan monolaurate. In 1982, based on long-term (2 years) studies in rats (WHO, 1982), a no observed adverse effect level (NOAEL) of 50,000 mg/kg diet (5%) was identified and considered equivalent to 2,500 mg/kg bw. By applying a safety factor of 100, a group ADI of 0–25 mg/kg bw for sorbitan esters was established.

The ANS Panel (EFSA, 2017) re-evaluated sorbitan monolaurate as a food additive together with other sorbitan esters (i.e. mono- and tristearate, monopalmitate and monooleate). In this opinion, two *in vitro* genotoxicity studies were described both made with sorbitan monolaurate: an *in vitro* chromosomal aberrations assay in cultured peripheral human lymphocytes and an *in vitro* mammalian cell gene mutation assay in L5178Y (Tk+/-) mouse lymphoma cells. Both these studies were performed according to Good Laboratory Practice (GLP) and following the relevant OECD Guidelines and were considered sufficient to exclude the genotoxicity of the substance. Furthermore, no relevant structural alert for both *in vitro* and *in vivo* genotoxicity were found for any of the sorbitan esters

when assessed by the OECD QSAR Toolbox. The FEEDAP Panel concludes that sorbitan monolaurate do not raise concern with respect to genotoxicity.

After reviewing the toxicity studies mentioned in the WHO evaluation performed in rats, monkeys and hamsters, the ANS Panel derived a NOAEL of 2,100 mg sorbitan monolaurate/kg bw per day and 2,300 mg sorbitan monolaurate/kg bw per day for males and females, respectively. The NOAEL was derived from a study in which Wistar rats (15 males and 15 females) were fed sorbitan monolaurate at dietary levels of 0, 2.5, 5.0 and 10% for 90 days corresponding to 0, 2,100, 4,200 and 8,000 mg sorbitan monolaurate/kg bw per day for males, and 0, 2,300, 4,500 and 8,400 mg sorbitan monolaurate/kg bw per day for females. However, no suitable long-term studies with sorbitan monolaurate could be identified.

Based on kidney lesions, the ANS identified a NOAEL of 2% for sodium monostearate (corresponding to 2,600 mg/kg bw per day) in male mice exposed to 0%, 0.5%, 2% or 4% of the additive for 80 weeks (Hendy et al., 1978). In that study, no increase in tumour incidences was found. The ANS Panel also considered that 'the available reproductive and developmental toxicity studies with sorbitan monostearate have limitations but no adverse effects were reported'.

The ANS Panel noted that (i) similar kinetics is expected for all the considered sorbitan esters, (ii) it is presumable that the kidney adverse effects used to derive the NOAEL for sodium monostearate are due to the sorbitan moiety, which is shared by all the esters under evaluation and (iii) the metabolic fate of all fatty acids deriving from ester hydrolysis is expected to be the same irrespective of the number of their carbon atoms.

According to these assumptions, the ANS Panel adopted a read-across approach and concluded that there was no need to set a separate ADI for sorbitan monolaurate and the other considered esters. Based on the long-term mice study on sorbitan monostearate (Hendy et al., 1978), the ANS Panel established a group ADI of 10 mg sorbitan/kg bw per day for sorbitan monolaurate and all the examined esters, singly or in combination, taking into account the ratio between the molecular weight of sorbitan monostearate (430.62) and of sorbitan (164.16) and applying a safety factor of 100.

The FEEDAP Panel follows the approach of the EFSA ANS Panel (2017) with its proposed group ADI of 10 mg sorbitan/kg bw per day for all sorbitan monoesters, singly or in combination. When applied to sorbitan monolaurate, this would correspond (based on its molecular weight) to an ADI of 21 mg sorbitan monolaurate/kg bw per day.

3.2.3. Safety for the target species

To support the safety of sorbitan monolaurate for all animal species, the applicant has performed three tolerance studies, one with chickens for fattening, one with dairy cows and one with weaned piglets.

3.2.3.1. Safety for chickens for fattening

A total of 756 one-day-old male chickens (Ross 308) was fed diets supplemented with 0, 85 (1× the maximum recommended dose) or 8,500 (100× the maximum recommended dose) mg sorbitan monolaurate/kg feed.¹⁶ Group size was twelve replicates with 21 birds each. The diets (starter, from day 1 to day 14; grower, from day 15 to day 28; finisher, from day 29 to day 35), consisting mainly of maize, wheat and soybean meal, were isonitrogenous (starter: 22.0% crude protein (CP); grower: 20.5% CP; finisher: 19.5% CP). The concentration of the additive was analytically confirmed. Feeds (mash form) and water were offered *ad libitum* for 35 days. Health status and mortality were monitored daily and most probable cause of death determined by necropsy. Feed intake (pen) and body weight (individual) were recorded at the beginning, and days 7, 14, 21, 28 and 35 of the experiment and average daily body weight gain and feed to gain ratio were calculated. At the end of the experiment, a blood sample was taken from two chickens per pen (randomly selected) for routine blood haematology¹⁷ and biochemistry.¹⁸ An analysis of variance (ANOVA) was performed with the data considering the pen for zootechnical parameters or the bird (blood analysis) as the experimental unit and group means were compared by Tukey's test. Significance level was set at $p < 0.05$.

¹⁶ Technical dossier/Supplementary information October 2017/Section III/Annex III 1.

¹⁷ Red blood cell count (RBC), haematocrit, haemoglobin, white blood cell count (WBC), white blood cell differentials (segmented neutrophils, lymphocytes, monocytes, eosinophils, basophils, erythroblasts).

¹⁸ Total protein, urea, cholesterol, alanine aminotransferase (ALT), aspartate aminotransferase (AST), gamma-glutamyltranspeptidase (GGT), bilirubin, albumin, globulin, calcium, phosphate inorg.

Mortality and culling of birds were low in each treatment (in total < 4%). Performance parameters were not affected by treatments and mean values were for daily feed intake 94.5 g/day, for final body weight 2.28 kg, for body weight gain 63.8 g/day and for feed to gain ratio 1.47. No treatment effects were observed either in the haematological and biochemical parameters. The sorbitan monolaurate supplementation up to 100-fold the recommended dose of 85 mg/kg feed did not adversely affect the health and performance of the chickens.

3.2.3.2. Safety for dairy cows

A total of 60 Holstein primi- and multiparous cows was fed total mixed ration (TMR) mainly composed of maize silage, wheat silage, ryegrass hay, fescue hay, alfalfa hay, maize, barley, and soybean meal supplemented with 0, 85 (1× the maximum recommended dose) or 850 (10× the maximum recommended dose) mg sorbitan monolaurate/kg of complete feed (88% dry matter).¹⁹ Group size was 20 cows which were housed in one pen, but fed individually to specific bins under an electronic feed monitoring system. The diets were calculated to be isonitrogenous (16.2% CP) and isocaloric (about 6.82 MJ net energy for lactation (NEL)/kg). The concentration of the additive was analytically confirmed. TMR and water were offered *ad libitum* for 56 days. Health status and mortality were monitored daily. Individual feed intake, body weight, milk production and milk composition were recorded daily. Milk samples were collected from each cow once a week to determine somatic cell counts. At the end of the experiment, a blood sample was taken from all animals per treatment for haematology²⁰ and clinical biochemistry.²¹ Data for performance parameters were analysed with a mixed model considering the fixed effects of treatment, time of sampling, parity and their three-way interactions, plus the random effect of cow with days in milk as a covariate, with the animal as experimental unit. Data for blood parameters were analysed with one-way ANOVA considering the fixed effect of treatment, with the animal as the experimental unit. Significance level was set at $p < 0.05$.

No mortality occurred. Mean values were for daily feed intake 23.0 kg dry matter/day and for milk yield 38.4 kg/day. No negative effects were observed in any measured performance parameter in the groups receiving sorbitan monolaurate compared to the control group. Among the haematological parameters, the percentage of basophils was significantly higher in the recommended dose group, compared to the control, but not in the overdose group. Chlorine and sodium concentrations were significantly lower in the overdose group, compared to the control. Although the difference observed were significant, the changes were small and are not considered of toxicological concern. No other treatment-related effects were observed in the haematological or in the biochemical parameters. The sorbitan monolaurate supplementation up to 10-fold the recommended dose of 85 mg/kg feed did not adversely affect the health and performance of dairy cows.

3.2.3.3. Safety for weaned piglets

A total of 72 castrated male and 72 female piglets (DanBred × Goland, 34 days of age, body weight 7.7 kg) was fed diets supplemented with 0, 85 (1× the maximum recommended dose) or 8,500 (100× the maximum recommended dose) mg sorbitan monolaurate/kg feed.²² Group size was 12 replicates with four pigs each (representing six pens with castrated males and six pens with females per treatment). The diets (prestarter, from day 1 to day 14; starter, from day 15 to day 42), consisting mainly of barley, wheat, maize, and soybean meal, were isonitrogenous (prestarter: 17.4% CP; starter: 17.1% CP) and isocaloric (prestarter: 10.6 MJ net energy (NE)/kg; starter: 10.5 MJ NE/kg). The concentration of the additive was analytically confirmed. Feeds (mash form) and water were offered *ad libitum* for 42 days. Health status and mortality were monitored daily and most probable cause of

¹⁹ Technical dossier/Supplementary information October 2017/Section III/Annex III 2.

²⁰ Red blood cell count (RBC), haemoglobin (Hb), packed cell volume (PCV), reticulocytes, mean corpuscular volume (MCV), mean corpuscular haemoglobin (MCH), mean corpuscular haemoglobin concentration (MCHC), platelets, mean platelet volume (MPV), white blood cell count (WBC), white blood cell differentials (neutrophils, lymphocytes, monocytes, eosinophils, basophils).

²¹ Alkaline phosphatase, amylase, gamma-glutamyltranspeptidase (GGT), alanine aminotransferase (ALT), aspartate aminotransferase (AST), lactate dehydrogenase (LDH), creatine phosphokinase (CPK), calcium, phosphorous, magnesium, potassium, sodium, chlorine, cholesterol, lactic acid, albumin, total protein, urea, creatinine, non-esterified fatty acids (NEFA), glucose and total bilirubin.

²² Technical dossier/Supplementary information October 2017/Section III/Annex III 3.

death determined by necropsy. Feed intake and body weight were recorded at the beginning, and days 7, 14, 21, 28, 35 and 42 of the experiment and average daily body weight gain and feed to gain ratio were calculated. At the end of the experiment, a blood sample was taken from two piglets per pen (representing twelve castrated males and twelve females per treatment) for routine blood haematology²³ and biochemistry.²⁴ An ANOVA was performed with the data considering the pen or the piglet (blood analysis) as the experimental unit and group means were compared by Tukey's test (performance) or Dunnett's test (blood analysis). Significance level was set at $p < 0.05$.

No mortality occurred. Performance parameters were not affected by treatments and mean values were for daily feed intake 768.5 g/day, for final body weight 28.1 kg, for body weight gain 484.9 g/day and for feed to gain ratio 1.59. The number of white blood cells was significantly higher in the overdose group compared to the control. The total bilirubin concentration was lower in the overdose group and Ca concentrations and ALT activity were lower in the use level group, compared to the control group. Although the difference observed were significant, the changes were small and are not considered of toxicological concern. No other treatment-related effects were observed in the haematological or in the biochemical parameters. The sorbitan monolaurate supplementation up to 100-fold the recommended dose of 85 mg/kg feed did not adversely affect the health and performance of weaned piglets.

3.2.3.4. Conclusions on safety for the target species

The results of three tolerance studies showed that dairy cows tolerated a concentration of 850 mg sorbitan monolaurate/kg feed (10× the proposed maximum content) and chickens for fattening and weaned piglets tolerated a concentration of 8,500 mg sorbitan monolaurate/kg feed (100× the proposed maximum content). The FEEDAP Panel therefore concludes that sorbitan monolaurate is safe for these animal species at the proposed maximum content of 85 mg/kg complete feed and extends this conclusion to all animal species.

3.2.4. Safety for the consumer

Based on the NOAEL of 2,600 mg sorbitan monostearate/kg bw per day, taking into account the ratio between the molecular weight of sorbitan monostearate (430.62 g/mol) and sorbitan (164.16 g/mol), and applying an uncertainty factor of 100, the ANS Panel proposed a group ADI of 10 mg sorbitan/kg bw per day expressed as sorbitan for sorbitan esters (E 491–495) singly or in combination. The FEEDAP Panel calculated that the corresponding ADI for sorbitan monolaurate would be 21 mg/kg bw.

Due to the extensive metabolism of sorbitan monolaurate at the intestinal level, no residues of the unchanged additive would be present in target animal tissues and products. The main intestinal metabolite sorbitan can be absorbed, and then excreted in urine unchanged, only very limited amounts being found in the whole body. Therefore, the administration of sorbitan monolaurate in complete feeds is expected to generate negligible amounts of residues of sorbitan and derived metabolites in food products of animal origin.

The consumption of tissues and products from animals administered the maximum recommended concentration of sorbitan monolaurate proposed for complete feeds would not measurably add to the exposure of the consumers. The FEEDAP Panel concludes that the use of sorbitan monolaurate in animal nutrition under the proposed conditions of use would not pose a risk for the consumer.

3.2.5. Safety for the user

3.2.5.1. Inhalation toxicity

No inhalation toxicity studies were available, but as sorbitan monolaurate is an oily liquid users are not expected to be exposed to it by inhalation during normal handling of the additive.

²³ Red blood cell count (RBC), haematocrit, haemoglobin, mean corpuscular volume, mean corpuscular haemoglobin, mean corpuscular haemoglobin concentration, platelets, white blood cell count (WBC), white blood cell differentials (neutrophils, lymphocytes, monocytes, eosinophils, basophils).

²⁴ Glucose, calcium, phosphorus inorg., total cholesterol, triglycerides, phospholipids, uric acid, creatinine, lactate dehydrogenase, alkaline phosphatase, alanine aminotransferase (ALT), aspartate aminotransferase (AST), total bilirubin.

3.2.5.2. Skin and eyes

Sorbitan monolaurate was tested for skin and eye irritancy using New Zealand rabbits.²⁵ Solutions of 1%, 10%, 60% or 100% sorbitan monolaurate were applied to clipped skin for 10 days. After 3 days of treatment, 100% caused intense erythema and oedema, 10% and 60% caused less intense erythema and oedema, and 1% caused no changes to exposed skin. After 10 days of treatment, erythema and oedema were seen in all treated groups and the 60% and 100% treatments also caused skin thickening. It was concluded that sorbitan monolaurate is irritant to rabbit skin. Although solutions of 30% and 60% sorbitan monolaurate did not cause irritancy when applied to the eyes of rabbits, considering that it was shown to be irritant to skin, it would be prudent to regard it as a potential irritant to the eyes of exposed users.

Sorbitan monolaurate was tested at aqueous solution of 30% and 100% in a Schwartz Prophetic Patch Test (two exposures of 72 h, seven days apart) for allergens using 30 and 50 human subjects, respectively.²⁶ No skin reactions were caused, indicating that none of the subjects were allergic to sorbitan laurate.

3.2.5.3. Conclusions on safety for the user

Sorbitan monolaurate is regarded as an irritant to skin and eyes but is not considered a skin sensitiser. It is not expected to be a risk for the users exposed via inhalation.

3.2.6. Safety for the environment

According to the Technical Guidance for assessing the safety of feed additives for the environment (EFSA, 2008a), when performing Phase I assessment, 100% of the parent compound is considered to enter the environment.

Phase I assessment

Exposure assessment

The active ingredient sorbitan monolaurate is not a physiological/natural substance of established safety for the environment. Consequently, a Phase I assessment has to be conducted to determine the predicted environmental concentrations (PECs) of the feed additive in relevant environmental compartments.

The applicant supplied a phase I assessment for sorbitan monolaurate when used as a feed additive for terrestrial and aquatic farm animals.

Additives for terrestrial animals

The PECs for sorbitan monolaurate in soil, groundwater and surface water were calculated (EFSA, 2008b), based on inclusion of the additive at a concentration of 85 mg/kg complete feed for all target animals and 100% excretion.

The PEC_{soil} ranged from 0.37 to 1.7 mg/kg soil from the use of sorbitan monolaurate in feed for turkeys and lambs for fattening, respectively.

The PEC_{groundwater} ranged from 1.0 to 4.6 µg/L and PEC_{surfacewater} ranged from 0.3 to 1.5 µg/L (both ranges for turkeys and lambs for fattening, respectively).

Additives for fish

The PECs from the use of sorbitan monolaurate in fish farmed in sea cages was calculated assuming that 100% of the maximum dose (85 mg/kg feed) is excreted to the sediment as the parent compound. The PEC_{sediment} is 0.18 mg/kg wet weight (ww) which exceeds the trigger value of 10 µg/kg ww.

The PEC_{swaq} from the use of sorbitan monolaurate in fish farmed in raceways, ponds, tanks and recirculation systems was calculated assuming that 100% of the maximum dose (85 mg/kg feed) is released to the surface water. The PEC_{swaq} ranged from 0.06 to 0.21 µg/L from use of the additive in different fish species. The use of the additive for salmon would give a PEC_{swaq} below the trigger value of 0.1 µg/L, whereas the use for rainbow trout, seabass/seabream and turbot would slightly exceed the trigger value.

²⁵ Technical dossier/Section III/Annex III.8.

²⁶ Technical dossier/Section III/Annex III.5.

Conclusions phase I assessment

As PEC_{soil} exceeded the trigger value of 10 $\mu\text{g}/\text{kg}$, and $PEC_{groundwater}$ and $PEC_{surfacewater}$ all exceeded the trigger values of 0.1 $\mu\text{g}/\text{L}$, a Phase II assessment is required for sorbitan monolaurate. Since the PEC_{swaq} was around the trigger value no further assessment is required for this environmental compartment.

Phase II assessment

Refinement of PEC

Degradation studies indicate that sorbitan monolaurate is readily degradable (US EPA, 2010), and with an estimated K_{ow} of 3.15 (US EPA, 2005) is not expected to bioaccumulate. Limited data are available on the ecotoxicity of sorbitan monolaurate. Studies in rats indicate that approximately 90% of sorbitan monostearate is hydrolysed to its fatty acid moiety and the corresponding anhydrides of sorbitol. Assuming similar metabolism of sorbitan monolaurate, a limited proportion of the additive will be excreted to the environment. However, in the absence of quantitative data, it is not possible to calculate refined PEC values.

The FEEDAP Panel considers that the lack of data and the inherent uncertainties do not allow the environmental risk assessment to be completed.

3.3. Efficacy

Sorbitan monolaurate is authorised for use as a food additive with the function of emulsifier. The technological effect underlying its use as a food additive could reasonably be expected to be seen when used in feed.

4. Conclusions

Sorbitan monolaurate is safe for all animal species at the proposed maximum content of 85 mg/kg complete feed.

The use of sorbitan monolaurate in animal nutrition is not expected to pose a risk for the consumer under the proposed conditions of use.

Users are unlikely to be exposed to sorbitan monolaurate via inhalation. Sorbitan monolaurate is irritant to skin and eyes and it is not considered a skin sensitiser.

Owing the lack of data, the FEEDAP Panel cannot conclude on the safety of the additive for the environment.

Sorbitan monolaurate is authorised for use as a food additive with the function of emulsifier. The technological effect underlying its use as a food additive could reasonably be expected to be seen when used in feed.

Documentation provided to EFSA

- 1) Sorbitan monolaurate for all animal species. November 2010. Submitted by Kemin Europa N.V.
- 2) Sorbitan monolaurate for all animal species. Supplementary information. August 2015. Submitted by Submitted by Kemin Europa N.V.
- 3) Sorbitan monolaurate for all animal species. Supplementary information. October 2017. Submitted by Submitted by Kemin Europa N.V.
- 4) Evaluation report of the European Union Reference Laboratory for Feed Additives on the Methods(s) of Analysis for sorbitan monolaurate.
- 5) Comments from Member States.

Chronology

Date	Event
05/11/2010	Dossier received by EFSA
11/12/2013	Reception mandate from the European Commission
22/04/2014	Application validated by EFSA – Start of the scientific assessment
24/07/2014	Comments received from Member States

Date	Event
24/07/2014	Reception of the Evaluation report of the European Union Reference Laboratory for Feed Additives
10/10/2014	Request of supplementary information to the applicant in line with Article 8(1)(2) of Regulation (EC) No 1831/2003 – Scientific assessment suspended. <i>Issues: characterisation</i>
22/12/2014	Request of supplementary information to the applicant in line with Article 8(1)(2) of Regulation (EC) No 1831/2003 – Scientific assessment suspended. <i>Issues: safety for target species</i>
07/08/2015	Reception of supplementary information from the applicant - Scientific assessment re-started
05/07/2016	Request of supplementary information to the applicant in line with Article 8(1)(2) of Regulation (EC) No 1831/2003 – Scientific assessment suspended <i>Issues: Safety for the target species</i>
04/10/2017	Reception of supplementary information from the applicant - Scientific assessment re-started
27/02/2019	Opinion adopted by the FEEDAP Panel. End of the Scientific assessment

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Abbreviations

ADI	acceptable daily intake
ADME	absorption, distribution, metabolism and excretion
ANS	EFSA Scientific Panel on Additives and Nutrient Sources added to Food
ANOVA	analysis of variance
bw	body weight
CAS	Chemical Abstracts Service
CP	crude protein
CV	coefficient of variation
DM	dry matter
ECHA	European Chemicals Agency
EINECS	European INventory of Existing Commercial chemical Substances
EURL	European Union Reference Laboratory
FAO	Food Agricultural Organization
FEEDAP	Panel on Additives and Products or Substances used in Animal Feed
GC	gas chromatography
GLP	Good laboratory practice
JECFA	The Joint FAO/WHO Expert Committee on Food Additives
K_{ow}	<i>n</i> -octanol/water partition coefficient
$\log K_{ow}$	logarithm of octanol–water partition coefficient
NEL	net energy for lactation
NOAEL	no observed adverse effect level
NTP	National Toxicology Program
OECD	Organisation for Economic Co-operation and Development
PCBs	polychlorinated biphenyl
PCDD/F	polychlorinated dibenzodioxins/dibenzofurans
PEC	predicted environmental concentration
PNEC	predicted no effect concentrations
SCF	Scientific Committee on Food
TEQ	toxic equivalent
TMR	total mixed ration
UF	uncertainty factor
WHO	World Health Organization

Annex A – Executive Summary of the Evaluation Report of the European Union Reference Laboratory for Feed Additives on the Method(s) of Analysis for sorbitan monolaurate

In the current application, authorisation is sought under article 10(2) for Sorbitan monolaurate under the category/functional group 1(c) 'technological additives/'emulsifiers' according to the classification system of Annex I of Regulation (EC) No 1831/2003. Specifically, the authorisation is sought for the use of the feed additive for all animal species and categories. Sorbitan monolaurate is a yellow-to-amber oily liquid, consisting of a minimum of 95% of a mixture of partial esters of sorbitol, sorbitan and isosorbide with edible commercial lauric acid; the later comprises mainly lauric acid (ca. 40–60%), myristic acid (ca. 14–25%) and palmitic acid (ca. 7–15%). The Applicant states that the specific purity criteria set in the Commission Directive 2008/84/EC for the food additive are applicable for the feed additive. Sorbitan monolaurate is intended to be added to other feed additives (mainly antioxidants) in order to assist their uniform distribution when added to other feed ingredients. No recommended minimum or maximum concentration levels were proposed by the Applicant. However, the typical maximum inclusion level is equivalent to 5 g of the feed additive/kg complete feedingstuffs. For the characterisation of Sorbitan monolaurate in the feed additive, the Applicant submitted the internationally recognised FAO JECFA monographs dedicated for Sorbitan monolaurate, based on the determination of – saponification-, - acid-, - hydroxyl- values; and – the assay of polyols and fatty acids, as recommended by Commission Directive 2008/84/EC. Even though no performance characteristics were provided, the EURL recommends for official control the methods described in the above mentioned FAO JECFA monographs to characterise Sorbitan monolaurate in the feed additive. For the characterisation of fatty acids in the feed additive, the gas chromatography (GC) method described in the European Pharmacopoeia monographs (Eur. Ph. 6.0, 1040 and 20422) may be applied. The accurate determination of Sorbitan monolaurate in premixtures and feedingstuffs is not achievable experimentally. Therefore, the EURL is not able to evaluate nor recommend any method for official control to determine Sorbitan monolaurate in premixtures and feedingstuffs. 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.