SCIENTIFIC OPINION

EFSA Journal

ADOPTED: 25 May 2020

doi: 10.2903/j.efsa.2020.6162

Safety for the environment 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 currently authorised in the European Union and it is intended to be used as a technological additive (functional group of emulsifiers), in feedingstuffs for all animal species, at a maximum concentration of 85 mg/kg complete feed. In 2019, the EFSA Panel on Additives and Products or Substances used in Animal Feed (FEEDAP) issued an opinion on the safety and efficacy of sorbitan monolaurate. Owing the lack of data, the FEEDAP Panel could not conclude on the safety of the additive for the environment. The applicant submitted new data (fate and degradation as well as ecotoxicity data) that were evaluated in the present opinion. The absorption, distribution, metabolism and excretion of structurally related compounds (sorbitan monostearate and sorbitan trioleate) indicate that the additive is expected to be partially metabolised. In addition, sorbitan monolaurate and some related compounds are readily biodegradable. The limited available data on the effects of sorbitan monolaurate in marine crustaceans and in marine sediment indicate that the ecotoxicity of the additive is low, in consistency with the very low acute toxicity of sorbitan esters. Overall, the FEEDAP Panel concludes that a risk of sorbitan monolaurate to terrestrial and aquatic environment is unlikely. Therefore, no safety concerns for the environment are expected from the use of the additive under assessment according to the established conditions of use.

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

Requestor: European Commission

Question number: EFSA-Q-2019-00595

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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, Kos Durjava M, Kouba M, López-Alonso M, López Puente S, Marcon F, Mayo B, Pechová A, Petkova M, Ramos F, Sanz Y, Villa RE, Woutersen R, Bories G, Finizio A, Focks A, Teodorovic I, Manini P and Tarrés-Call J, 2020. Scientific Opinion on the safety for the environment of sorbitan monolaurate as a feed additive for all animal species. EFSA Journal 2020;18(6):6162, 12 pp. https://doi.org/10.2903/j.efsa.2020.6162

ISSN: 1831-4732

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

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1. Introduction

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

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

The applicant, Kemin Europa N.V, is seeking a Community authorisation of Sorbitan Monolaurate as feed additive to be used as an emulsified for all animal species (Table 1).

Table 1: Description of the substances

Category of additive	Technological additive
Functional group of additive	Emulsifier
Description	Sorbitan monolaurate (Kemin)
Target animal category	All animal species
Applicant	Kemin Europa N.V.
Type of request	New opinion

On 27 February 2019, the Panel on Additives an Products or Substances used in Animal Feed of the European Food Safety Authority ("Authority"), in its opinion on the safety of the product, could not conclude on the safety of Sorbitan monolaurate in all animal species, under the conditions of use as posed by the applicant. Owing the lack of data, the FEEDAP Panel could not conclude on the safety of the additive for the environment. It was suggested to check for the possibility to demonstrate the safety of the additive.

The Commission gave the possibility to the applicant to submit complementary information in order to complete the assessment and to allow a revision of Authority's opinion. The new data have been received on 2 April 2019.

In view of the above, the Commission asks the Authority to deliver a new opinion on Sorbitan monolaurate as feed additive for all animal species based on the additional data submitted by the applicant.

1.2. Additional information

The re-evaluation of the safety of sorbitan monolaurate for the environment is the object of the current risk assessment. It is currently authorised as a technological additive, functional group (c) emulsifier, for all animal species.

Sorbitan monolaurate (E 493) is approved as a food additive (Commission Regulation (EU) No 1129/2011) in a wide range of commonly consumed foods (up to 10 g/kg), including dietary food supplements (*quantum satis*). Sorbitan stearate (E 491), sorbitan tristearate (E 492), sorbitan oleate (E 494), sorbitan palmitate (E 495) and sorbitol (E 420) are authorised as food additives in the EU.

The European Food Safety Authority (EFSA) FEEDAP Panel adopted, in 2019, an opinion on the safety and efficacy of sorbitan monolaurate as a feed additive for all animal species. In that opinion, owing the lack of data, the FEEDAP Panel could not conclude on the safety of the additive for the environment.

2. Data and methodologies

2.1. Data

The present assessment is based on data submitted by the applicant in the form of additional information[2] to a previous application on the same product.[3]

[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] FEED dossier reference: FAD-2019-0060.
[3] FEED dossier reference: FAD-2010-0333.

2.2. Methodologies

The approach followed by the FEEDAP Panel to assess the safety of sorbitan monolaurate is in line with the principles laid down in Regulation (EC) No 429/2008[4] and the relevant guidance documents: Guidance for assessing the safety of feed additives for the environment (EFSA, 2008).

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.

The additive was characterised in a previous opinion (EFSA FEEDAP Panel, 2019). It consists of sorbitol (and its anhydrides) esterified with fatty acids derived from coconut oil. The additive is an oily liquid, insoluble in water, and has a density of about 1,030 kg/m^3.

The typical fatty acid profile of the additive sorbitan monolaurate reflects the fatty acid composition of coconut oil and according to the applicant, it is specified to contain a number of compounds reported in Table 2.

Table 2: Typical fatty acid profile of the additive sorbitan monolaurate

Compound (chemical name and linear formula)	Content (%)
Lauric acid (dodecanoic acid, $CH_3(CH_2)_{10}COOH$)	40–60
Myristic acid (1-tetradecanoic acid, $CH_3(CH_2)_{12}COOH$)	14–25
Palmitic acid (hexadecenoic acid, $CH_3(CH_2)_{14}COOH$)	7–15
Oleic acid ((9*Z*)-octadec-9-enoic acid, $CH_3(CH_2)_7CH{=}CH(CH_2)_7COOH$)	< 11
Caprylic acid (octanoic acid, $CH_3(CH_2)_6COOH$)	< 10
Capric acid (decanoic acid, $CH_3(CH_2)_8COOH$)	< 10
Stearic acid (octadecanoic acid, $CH_3(CH2)_{16}COOH$)	< 7
Linoleic acid ((9Z,12Z)-octadeca-9,12-dienoic acid, $CH_3(CH_2)_4CH{=}CHCH_2CH{=}CH(CH_2)_7COOH$)	< 3

In the previous opinion, the FEEDAP Panel could not conclude on the safety of the additive for the environment due to lack of data and inherent uncertainties. The applicant has submitted additional information in support to the safety for the environment.

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

3.1. Safety for the environment

In the previous opinion, the FEEDAP Panel performed a Phase I environmental risk assessment and noted that the predicted environmental concentrations (PECs) for soil, groundwater and surface water were exceeded. Since the PEC surface water for the aquatic compartment was around the trigger value, no further assessment was considered required for this environmental compartment (EFSA FEEDAP Panel, 2019).

In the same opinion, it was not possible to refine the above PECs in Phase II, due to the absence of quantitative data and it was noted the following: *Degradation studies indicate that sorbitan monolaurate is readily degradable (US EPA, 2010), and with an estimated log Kow 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.*

Based on the above, in 2019, the FEEDAP Panel concluded that *the lack of data and the inherent uncertainties do not allow the environmental risk assessment to be completed.*

In order to fulfil the lack of data identify in the previous assessment, the applicant submitted one study on degradation in marine water of sorbitan monolaurate,[5] one on toxicity in marine sediment

[4] 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.

[5] Technical dossier/Annex SIn 3.

testing sorbitan monolaurate,[6] and one on toxicity in marine water testing sorbitan monolaurate and sorbitan monooleate.[7] In addition, a review of the literature on the safety of sorbitan esters for the environment was performed.[8]

The FEEDAP Panel assessed the new information available and considered in particular the following: (i) the outcome of the literature review on sorbitan esters, (ii) the available data on the Absorption, distribution, metabolism and excretion (ADME) of structurally related compounds (sorbitan esters), (ii) the study on the aerobic degradability of sorbitan monolaurate in seawater and (iii) the ecotoxicity data on marine crustaceans and in marine sediment organisms.

In performing the assessment, the FEEDAP Panel considered the additive as a mixture of different derivates of sorbitol and fatty acids, naturally present in plants/animal products used as food or feed (Table 3).

Table 3: Natural occurrence of the compounds of the additive

Compound	CAS number (sorbitan ester)	Naturally present in
Lauric acid	143-07-7 (1338-39-2)	Laurel oil, palm kernel oil, watermelon seed, pumpkin seed [E 493]
Myristic acid	544-63-8 (56645-05-7)	Palm kernel oil, coconut oil, nutmeg
Palmitic acid	57-10-3 (26266-57-9)	Palm tree (Mediterranean coast), canola oil (EU), linseed oil (EU) [E 495]
Oleic acid	112-80-1 (1338-43-8)	Olive oil, canola oil (EU), linseed oil, sunflower oil [E 494]
Caprylic acid	124-07-2 (60177-36-8)	Palm kernel oil, coconut oil.
Capric acid	334-48-5	Palm kernel oil, coconut oil.
Stearic acid	57-11-4 (1338-41-6)	Canola oil, linseed oil, cotton oil, sunflower oil, rapeseed, palm kernel oil [E491]
Linoleic acid	60-33-3	Linseed oil, poppyseed oil, sunflower oil, maize oil.
Sorbitol	50-70-4	Sugar alcohol present in stone fruits, and in trees of the genus *Surbus*, present in Europe [E420]

3.1.1. Literature review on sorbitan esters

The applicant has reviewed the scientific literature in two database platforms (Science direct and Livivo). Search strategies used included 'sorbitan AND toxicity AND availability', 'sorbitan AND environment AND earthworm', 'sorbitan AND environment'. The search was restricted to reports published within the period 1992–2020 and written in the English language. Those not publicly available were excluded.[9] After screening for relevance, 11 papers were selected from a total of 179 hits for closer attention: Alwadani and Fatehi (2018), Chen et al. (2001), Franzetti et al. (2006), Harvey et al. (2011), Kim and Weber (2005), Krogh et al. (2003), Li and Yang (2010), Toshima et al. (1992), Wirz et al. (2015), Xi et al. (2016) and Zheng et al. (2012).

The FEEDAP Panel noted that ecotoxicity studies reviewed in the scientific literature submitted by the applicant tested sorbitan monolaurate and similar substances (e.g. sorbitan monooleate, sorbitol polyoxyethylene) that are still considered relevant as supportive evidence. The chemical structure of these substances is available in Appendix A.

The scientific papers of Toshima et al. (1992), Harvey et al. (2011); Krogh et al. (2003); Li and Yang (2010), Zheng et al. (2012), and Xi et al. (2016), were considered not relevant for the hazard characterisation of the additive because the endpoints measured or because they were designed for different purposes. The remaining scientific papers are described in the following sections.

[6] Technical dossier/Annex SIn 1.
[7] Technical dossier/Annex Sin 2.
[8] Technical dossier/Annex SIn 4.
[9] Technical dossier/Supplementary information February 2020/FAD-2019-0333 supplementary information, table 18.

3.1.2. ADME of structurally related compounds – metabolism of sorbitan esters

The metabolic fate of sorbitan monostearate has been studied in the rat. After administration of a single dose of ^{14}C-sorbitan monostearate (labelled on the polyol moiety), 90% and 50% (oily and water emulsion form, respectively) of the emulsifier were hydrolysed to stearic acid and anhydrides of sorbitol that were extensively excreted (44% and 66%) in the urine; only a fraction of sorbitol anhydrides was oxidised to $^{14}CO_2$ (14–24% of the administered radioactivity); very low amounts of radioactivity (< 0.1%) were measured in tissues; continuous administration (28 days) of the same labelled compound showed no accumulation of the additive in the fat (Wick and Joseph, 1952, 1953). Similar studies performed with sorbitan ^{14}C-monostearate (labelled on the fatty acid) showed that the stearate moiety had a coefficient of digestibility of 53.3%; fractionation of carcass fat showed that ^{14}C was incorporated into fatty acids, glycerol and non-identified residues (Wick and Joseph, 1953; Oser and Oser, 1957).

The metabolic fate of sorbitan trioleate has been studied in the rat. After administration of a single oral dose of sorbitan ^{14}C-trioleate (labelled in the oleate moiety), 42% was found in the faeces and gastrointestinal tract, indicating that the compound was incompletely absorbed; $^{14}CO_2$ excretion amounted to 30–35%, urinary excretion to 3%; the liver contained about 3% and the carcass about 22%. After administration of the ^{14}C-sorbitan-trioleate (labelled in the polyol moiety), less than 2% of the label was recovered as $^{14}CO_2$; the proportions not absorbed were 24% when administrated in a water emulsion but 37% from an oily solution; urinary excretion amounted 88%; the liver contained about 1% and the carcass about 6% of the administered radioactivity (Treon et al., 1967).

It was shown that the bioavailability of mono-, di- and tri-esters of sorbitan was similar (Mattson and Nolen, 1972).

The ANS Panel, in its opinion of 2017, considered that the different sorbitan esters will follow the same metabolic and excretion pathways as sorbitan monostearate (E491). The FEEDAP Panel assumes that the above-mentioned results would qualitatively/semiquantitatively apply to the homologous fatty esters of sorbitan constitutive of the additive under assessment.

The pancreas is considered to be the major source of digestive carboxylic ester hydrolases in fish as it is in mammals (review from Tocher, 2003). The same has been shown to occur in birds (review from Krogdahl, 1985). Consequently, the sorbitan moiety of sorbitan monolaurate should be released the same in the digestive tract of these species and undergo a similar metabolic fate as in the rat.

Based on the data from structurally related compounds, the Panel considers that the additive (esters of fatty acids and sorbitol (and its anhydrides) is partially absorbed and metabolised and metabolites of sorbitan are excreted by urine. The exact amount of the additive that is metabolised cannot be determined from the data available. The data available on structurally related compounds allow to estimate that about 20% of the absorbed fraction is exhaled in the form of CO_2, and that about 20–50% (when administered in a water vehicle or in an oily vehicle, respectively) of the absorbed fraction is excreted in urine as sorbitan or metabolites.

3.1.3. Ready biodegradability of sorbitan monolaurate and sorbitan esters

The aerobic degradability (biochemical oxygen demand of insoluble substances [BODIS test]) of sorbitan monolaurate in seawater was tested.[10] The test substance was biodegraded by 54% over 28 days and showed only a slight inhibition of 8% to seawater bacteria. The test was extended for an additional 7 days to establish whether degradation was continuous after the test period. Sorbitan monolaurate achieved a plateau by day 35 in the 7 days extended test.

Chen et al. (2001), investigating the biodegradability of surfactants in activated sludge, found that sorbitan monooleate was readily degraded (90%) by activated sludge within 100 h.

Kim and Weber (2005) reported about the degradation of a number of polycyclic aromatic hydrocarbons with and without polyoxyethylene-sorbitan-monolaurate. Its biodegradation in a soil-free liquid bacteria culture was limited to 17.8% of the initial dose, degradation in soil systems was not tested. The degradation potential for polyoxyethylene-sorbitan-monolaurate in soil-free systems is limited.

Franzetti et al. (2006) reported about sorption and biodegradation of polyoxyethylene-sorbitan-monolaurate. The compound showed moderate sorption (sorption/desorption coefficient [Kd] of 37 L/kg), but at higher concentrations, it showed non-linear 'cooperative sorption' behaviour. Biodegradation was

[10] Technical dossier/Supplementary information February 2020/Annex Sin3 Degradability.

assessed indirectly by liquid respirometry with the conclusion that the compound is extremely degradable and is completely mineralised.

Sorbitan monolaurate is readily biodegradable (US Epa, 2010), achieving 57% of its theoretical biochemical oxygen demand over a 14-day period.

Wirz et al. (2015) assessed the environmental risk posed by excipients from a galenic pharmaceutical production (including sorbitol (CAS: 50-70-4) and polyoxyethylene-sorbitan-monolaurate (CAS: 9005-64-5)) to receiving water bodies upon wastewater treatment process. From the results, it can be seen that compounds similar to sorbitan monolaurate (e.g. polyoxyethylene-sorbitan-monolaurate, stearic acid, sorbitol) are highly biodegradable and the risk for aquatic biota is highly unlikely.

These studies indicate that sorbitan monooleate as well as chemically similar molecules are readily degradable in activated sludge.

3.1.4. Ecotoxicity data

Franzetti et al. (2006) reported about microbial toxicity of polyoxyethylene-sorbitan-monolaurate. The compound showed very low toxicity in the MICROTOX® bioassay (EC_{50} 7.0 g/L).

A limited set of relevant ecotoxicological information is mentioned in only one paper, Wirz et al. (2015) where some PEC and Predicted no effect concentration (PNEC) values are reported.[11]

The applicant submitted the following studies on aquatic organisms in which sorbitan monolaurate and/or sorbitan monooleate were used as test items.

Marine water toxicity

The toxicity of sorbitan monolaurate and sorbitan monooleate was tested in a study following good laboratory practices (GLPs) performed according to ISO 14669:1999 with the marine crustacean *Acartia tonsa*.[12] Sorbitan monolaurate exhibited a 48-h LC_{50} value of 452.8 mg/L and sorbitan monooleate a 48-h LC_{50} > 10,000 mg/L.

Marine sediment toxicity

Sorbitan monolaurate was tested in a sediment toxicity test with the intertidal amphipod *Corophium volutator*.[13] According to the method, test duration was 10 days. Sorbitan monolaurate was characterised as poorly soluble and therefore was added to the test system via dried sediment. Well-defined information was provided on the source of test species and sediment (Bay of Suckquoy, Scotland), acclimation period (4 days) and test conditions. Tests were conducted (under controlled illumination and temperature) in 1 L capacity glass beakers each containing 2 cm depth of amended sediment and 850 mL of overlying seawater. Three replicates were prepared for each test concentration; controls were replicated five times. In total, 60 organisms were exposed per concentration of the test item and 100 for control. The target wet weight nominal concentrations ranged from 10 to 10,000 mg/kg (10, 100, 320, 1,000, 10,000). The validity criteria were fulfilled. Based on the obtained results, sorbitan monolaurate exhibited a 10-day LC_{50} value of 1,141 mg/kg (dry weight) to the marine amphipod *Corophium volutator* in the sediment phase.

The ecotoxicity of sorbitan monolaurate to marine sediment organisms is very low as well as to marine water species.

3.1.5. Conclusions on the safety for the environment

The additive is a mixture of different compounds. Biodegradation studies and ADME data are available only for a few compounds of the additive. Few ecotoxicity data on sorbitan esters are available, mainly related to marine environment.

Sorbitan ester of	Content (%)	ADME	Biodegradability	Ecotoxicity	Literature review
Lauric acid	40–60		X	X (marine water)	X (biodegradability)

[11] Sources for the PNEC values for polyoxyethylene-sorbitan-monolaurate originated from a material safety data sheet of polyethylene glycol 6000- CAS No 25322-68-3 (Clariant, 2011), and for sorbitol the reference was ECHA (2006) for the receiving water; and Gonzalez et al., (1972) and Straub et al. (2014) for the wastewater treatment plant.

[12] Technical dossier/Supplementary information February 2020/Annex Sin2 Aquatic.

[13] Technical dossier/Supplementary information February 2020/Annex Sin1 Sediment.

Sorbitan ester of	Content (%)	ADME	Biodegradability	Ecotoxicity	Literature review
Myristic acid	14–25				
Palmitic acid	7–15				
Oleic acid	< 11	X (trioleate)		X (marine sediment) X (marine water)	X (biodegradability)
Caprylic acid	< 10				
Capric acid	< 10				
Stearic acid	< 7	X			
Linoleic acid	< 3				

A complete ecotoxicological data set is not available. Nevertheless, the FEEDAP Panel considers that even with a limited amount of studies, some conclusions on the safety for the environment of sorbitan monolaurate can be drawn through a weight of evidence assessment (EFSA Scientific Committee, 2017). Information from different lines of evidence was integrated including:

i) the available data on the ADME of structurally related compounds, sorbitan monostearate and sorbitan trioleate, which indicate that the additive is expected to be metabolised at least in part, as about 20% of the absorbed fraction is exhaled in the form of CO_2, and that about 20–50% of the absorbed fraction is excreted in urine as sorbitan or metabolites,
ii) the readily aerobic degradability of sorbitan monolaurate in water and seawater, supported by evidence available from the literature on structurally related compounds, sorbitan monooleate and polyoxyethylene-sorbitan-monolaurate,
iii) the limited available ecotoxicity data for sorbitan monolaurate and marine crustaceans and in marine sediment organisms, which indicate that the ecotoxicity of the additive is low, in consistency with the very low acute toxicity of sorbitan esters.

Overall, the FEEDAP Panel concludes that an environmental risk of sorbitan monolaurate to terrestrial and aquatic organisms is unlikely. Therefore, no safety concerns for the environment are expected from the use of the additive under assessment according to the proposed conditions of use.

4. Conclusions

No safety concerns for the environment are expected from the use of the additive under assessment according to the established conditions of use.

5. Documentation as provided to EFSA/Chronology

Date	Event
02/04/2019	Dossier received by EFSA. Sorbitan monolaurate for all animal species. Submitted by Kemin Europa N.V
10/07/2019	Reception mandate from the European Commission
19/09/2019	Application validated by EFSA – Start of the scientific assessment
04/12/2019	Request of supplementary information to the applicant in line with Article 8(1)(2) of Regulation (EC) No 1831/2003 – Scientific assessment suspended. *Issues: safety for the environment*
19/02/2020	Reception of supplementary information from the applicant - Scientific assessment re-started
25/05/2020	Opinion adopted by the FEEDAP Panel. End of the Scientific assessment

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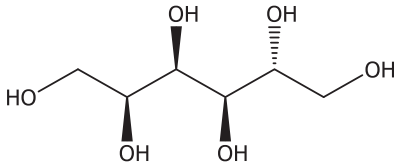
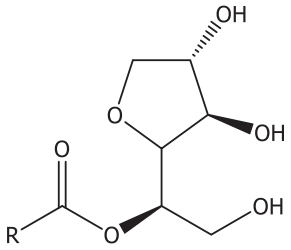
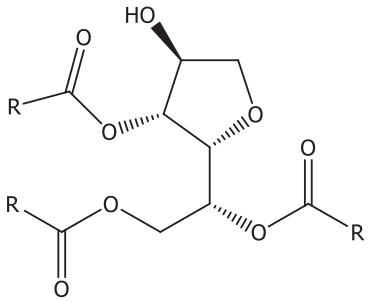
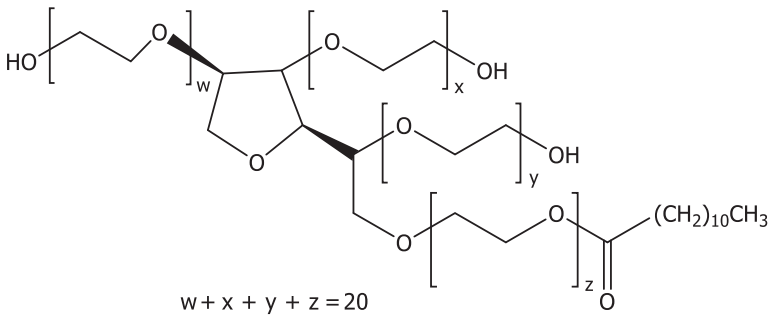
Abbreviations

ADME	Absorption, distribution, metabolism and excretion
CAS	Chemical Abstracts Service
BODIS test	Test of biochemical oxygen demand of insoluble substances
DM	dry matter
EC_{50}	the concentration of a test substance which results in 50% of the test organisms being adversely affected, i.e. both mortality and sublethal effects
GLP	Good laboratory practice
Kd	sorption/desorption coefficient
LC_{50}	the concentration of a test substance which results in a 50% mortality of the test species
Log Kow	logarithm of octanol-water partition coefficient
MW	molecular weight
PEC	Predicted environmental concentration
PNEC	Predicted no effect concentration
US EPA	United States environmental protection Agency

Appendix A – Chemical structure of the compounds of the additive and similar compounds relevant for the assessment

Chemical structure of the different compounds of the additive and similar compounds considered relevant for the assessment, retrieved from the literature review.

	Sorbitol	
	Sorbitan caprylateSorbitan caprateSorbitan monolaurateSorbitan myristateSorbitan monopalmitateSorbitan monostearateSorbitan monooleateSorbitan linoleate	$R=CH_3(CH_2)_6$ $R=CH_3(CH_2)_8$ $R=CH_3(CH_2)_{10}$ $R=CH_3(CH_2)_{12}$ $R=CH_3(CH_2)_{14}$ $R=CH_3(CH_2)_{16}$ $R=CH_3(CH_2)_7CH=CH(CH_2)_7$ $R=CH_3(CH_2)_4CH=CHCH_2CH=CH(CH_2)_7$
	Sorbitan trioleate	$R=CH_3(CH_2)_7CH=CH(CH_2)_7$
 w + x + y + z = 20		Polyoxyethylene-sorbitan-monolaurate