SCIENTIFIC OPINION

Scientific Opinion on the safety and efficacy of primary aliphatic saturated or unsaturated alcohols/aldehydes/acids/acetals/esters with a second primary, secondary or tertiary oxygenated functional group including aliphatic lactones (chemical group 9) when used as flavourings 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

ABSTRACT

Chemical group 9 consists of primary aliphatic saturated or unsaturated alcohols/aldehydes/acids/acetals/esters with a second primary, secondary or tertiary oxygenated functional group including aliphatic lactones, of which 30 are currently authorised for use as flavours in food. The FEEDAP Panel was unable to perform an assessment of 2-oxopropanal because of issues related to the purity of the compound. The FEEDAP Panel concludes that lactic acid, succinic acid, fumaric acid, 4-oxovaleric acid, ethyl lactate, butyl lactate, butyl-O-butyryllactate, hex-3-enyl lactate, hexyl lactate, ethyl acetoacetate, ethyl 4-oxovalerate, diethylsuccinate and diethyl malonate are considered to be safe for all animal species at the use levels proposed when used as feed flavourings; octano-1,4-lactone, nonano-1,4-lactone, decano-1,4-lactone and undecano-1,4-lactone are safe at 20 mg/kg complete feed; butyro-1,4-lactone, pentano-1,4-lactone, hexano-1,4-lactone, heptano-1,4-lactone, octano-1,5-lactone, nonano-1,5-lactone, decano-1,5-lactone and undecano-1,5-lactone at 5 mg/kg complete feed; dodecano-1,4-lactone, dodecano-1,5-lactone, tetradecano-1,5-lactone, and pentadecano-1,15-lactone at a maximum of 1.5 mg/kg complete feed for cattle, salmonids and non food producing animals and of 1 mg/kg complete feed for pigs and poultry. No safety concern was identified for the consumer from the use of compounds belonging to CG 9 up to the highest safe level in feedingstuffs for all animal species. All compounds should be considered as irritants to skin, eyes and respiratory tract, and as skin sensitizers. The compounds do not pose a risk to the environment when used at concentrations considered safe for the target species. Since all compounds are used in food as flavourings, no further demonstration of efficacy is necessary.

[1] On request from the European Commission, Question No EFSA-Q-2010-01177, adopted on 17 October 2012.

[2] Panel members: Gabriele Aquilina, Alex Bach, Vasileios Bampidis, Maria De Lourdes Bastos, Gerhard Flachowsky, Josep Gasa-Gasó, Mikolaj Gralak, Christer Hogstrand, Lubomir Leng, Secundino López-Puente, Giovanna Martelli, Baltasar Mayo, Derek Renshaw, Guido Rychen, Maria Saarela, Kristen Sejrsen, Patrick Van Beelen, Robert John Wallac and Johannes Westendorf. Correspondence: FEEDAP@efsa.europa.eu

[3] Acknowledgement: The Panel wishes to thank the members of the Working Group on Feed Flavourings, including Georges Bories, Paul Brantom, Andrew Chesson, Joop de Knecht, Jürgen Gropp, Anne-Katrine Lundebye Haldorsen, and Guido Rychen, for the preparatory work on this scientific opinion.

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KEY WORDS

Sensory additives, flavourings, primary aliphatic saturated or unsaturated alcohols/aldehydes/acids/acetals/esters with a second primary, secondary or tertiary oxygenated functional group including aliphatic lactones, chemical group 9, 2-oxopropanal, lactic acid, 4-oxovaleric acid, succinic acid, fumaric acid, ethyl acetoacetate, ethyl lactate, butyl lactate, ethyl 4-oxovalerate, diethyl succinate, diethyl malonate, butyl O-butyryllactate, hex-3-enyl lactate, hexyl lactate, nonano-1,4-lactone, undecano-1,4-lactone, pentadecano-1,15-lactone, butyro-1,4-lactone, decano-1,5-lactone, dodecano-1,5-lactone, undecano-1,5-lactone, pentano-1,4-lactone, nonano-1,5-lactone, octano-1,5-lactone, tetradecano-1,5-lactone, decano-1,4-lactone, dodecano-1,4-lactone, heptano-1,4-lactone, hexano-1,4-lactone and octano-1,4-lactone

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 safety and efficacy of 30 compounds (primary aliphatic saturated or unsaturated alcohols/aldehydes/ acids/acetals/esters with a second primary, secondary or tertiary oxygenated functional group including aliphatic lactones belonging to chemical group 9) when used as flavourings for all animal species. All 30 compounds are currently authorised for use as flavours in food and have all been detected in plant materials, in fruits or in processed foods. However the reports of their distribution vary greatly.

The FEEDAP Panel was unable to perform an assessment of 2-oxopropanal because of issues related to the purity of the compound.

The FEEDAP Panel concludes that lactic acid, succinic acid, fumaric acid, 4-oxovaleric acid, ethyl lactate, butyl lactate, butyl-O-butyryllactate, hex-3-enyl lactate, hexyl lactate, ethyl acetoacetate, ethyl 4-oxovalerate, diethylsuccinate and diethyl malonate are considered to be safe for all animal species at the use levels proposed when used as feed flavourings; octano-1,4-lactone, nonano-1,4-lactone, decano-1,4-lactone and undecano-1,4-lactone, and are safe at 20 mg/kg complete feed (with a margin of safety ranging from 1 to 3.5); butyro-1,4-lactone, pentano-1,4-lactone, hexano-1,4-lactone, heptano-1,4-lactone, octano-1,5-lactone, nonano-1,5-lactone, decano-1,5-lactone and undecano-1,5-lactone at 5 mg/kg complete feed (with a margin of safety ranging from 4 to 14); dodecano-1,4-lactone, dodecano-1,5-lactone, tetradecano-1,5-lactone, and pentadecano-1,15-lactone at a maximum of 1.5 mg/kg complete feed for cattle, salmonids and non food producing animals and of 1 mg/kg complete feed for pigs and poultry. The absence of a margin of safety would not allow the simultaneous administration in feed and water for drinking of these substances.

No safety concern would arise for the consumer from the use of compounds belonging to CG 9 up to the highest safe level in feedingstuffs for all animal species.

The FEEDAP Panel considers it prudent to treat all compounds under assessment as irritants to skin, eyes and respiratory tract, and as skin sensitizers.

The compounds considered to be safe for the target species are extensively metabolised by the target species and excreted as innocuous metabolites and carbon dioxide. Therefore no environmental risk assessment is considered necessary.

Since all 29 compounds are used in food as flavourings, and their function in feed is essentially the same as that in food, no further demonstration of efficacy is necessary.

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BACKGROUND

Regulation (EC) No 1831/2003[4] 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; in addition, 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 time limit or pursuant to Directive 82/471/EEC.

The European Commission received a request from the Feed Flavourings Authorisation Consortium European Economic Interest Grouping (FFAC EEIG)[5] for authorisation of the 30 substances listed in Table 1 belonging to chemical group 9 (primary aliphatic saturated or unsaturated alcohols/aldehydes/acids/acetals/esters with a second primary, secondary or tertiary oxygenated functional group including aliphatic lactones) to be used as feed additives for all animal species (category: sensory additives; functional group: flavourings) 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 4(1) (authorisation of a feed additive or new use of a feed additive) and 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.[6] 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 24 November 2011.

The additives are listed as food and feed flavourings in the register of Flavouring substances (CD 217/1999)[7] and in the European Union Register of Feed Additives, respectively. They have not been previously assessed by EFSA for this purpose.

The 30 substances belonging to CG 9 except succinic acid and hexyl lactate have been previously assessed by JECFA (1999, 2000 and 2002). According to Regulation (EC) No 1565/2000,[8] 'Substances classified by JECFA as to present no safety concern at the current levels of intake with the exception of substances which have been accepted on the sole basis that their estimated intake is lower than the threshold of concern of 1.5 µg per person per day, as laid down in the reports of the 46th, 49th, 51st and 53rd JECFA meetings need not to be re-evaluated.' Sixteen substances evaluated by JECFA in 1999 and six substances evaluated in 2000, were not further evaluated by EFSA. 2-Oxopropanal, lactic acid, ethyl lactate, butyl lactate, butyl-O-butyryllactate and hex-3-enyl lactate have been assessed by both JECFA (2002) and EFSA (2009b) as food flavourings. Succinic acid and hexyl lactate have been assessed by EFSA only (2009a).

[4] 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.

[5] Feed Flavourings Authorisation Consortium European Economic Interest Grouping (FFAC EEIG), Avenue Louise 130A, B-1050, Brussels, Belgium.

[6] EFSA Dossier reference: FAD-2010-0097.

[7] Commission Decision of 23 February 1999 adopting a register of flavouring substances used in or on foodstuffs drawn up in application of Regulation (EC) No 2232/96 of the European Parliament and of the Council of 28 October 1996. OJ L 84, 27.3.1999, p. 1.

[8] Commission Regulation (EC) No 1565/2000 of 18 July 2000 laying down the measures necessary for the adoption of an evaluation programme in application of Regulation (EC) No 2232/96 of the European Parliament and of the Council. OJ L 180, 19.7.2000, p. 8.

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, consumer, user and the environment and the efficacy of the active substances listed in Table 1, when used under the conditions described in Table 1.

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

Additive	Chemical defined flavourings from Chemical Group 9: 2-Oxopropanal 4-Oxovaleric acid Butyl lactate Butyl-O-butyryllactate Butyro-1,4-lactone Decano-1,4-lactone Decano-1,5-lactone Diethyl malonate Diethyl succinate Dodecano-1,4-lactone Dodecano-1,5-lactone Ethyl 4-oxovalerate Ethyl acetoacetate Ethyl lactate Fumaric acid Heptano-1,4-lactone Hex-3-enyl lactate Hexano-1,4-lactone Hexyl lactate Lactic acid Nonano-1,4-lactone Nonano-1,5-lactone Octano-1,4-lactone Octano-1,5-lactone Pentadecano-1,15-lactone Pentano-1,4-lactone Succinic acid Tetradecano-1,5-lactone Undecano-1,4-lactone Undecano-1,5-lactone
Registration number/EC No/No (if appropriate)	-
Category(ies) of additive	2. Sensory additives
Functional group(s) of additive	b) flavouring compounds

Description			
Composition, description	Chemical formula	Purity criteria (if appropriate)	Method of analysis (if appropriate)
2-Oxopropanal (CAS No 78-98-8)	$C_3H_4O_2$	95%	Gas Chromatography – Mass Spectrometry (GC-MS)
4-Oxovaleric acid (CAS No 123-76-2)	$C_5H_8O_3$	97%	Gas Chromatography – Mass Spectrometry (GC-MS)
Butyl lactate (CAS No 138-22-7)	$C_7H_{14}O_3$	95%	Gas Chromatography – Mass Spectrometry (GC-MS)
Butyl-O-butyryllactate (CAS No 7492-70-8)	$C_{11}H_{20}O_4$	95%	Gas Chromatography – Mass Spectrometry (GC-MS)
Butyro-1,4-lactone (CAS No 96-48-0)	$C_4H_6O_2$	98%	Gas Chromatography – Mass Spectrometry (GC-MS)
Decano-1,4-lactone (CAS No 706-14-9)	$C_{10}H_{18}O_2$	95%	Gas Chromatography – Mass Spectrometry (GC-MS)
Decano-1,5-lactone (CAS No 705-86-2)	$C_{10}H_{18}O_2$	98%	Gas Chromatography – Mass Spectrometry (GC-MS)

Diethyl malonate (CAS No 105-53-3)	$C_7H_{12}O_4$	97%	Gas Chromatography – Mass Spectrometry (GC-MS)
Diethyl succinate (CAS No 123-25-1)	$C_8H_{14}O_4$	98%	Gas Chromatography – Mass Spectrometry (GC-MS)
Dodecano-1,4-lactone (CAS No 2305-05-7)	$C_{12}H_{22}O_2$	97%	Gas Chromatography – Mass Spectrometry (GC-MS)
Dodecano-1,5-lactone (CAS No 713-95-1)	$C_{12}H_{22}O_2$	98%	Gas Chromatography – Mass Spectrometry (GC-MS)
Ethyl 4-oxovalerate (CAS No 539-88-8)	$C_7H_{12}O_3$	98%	Gas Chromatography – Mass Spectrometry (GC-MS)
Ethyl acetoacetate (CAS No 141-97-9)	$C_6H_{10}O_3$	97.5%	Gas Chromatography – Mass Spectrometry (GC-MS)
Ethyl lactate (CAS No 97-64-3)	$C_5H_{10}O_3$	97%	Gas Chromatography – Mass Spectrometry (GC-MS)
Fumaric acid (CAS No 110-17-8)	$C_4H_4O_4$	99.5%	Gas Chromatography – Mass Spectrometry (GC-MS)
Heptano-1,4-lactone (CAS No 105-21-5)	$C_7H_{12}O_2$	98%	Gas Chromatography – Mass Spectrometry (GC-MS)
Hex-3-enyl lactate (CAS No 61931-81-5)	$C_9H_{16}O_3$	96%	Gas Chromatography – Mass Spectrometry (GC-MS)
Hexano-1,4-lactone (CAS No 695-06-7)	$C_6H_{10}O_2$	98%	Gas Chromatography – Mass Spectrometry (GC-MS)
Hexyl lactate (CAS No 20279-51-0)	$C_9H_{18}O_3$	95%	Gas Chromatography – Mass Spectrometry (GC-MS)
Lactic acid (CAS No 598-82-3, 50-21-5, 79-33-4)	$C_3H_6O_3$	95%	Gas Chromatography – Mass Spectrometry (GC-MS)
Nonano-1,4-lactone (CAS No 104-61-0)	$C_9H_{16}O_2$	98%	Gas Chromatography – Mass Spectrometry (GC-MS)
Nonano-1,5-lactone (CAS No 3301-94-8)	$C_9H_{16}O_2$	98%	Gas Chromatography – Mass Spectrometry (GC-MS)
Octano-1,4-lactone (CAS No 104-50-7)	$C_8H_{14}O_2$	95%	Gas Chromatography – Mass Spectrometry (GC-MS)
Octano-1,5-lactone (CAS No 698-76-0)	$C_8H_{14}O_2$	98%	Gas Chromatography – Mass Spectrometry (GC-MS)
Pentadecano-1,15-lactone (CAS No 106-02-5)	$C_{15}H_{28}O_2$	98%	Gas Chromatography – Mass Spectrometry (GC-MS)
Pentano-1,4-lactone (CAS No 108-29-2)	$C_5H_8O_2$	95%	Gas Chromatography – Mass Spectrometry (GC-MS)
Succinic acid (CAS No 110-15-6)	$C_4H_6O_4$	99%	Gas Chromatography – Mass Spectrometry (GC-MS)
Tetradecano-1,5-lactone (CAS No 2721-22-4)	$C_{14}H_{26}O_2$	97%	Gas Chromatography – Mass Spectrometry (GC-MS)
Undecano-1,4-lactone (CAS No 104-67-6)	$C_{11}H_{20}O_2$	98%	Gas Chromatography – Mass Spectrometry (GC-MS)
Undecano-1,5-lactone (CAS No 710-04-3)	$C_{11}H_{20}O_2$	98%	Gas Chromatography – Mass Spectrometry (GC-MS)

Trade name (if appropriate)	-
Name of the holder of authorisation (if appropriate)	-

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 species	-	-	-	-

and categories				

Other provisions and additional requirements for the labelling	
Specific conditions or restrictions for use (if appropriate)	-
Specific conditions or restrictions for handling (if appropriate)	All feedingstuffs and water for drinking, as part of a premixture only
Post-market monitoring (if appropriate)	-
Specific conditions for use in complementary feedingstuffs (if appropriate)	-

Maximum Residue Limit (MRL) (if appropriate)			
Marker residue	Species or category of animal	Target tissue(s) or food products	Maximum content in tissues
-	-	-	-

ASSESSMENT

1. Introduction

The Chemical Group (CG) 9 for flavouring substances is defined in Commission Regulation (EC) No 1565/2000[9] as 'primary aliphatic saturated or unsaturated alcohols/aldehydes/acids/acetals/esters with a second primary, secondary or tertiary oxygenated functional group including aliphatic lactones'. The present application concerns 30 compounds, which can be assigned to this CG. The flavours included in this assessment have all been detected in plant materials, fruits or in processed foods (e.g., cheese, wine, and cider)*;* however, the reports of their distribution vary greatly.

The 30 compounds belonging to CG 9 except succinic acid and hexyl lactate have been previously assessed by JECFA (1999, 2000 and 2002). According to Regulation (EC) No 1565/2000,[9] 'Substances classified by JECFA as to present no safety concern at the current levels of intake with the exception of substances which have been accepted on the sole basis that their estimated intake is lower than the threshold of concern of 1.5 µg per person per day, as laid down in the reports of the 46th, 49th, 51st and 53rd JECFA meetings need not to be re-evaluated.' Sixteen substances evaluated by JECFA in 1999 and six substances evaluated in 2000 were not further evaluated by EFSA. 2-Oxopropanal, lactic acid, ethyl lactate, butyl lactate, butyl-O-butyryllactate and hex-3-enyl lactate have been assessed by both JECFA (2002) and EFSA (2009b) as food flavourings. Succinic acid and hexyl lactate have been assessed by EFSA only (2009a). The 30 compounds are currently listed in the European Union database of flavouring substances and as such authorised for use in food.

A consortium of companies (FFAC) supplying flavours to the feed industry has requested authorisation for the use of the substances listed in Table 2 as additives to feed and water for drinking (category: sensory additives, flavouring compounds) for use in all animal species.

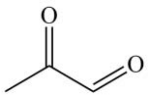
Regulation (EC) No 429/2008[10] allows substances already approved for use in human food to be assessed with a more limited procedure than for other feed additives. However, the use of this procedure is always subject to the condition that food safety assessment is relevant to the use in feed.

2. Characterisation

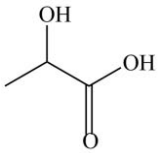
2.1. Characterisation of the flavouring additives

The molecular structures of the additives under application are shown in Figure 1 and their physico-chemical characteristics are summarised in Table 2.

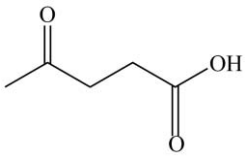
2-Oxopropanal (07.001)



Lactic acid (08.004)



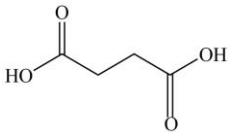
4-Oxovaleric acid (08.023)



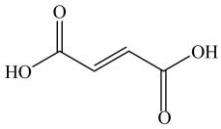
[9] Commission Regulation (EC) No 1565/2000 of 18 July 2000 laying down the measures necessary for the adoption of an evaluation programme in application of Regulation (EC) No 2232/96 of the European Parliament and of the Council. OJ L 180, 19.7.2000, p. 8.

[10] 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. 1-65.

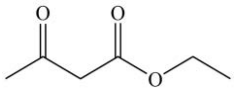
Succinic acid (08.024)



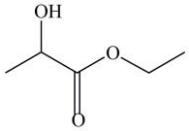
Fumaric acid (08.025)



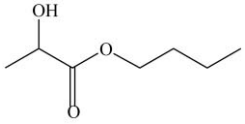
Ethyl acetoacetate (09.402)



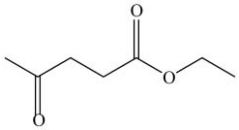
Ethyl lactate (09.433)



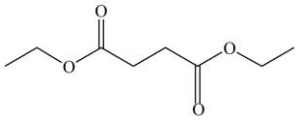
Butyl lactate (09.434)



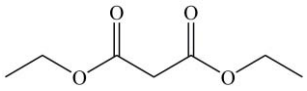
Ethyl 4-oxovalerate (09.435)



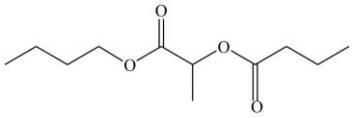
Diethyl succinate (09.444)



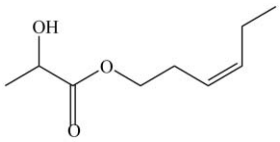
Diethyl malonate (09.490)



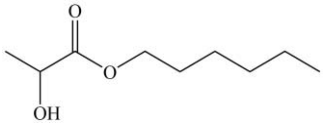
Butyl-O-butyryllactate (09.491)



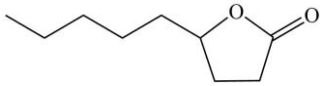
Hex-3-enyl lactate (09.545)



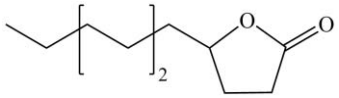
Hexyl lactate (09.580)



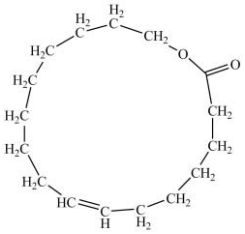
Nonano-1,4-lactone (10.001)



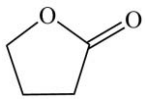
Undecano-1,4-lactone (10.002)



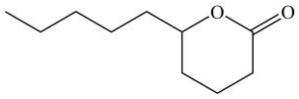
Pentadecano-1,15-lactone (10.005)



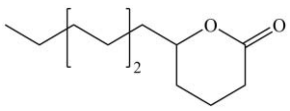
Butyro-1,4-lactone (10.006)



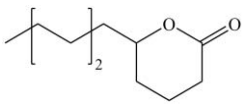
Decano-1,5-lactone (10.007)



Dodecano-1,5-lactone (10.008)

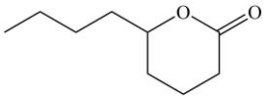


Undecano-1,5-lactone (10.011)

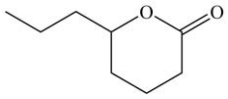


Pentano-1,4-lactone (10.013)

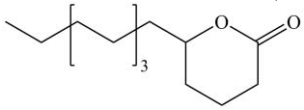
Nonano-1,5-lactone (10.014)



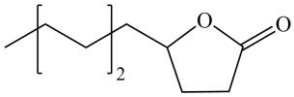
Octano-1,5-lactone (10.015)



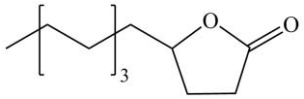
Tetradecano-1,5-lactone (10.016)



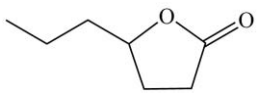
Decano-1,4-lactone (10.017)



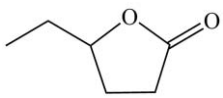
Dodecano-1,4-lactone (10.019)



Heptano-1,4-lactone (10.020)



Hexano-1,4-lactone (10.021)



Octano-1,4-lactone (10.022)

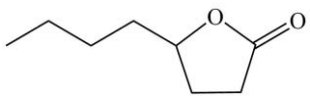


Figure 1: Molecular structures and FLAVIS numbers of flavourings of CG 9

Table 2: Chemically defined flavourings of CG 9 under application

EU Register name	CAS No.	Flavis No.	Molecular formula	Molecular weight	Physical status	Log K_{ow}
2-Oxopropanal	78-98-8	07.001	$C_3H_4O_2$	72.06	Liquid	-1.5
Lactic acid	598-82-3[#]	08.004	$C_3H_6O_3$	90.08	Solid	-0.72
4-Oxovaleric acid	123-76-2	08.023	$C_5H_8O_3$	116.12	Liquid	-0.49
Succinic acid	110-15-6	08.024	$C_4H_6O_4$	118.09	Solid	-0.59
Fumaric acid	110-17-8	08.025	$C_4H_4O_4$	116.07	Solid	0.46
Ethyl acetoacetate	141-97-9	09.402	$C_6H_{10}O_3$	130.14	Liquid	0.25
Ethyl lactate	97-64-3	09.433	$C_5H_{10}O_3$	118.13	Liquid	-0.18
Butyl lactate	138-22-7	09.434	$C_7H_{14}O_3$	149.19	Liquid	0.80
Ethyl 4-oxovalerate	539-88-8	09.435	$C_7H_{12}O_3$	144.17	Liquid	0.29
Diethyl succinate	123-25-1	09.444	$C_8H_{14}O_4$	174.2	Liquid	1.2
Diethyl malonate	105-53-3	09.490	$C_7H_{12}O_4$	160.17	Liquid	0.96
Butyl-O-butyryllactate	7492-70-8	09.491	$C_{11}H_{20}O_4$	216.28	Liquid	2.79*
Hex-3-enyl lactate	61931-81-5	09.545	$C_9H_{16}O_3$	172.22	Liquid	1.57*
Hexyl lactate	20279-51-0	09.580	$C_9H_{18}O_3$	174.24	Liquid	3.32
Nonano-1,4-lactone	104-61-0	10.001	$C_9H_{16}O_2$	156.22	Liquid	2.21*
Undecano-1,4-lactone	104-67-6	10.002	$C_{11}H_{20}O_2$	184.28	Liquid	3.06
Pentadecano-1,15-lactone	106-02-5	10.004	$C_{15}H_{28}O_2$	240.39	Solid	6.15
Butyro-1,4-lactone	96-48-0	10.006	$C_4H_6O_2$	86.09	Liquid	-0.64
Decano-1,5-lactone	705-86-2	10.007	$C_{10}H_{18}O_2$	170.25	Liquid	2.57*
Dodecano-1,5-lactone	713-95-1	10.008	$C_{12}H_{22}O_2$	198.31	Liquid	3.55*
Undecano-1,5-lactone	701-04-3	10.011	$C_{11}H_{20}O_2$	184.28	Liquid	3.06*
Pentano-1,4-lactone	108-29-2	10.013	$C_5H_8O_2$	100.12	Liquid	-0.13*
Nonano-1,5-lactone	3301-94-8	10.014	$C_9H_{16}O_2$	156.22	Liquid	2.08*
Octano-1,5-lactone	698-76-0	10.015	$C_8H_{14}O_2$	142.2	Liquid	1.59*
Tetradecano-1,5-lactone	2721-22-4	10.016	$C_{14}H_{26}O_2$	226.4	Liquid	4.53
Decano-1,4-lactone	706-14-9	10.017	$C_{10}H_{18}O_2$	170.25	Liquid	2.72
Dodecano-1,4-lactone	2305-05-7	10.019	$C_{12}H_{22}O_2$	198.31	Liquid	3.46*
Heptano-1,4-lactone	105-21-5	10.020	$C_7H_{12}O_2$	128.17	Liquid	1.19*
Hexano-1,4-lactone	695-06-7	10.021	$C_6H_{10}O_2$	114.14	Liquid	0.60
Octano-1,4-lactone	104-50-7	10.022	$C_8H_{14}O_2$	142.2	Liquid	1.72*

[#] Three CAS numbers have been used to identify lactic acid, two refer to DL-lactic acid (50-21-5 and CAS no 598-82-3) and one to the isomer L-lactic acid (79-33-4). They are all relevant to the assessment of this compound

* Generated from Epi-Suite 4.01

All 30 substances are produced by chemical synthesis. Typically several routes of synthesis are available and described in the dossier.[11]

Data was provided on the batch to batch variation in five batches of each additive (with the exception of oxopropanal, fumaric acid and tetradecano-1,5-lactone (one batch was available) and hexyl lactate (four batches)).[12] Except for 2-oxopropanal, the content of the active substance exceeded the JECFA specifications (Combined Compendium of Food Additives Specifications; JECFA, 2006) for all compounds (Table 3). 2-Oxopropanal is specified to contain a minimum of 40 % in aqueous solution. This description does not allow the setting of a specification or the extrapolation of consumer safety assessments of 2-oxopropanal to this product. Consequently, this additive is excluded from further consideration.

[11] Technical dossiers/Section II.

[12] Technical dossiers/Section II/Annex 2.1 and Supplementary Information June 2011.

Table 3: Identification of the substances and data on purity

EU Register name	JECFA specification %	Assay %	
		Average	Range
2-Oxopropanal	> 95[a]	45.3[b]	45.3
Lactic acid	> 95	96.3	95.0–97.0
4-Oxovaleric acid	> 97	99.6	99.1–100
Succinic acid	> 99	99.4	99.1–99.7
Fumaric acid	> 99.5	99.8[b]	99.8
Ethyl acetoacetate	> 97.5	99.7	99.2–99.9
Ethyl lactate	> 97	99.6	98.0–100
Butyl lactate	> 95	99.4	99.0–99.8
Ethyl 4-oxovalerate	> 98	98.6	98.1–100
Diethyl succinate	> 98	99.7	99.4–100
Diethyl malonate	> 97	99.8	99.5–100
Butyl-O-butyryllactate	> 95	99.6	99.4–99.8
Hex-3-enyl lactate	> 96	98.5	98.2–98.7
Hexyl lactate	> 95	98.7[c]	98.4–98.6
Nonano-1,4-lactone	> 98	99.3	98.8–99.7
Undecano-1,4-lactone	> 98	99.1	98.5–99.5
Pentadecano-1,15-lactone	> 98	99.2	98.8–99.6
Butyro-1,4-lactone	> 98	98.8	98.1–100
Decano-1,5-lactone	> 98	98.8	98.0–99.3
Dodecano-1,5-lactone	> 98	99.0	98.4–99.7
Undecano-1,5-lactone	> 98	98.2	98.0–98.5
Pentano-1,4-lactone	> 95	99.7	98.7–100
Nonano-1,5-lactone	> 98	98.3	98.0–98.6
Octano-1,5-lactone	> 98	99.5	98.5–99.9
Tetradecano-1,5-lactone	> 97	98.6[b]	98.6
Decano-1,4-lactone	> 95	99.5	98.6–99.8
Dodecano-1,4-lactone	> 97	98.8	98.4–99.3
Heptano-1,4-lactone	> 98	99.6	98.9–99.9
Hexano-1,4-lactone	> 98	99.5	98.7–99.8
Octano-1,4-lactone	> 95	99.5	99.3–99.9

[a] Only available as 40 % aqueous solution; [b] One batch available; [c] average of four batches

Potential contaminants are considered as part of the product specification and are monitored as part of the HACCP procedure applied by all consortium members. The parameters considered include residual solvents, heavy metals and other undesirable substances.

2.2. Stability

The minimum shelf life for all compounds is 12 months with the majority stable for a longer period when stored in closed containers under recommended conditions (in a cool and dry place). This assessment is made on the basis of compliance with the original specification after storage.

Although no data is required for the stability of volatile additives in premixes and feed, use in water for drinking introduces other issues relating to product stability, such as degradation due to microbial activity.

The FEEDAP Panel notes that 13 out of 29 compounds in CG 9 have low water solubility (Log K_{ow} > 2) which makes it difficult to assess the safety in water for drinking. As no data on the short term stability of the additive in water for drinking were provided, the FEEDAP Panel is not in the position to comment on this route of administration.

2.3. Conditions of use

The applicant proposes the use of the 29 additives in feed or water for drinking for all animal species without withdrawal. In all cases the applicant proposes a normal use level in feed and a high use level of five times the normal levels:

- a normal use level of 25 mg/kg and a high use level of 125 mg/kg for ethyl lactate and nonano-1,4-lactone
- a normal use level of 5 mg/kg and a high use level of 25 mg/kg for octano-1,4-lactone, decano-1,4-lactone and undecano-1,4-lactone
- a normal use level of 1 mg/kg and a high use level of 5 mg/kg for the remaining compounds

No specific proposals are made for levels to be used in water for drinking.

2.4. 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 chemically defined flavourings from Group 9 – Primary aliphatic saturated or unsaturated alcohols/aldehydes/acids/acetals/esters with a second primary, secondary or tertiary oxygenated functional group including aliphatic lactones in animal feed. The Executive Summary of the EURL report can be found in the Appendix.

3. Safety

The assessment of safety is based on the high use level proposed by the applicant (125 mg/kg complete feed for ethyl lactate and nonano-1,4-lactone, 25 mg/kg complete feed for octano-1,4-lactone, decano-1,4-lactone and undecano-1,4-lactone, and 5 mg/kg complete feed for the other additives).

3.1. Safety for the target species

Lactic acid, succinic acid and fumaric acid are normal components of cell metabolism and are considered to be safe up to the highest proposed use level. Esters of these acids (ethyl lactate, butyl lactate, butyl-O-butyryllactate, hex-3-enyl lactate and hexyl lactate, diethylsuccinate and diethyl malonate) are generally rapidly hydrolysed to the corresponding acids and alcohols and thus raise no concerns when used as flavours in animal feed at the proposed levels. Ethyl acetoacetate and ethyl 4-oxovalerate are hydrolysed to their respective acids and alcohols, which are either normal components of cell metabolism or readily degraded by similar pathways (see section 3.2.1). The use of these esters as flavours is thus considered to be safe without restrictions for all animal species.

No further consideration on the safety for the target species of these compounds is deemed necessary.

For the remaining 16 compounds the first approach to the safety assessment for target species takes account of the applied use levels in animal feed relative to the maximum reported exposure of humans on the basis of the metabolic body weight. The data for human exposure in the EU (EFSA, 2009a,b) range between 73 and 1600 µg/person/day, corresponding to 3.4 and 74.2 µg/mbw ($kg^{0.75}$)/day. Table 5 summarises the result of the comparison for representative target animals at the maximum proposed dose level in complete feed with human exposure. The body weight of target animals is taken from the default values shown in Table 5.

Table 4: Comparison of exposure of humans and target animals to 16 of the flavourings under application

Flavouring	Use level in feed (mg/kg)	Human exposure µg/mbw ($kg^{0.75}$)/day*	Target animal exposure µg/mbw ($kg^{0.75}$)/day		
			Salmon	Piglet	Dairy cow
Nonano-1,4-lactone	125	46.4	2941	13158	19425
Undecano-1,4-lactone	25	10.8	588	2632	3885
Pentadecano-1,15-lactone	5	3.4	118	526	777
Butyro-1,4-lactone	5	5.1	118	526	777
Decano-1,5-lactone	5	334	118	526	777
Dodecano-1,5-lactone	5	269	118	526	777
Undecano-1,5-lactone	5	13.9	118	526	777
Pentano-1,4-lactone	5	5.6	118	526	777
Nonano-1,5-lactone	5	6.0	118	526	777
Octano-1,5-lactone	5	10.7	118	526	777
Tetradecano-1,5-lactone	5	5.1	118	526	777
Decano-1,4-lactone	25	74.2	588	2632	3885
Dodecano-1,4-lactone	5	8.8	118	526	777
Heptano-1,4-lactone	5	7.9	118	526	777
Hexano-1,4-lactone	5	7.4	118	526	777
Octano-1,4-lactone	25	19.9	588	2632	3885

* mbw = metabolic body weight (kg 0.75) for a 60 kg person = 21.6

The data in Table 4 clearly indicate that the intake by the target animals usually exceeds that of humans, resulting from use in food for all 16 compounds. As a consequence, safety for the target species at the feed concentration applied cannot be derived from the risk assessment for food use.

As an alternative the maximum feed concentration which can be considered as safe for the target animal can be derived from the lowest No Observed Adverse Effect Level (NOAEL) when suitable data is available. Toxicological data could be found for some of the 16 lactone compounds. The studies have been recently reviewed by EFSA Panel on Food Contact Materials, Enzymes, Flavourings and Processing Aids (CEF; EFSA, 2012a).

A NOAEL of 112 mg/kg bw per day was derived for butyro-1,4-lactone (or γ-butyrolactone) from a two-year carcinogenicity study in rats (50M/50F, doses: 0, 112, 225 mg/kg bw per day for male rats; 0, 225, 450 mg/kg bw per day for female rats; administration route: gavage) and mice (50M/50F, doses: 0, 262, 525 mg/kg bw per day; administration route: gavage) (NTP, 1992). The NOAEL of 112 mg/kg is based on a reduced survival of male rats at the dose of 225 mg/kg bw per day. No histopathological abnormalities could be observed at any dose level. There was no evidence of carcinogenic activity of butyro-1,4-lactone at the doses tested in male and female rats and female mice. There was equivocal evidence of carcinogenicity of butyro-1,4-lactone in male $B6C3F_1$ mice based on marginally increased incidences of adrenal medulla pheochromocytomas and hyperplasia at the low dose group (262 mg/kg bw per day) but not at the high dose group 525 mg/kg bw per day). This effect was not considered of relevance to other species in the report of the National Toxicology Program (NTP, 1992) and the FEEDAP Panel agrees with these conclusions.

On the basis of the structural and metabolic similarity (see section 3.2.2), the FEEDAP Panel considered the 16 lactone compounds as a single group and a group NOAEL approach was taken. The NOAEL derived from the study with butyro-1,4-lactone is considered to be relevant to each member of this group and is not in conflict with data for any individual substances (EFSA, 2012a). Following the EFSA Guidance for sensory additives (EFSA, 2012b), a safety factor of 100 to account for intra-species variation (2), inter-species variation (10) and uncertainty about the toxicity of untested compounds (5) was applied to this value and, thus, the maximum safe intake and the maximum safe feed concentration for different target species was derived for the following compounds belonging to

CG 9: butyro-1,4-lactone, pentano-1,4-lactone, hexano-1,4-lactone, heptano-1,4-lactone, octano-1,4-lactone, nonano-1,4-lactone, decano-1,4-lactone, undecano-1,4-lactone, octano-1,5-lactone, nonano-1,5-lactone, decano-1,5-lactone and undecano-1,5-lactone. The results of the calculations are shown in Table 5.

Table 5: Derived maximum safe concentration in feed for different target animals for 12 compounds belonging to CG 2 (see the list in the paragraph above)

Target animal	Default settings		Maximum safe intake/feed concentration	
	BW (kg)	FI (g/d)	Intake (mg/d)	mg/kg feed
Salmonids	2	40	2	56
Veal calves (milk replacer)	100	2000	112	56
Cattle for fattening	400	8000	448	56
Pigs for fattening	100	3000	112	37
Sows	200	6000	224	37
Dairy Cows	650	20000	728	36
Turkeys for fattening	12	400	13	34
Piglets	20	1000	22	22
Chickens for fattening	2	120	2	19
Laying hens	2	120	2	19
Dogs	15	250	17	67
Cats	3	60	3	56

Because of the higher lipophylicity (LogKow > 3.5) and the potential difference in toxicokinetics dodecano-1,4-lactone, dodecano-1,5-lactone, tetradecano-1,5-lactone and pentadecano-1,15-lactone were excluded from the group NOAEL approach. For these Cramer Class I compounds the threshold of toxicological concern (TTC) approach was adopted to derive the maximum safe feed concentration. The calculated safe use level for these compounds is 1.5 mg/kg complete feed for cattle, salmonids and non food producing animals and 1 mg/kg complete feed for pigs and poultry.

3.1.1. Conclusions on the safety for target species

Lactic acid, succinic acid and fumaric acid are normal components of cell metabolism and are considered to be safe up to the highest proposed use level. Esters of these acids (ethyl lactate, butyl lactate, butyl-O-butyryllactate, hex-3-enyl lactate and hexyl lactate, diethylsuccinate and diethyl malonate) are generally rapidly hydrolysed to the corresponding acids and alcohols and thus raise no concerns when used as flavours in animal feed at the proposed levels. Ethyl acetoacetate and ethyl 4-oxovalerate are hydrolysed to their respective acids and alcohols which are either normal components of cell metabolism or readily degraded by similar pathways (see section 3.2.1).

For the remaining 16 lactones, the FEEDAP Panel concludes that the use of the following is safe for all animal species:

- octano-1,4-lactone, nonano-1,4-lactone, decano-1,4-lactone and undecano-1,4-lactone at 20 mg/kg complete feed with a margin of safety ranging from 1 to 3.5

- butyro-1,4-lactone, pentano-1,4-lactone, hexano-1,4-lactone, heptano-1,4-lactone, octano-1,5-lactone, nonano-1,5-lactone, decano-1,5-lactone and undecano-1,5-lactone at 5 mg/kg complete feed with a margin of safety ranging from 4 to 14

- dodecano-1,4-lactone, dodecano-1,5-lactone, tetradecano-1,5-lactone, and pentadecano-1,15-lactone at a maximum of 1.5 mg/kg complete feed for cattle, salmonids and non food producing animals and of 1 mg/kg complete feed for pigs and poultry. The absence of a

margin of safety would not allow the simultaneous administration in feed and water for drinking of these substances

The total dose from all sources should not exceed that obtained when given in feed alone. Consequently the concentrations used when substances are administered in water for drinking should be proportionally reduced. The exact ratio for inclusion when used in both feed and water for drinking is beyond the scope of data available to the FEEDAP Panel.

3.2. Safety for the consumer

The safety for the consumer of CG 9 compounds when used as food flavours has already been assessed by JECFA (1999, 2000 and 2002) and/or EFSA (2009a, 2009b). An Acceptable Daily Intake (ADI) of 1.25 mg/kg bw was established for nonano-1,4-lactone and undecano-1,4-lactone. All 29 compounds are currently authorised as food additives without limitations.

As the intake of all 29 compounds by target animals exceeds that of humans resulting from use in food by one to three orders of magnitude, the metabolic fate and potential transfer of significant amounts of residues in edible tissues and products has to be considered.

3.2.1. Esters, acids and aldehydes containing additional oxygenated functional groups

According to JECFA (2000 and 2002), studies on the absorption, metabolism and elimination of aliphatic primary alcohols, aldehydes, carboxylic acids, acetals and esters with additional oxygenated functional groups show that these substances are readily hydrolysed and absorbed and are completely metabolized. Many of these substances or their metabolites are endogenous in humans. Mono-esters (ethyl acetoacetate, ethyl 4-oxovalerate and aliphatic esters of lactic acid) and di-esters (diethyl succinate and diethyl malonate) are expected to undergo hydrolysis in humans to yield their corresponding alcohol and acid components (i.e. β- or γ-keto or α-hydroxy acids; or diacids), which would be further metabolised and excreted through the common pathways of detoxication of aliphatic alcohols and carboxylic acids. JECFA stated also that the presence of a second oxygenated functional group has little if any effect on hydrolysis of these esters.

Hydrolysis is catalysed by classes of enzymes recognised as carboxylesterases or esterases (Heymann, 1980), the most important of which are the β-esterases (Heymann, 1980; Anders, 1989). Acetyl esters are the preferred substrates of C-esterases (Heymann, 1980). Mammalian carboxylesterases represent a multigene family and play an important role in the hydrolytic biotransformation of a vast number of structurally diverse drugs (Satoh and Hosokawa 1998). Carboxylesterase activity also plays a significant role in detoxification processes in fish (Di Giulio and Hinton 2008; Tocher, 2003) as well as in birds (Beasley, 1999). The most probable metabolic reactions of the hydrolysis products are: oxidation of alcohols to aldehydes and acids; conjugations of alcohols and acids to glucuronides and sulphates; β-oxidation of carboxylic acids; ω-oxidation of carboxylic acids.

β-Keto acids and derivatives like acetoacetic acid undergo decarboxylation. Along with α-keto and α-hydroxyacids (lactic acid), they yield breakdown products, which are incorporated into normal biochemical pathways. The γ-keto-acids and related substances (4-oxovaleric acid) may undergo complete or partial β-oxidation to yield metabolites that are eliminated in the urine. Simple aliphatic di-carboxylic acids (succinic acid and fumaric acid) and their precursors (2-oxopropanal) are metabolised in the fatty acid β-oxidation pathway or tricarboxylic acid cycle (EFSA, 2009a).

3.2.2. Lactones

In its evaluation, JECFA (1999) recognized that lactones are formed by acid-catalysed intramolecular cyclisation of γ- or δ-hydroxycarboxylic acids. In an aqueous environment, a pH-dependent

equilibrium is established between the open-chain hydroxycarboxylate anion and the lactone ring. In basic and neutral media, such as blood, the open-chain hydroxycarboxylate anion is favoured while in acidic media, such as gastric juice and urine, the lactone ring is favoured. Enzymes, such as lactonase, may catalyse the hydrolysis reaction, but for simple saturated lactones, the ring-opening reaction and reverse cyclization are in equilibrium, mainly controlled by pH conditions. Both the aliphatic lactones and the ring-opened hydroxycarboxylic acids can be absorbed from the gastrointestinal tract. However, the simple lactones with low molecular weight being uncharged may cross the cell membrane more easily than the acidic form, which penetrates the cells as a weak electrolyte (Guidotti and Ballotti, 1970).

In humans, paraoxonase (PON1), a serum enzyme belonging to the class of A-carboxyesterases (Aldridge, 1953), is known to rapidly hydrolyse a broad range of aliphatic lactone substrates including β-, γ-, δ- and ω-lactones, lactones fused to alicyclic rings such as 2-(2- hydroxycyclopent-4-enyl)ethanoic acid γ-lactone (Billecke et al., 2000). Activities of paraoxonase isoenzymes (Q & R) in human blood exhibit a bimodal distribution that is accounted for by a Q/R (glutamine or arginine) polymorphism with Q-type homozygotes showing a lower activity than QR heterozygotes or R homozygotes (Humbert et al., 1993). Members of the serum paraoxonase (PON) family have also been identified in other vertebrates than humans and mammals, where they exhibit a wide range of physiologically important hydrolytic activities (Estin et al., 2009; Tucker and Halver 1986).

JECFA stated also that the hydroxycarboxylic acid obtained from lactone hydrolysis enters the fatty acid pathway and undergoes α-oxidation (linear saturated 4- or 6-hydroxycarboxylic acids formed from γ- or ε-lactones) or β-oxidation (linear saturated 5-hydroxycarboxylic acids formed from delta-lactones) and cleavage to form acetyl CoA and a chain-shortened carboxylic acid. The carboxylic acid is then reduced by 2-carbon fragments until either acetyl CoA or propionyl CoA is produced. These fragments are then metabolised in the citric acid cycle (Voet and Voet, 1990). In rats and dogs, $^{14}CO_1$-gamma-decalactone and $^{14}CO_1$-gammadodecalactone are metabolised in a manner similar to $^{14}CO_1$-lauric acid, with approximately 75 % of the labeled ^{14}CO being eliminated as carbon dioxide within 48 hours (Fassett, 1961).

Information on hydrolysis of aliphatic lactones is mainly derived from studies on butyro-1,4-lactone (γ-butyrolactone), which has been extensively studied in animals and humans. The majority of ^{14}C-labeled 4-hydroxybutanoate administered by intravenous injection to rats was recovered as $^{14}CO_2$ within 2.5 hours (Roth and Giarman, 1965). Oxidation of γ-butyrolactone to succinate by alcohol dehydrogenase and succinic semialdehyde dehydrogenase occurs primarily in the liver (Jakoby and Scott, 1959); succinate then participates in the citric acid cycle (Walkenstein et al., 1964; Möhler et al., 1976; Lee, 1977; Doherty and Roth, 1978). However, this pathway accounts for only a limited proportion of the metabolised compound. The main biotransformation route through which γ-butyrolactone is metabolised is β-oxidation as indicated by the presence of (S)-3,4-dihydroxybutyric acid, glycolic acid and 3-oxobutyric acid in the urine of human volunteers given orally 1.0 g γ-butyrolactone (Lee, 1977); other intermediates derived from β-oxidation have been previously detected in samples of human urine (Walkenstein et al., 1964).

3.2.3. Conclusions on the safety for the consumer

Primary aliphatic saturated or unsaturated alcohols, aldehydes, acids, acetals and esters with a second primary, secondary or tertiary oxygenated functional group including aliphatic lactones are rapidly converted to innocuous substances. Mammals, birds and fish share a similar metabolic capacity to handle these compounds. Consequently, no safety concern would arise for the consumer from the use of these compounds up to the highest safe level in feeds.

3.3. Safety for the user

No experimental data on the safety for the user was provided. In the material safety data sheets[13] hazards for skin and eye contact and respiratory exposure are recognised for 18 (lactic acid, 4-oxovaleric acid, succinic acid, fumaric acid, ethyl acetoacetate, ethyl lactate, butyl lactate, diethyl succinate, diethyl malonate, butyl O-butyryllactate, hex-3-enyl lactate, undecano-1,4-lactone, butyro-1,4-lactone, dodecano-1,5-lactone, undecano-1,5-lactone, dodecano-1,4-lactone, heptano-1,4-lactone, and octano-1,4-lactone) out of the 29 compounds. Seventeen compounds are classified as irritating to eyes and/or skin. For three compounds (lactic acid, succinic acid and 2-ethyl lactate) the risk of serious damage to eyes is reported. Eleven compounds (lactic acid, succinic acid, ethyl lactate, butyl lactate, diethyl succinate, butyl O-butyryllactate, hex-3-enyl lactate, undecano-1,4-lactone, dodecano-1,5-lactone, undecano-1,5-lactone and dodecano-1,4-lactone) are identified as 'irritating to the respiratory system'. For the remaining substances, no hazards are identified, probably because the substances have not yet been tested.

The FEEDAP Panel considers it prudent to treat all compounds under assessment as irritants to skin, eyes and respiratory tract, and as skin sensitizers.

3.4. Safety for the environment

The compounds considered to be safe for the target species are extensively metabolised by the target species and excreted as innocuous metabolites and carbon dioxide. Therefore no environmental risk is foreseen.

4. Efficacy

Since all 29 compounds are used in food as flavourings, and their function in feed is essentially the same as that in food no further demonstration of efficacy is necessary.

CONCLUSIONS

The FEEDAP Panel was unable to perform an assessment of 2-oxopropanal because of issues related to the purity of the compound.

The following compounds are considered to be safe for all animal species at the use levels proposed when used as feed flavourings:

- lactic acid, succinic acid, fumaric acid, 4-oxovaleric acid, ethyl lactate, butyl lactate, butyl-O-butyryllactate, hex-3-enyl lactate, hexyl lactate, ethyl acetoacetate, ethyl 4-oxovalerate, diethylsuccinate and diethyl malonate

For the remaining 16 lactones, the FEEDAP Panel concludes that the use of the following is safe for all animal species:

- octano-1,4-lactone, nonano-1,4-lactone, decano-1,4-lactone and undecano-1,4-lactone at 20 mg/kg complete feed with a margin of safety ranging from 1 to 3.5

- butyro-1,4-lactone, pentano-1,4-lactone, hexano-1,4-lactone, heptano-1,4-lactone, octano-1,5-lactone, nonano-1,5-lactone, decano-1,5-lactone and undecano-1,5-lactone at 5 mg/kg complete feed with a margin of safety ranging from 4 to 14

[13] Technical dossier/Section II/Annex II.3.

– dodecano-1,4-lactone, dodecano-1,5-lactone, tetradecano-1,5-lactone and pentadecano-1,15-lactone at a maximum of 1.5 mg/kg complete feed for cattle, salmonids and non food producing animals and of 1 mg/kg complete feed for pigs and poultry. The absence of a margin of safety would not allow the simultaneous administration in feed and water for drinking of these substances.

No safety concern would arise for the consumer from the use of compounds belonging to CG 9 up to the highest safe level in feedingstuffs for all animal species.

The FEEDAP Panel considers it prudent to treat all compounds under assessment as irritants to skin, eyes and respiratory tract, and as skin sensitizers.

The compounds considered to be safe for the target species are extensively metabolised by the target species and excreted as innocuous metabolites and carbon dioxide. Therefore no environmental risk is foreseen.

Since all 29 compounds are used in food as flavourings, and their function in feed is essentially the same as that in food, no further demonstration of efficacy is necessary.

DOCUMENTATION PROVIDED TO EFSA

1. Chemically defined flavourings from Flavouring Group 09 - Primary aliphatic saturated or unsaturated alcohols/aldehydes/acids/acetals/esters with a second primary, secondary or tertiary oxygenated functional group including aliphatic lactones (CDG 9) for all animal species and categories. October 2010. Submitted by Feed Flavourings Authorisation Consortium European Economic Interest Grouping (FFAC EEIG).

2. Chemically defined flavourings from Flavouring Group 09 - Primary aliphatic saturated or unsaturated alcohols/aldehydes/acids/acetals/esters with a second primary, secondary or tertiary oxygenated functional group including aliphatic lactones (CDG 9) for all animal species and categories. Supplementary information. June 2011. Submitted by Feed Flavourings Authorisation Consortium European Economic Interest Grouping (FFAC EEIG).

3. Chemically defined flavourings from Flavouring Group 09 - Primary aliphatic saturated or unsaturated alcohols/aldehydes/acids/acetals/esters with a second primary, secondary or tertiary oxygenated functional group including aliphatic lactones (CDG 9) for all animal species and categories. Supplementary information. April 2012. Submitted by Feed Flavourings Authorisation Consortium European Economic Interest Grouping (FFAC EEIG).

4. Evaluation report of the European Union Reference Laboratory for Feed Additives on the methods(s) of analysis for Chemically Defined Flavourings – Group 9 (CDG 9 Primary aliphatic saturated or unsaturated alcohols/aldehydes/acids/acetals/esters with a second primary, secondary or tertiary oxygenated functional group including aliphatic lactones).

5. Comments from Member States received through the ScienceNet.

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APPENDIX

Executive Summary of the Evaluation Report of the European Union Reference Laboratory for Feed Additives on the Method(s) of Analysis for Chemically Defined Flavourings – Group 09 (CDG09, Primary aliphatic saturated or unsaturated alcohols/aldehydes/acids/acetals/esters with a second primary, secondary or tertiary oxygenated functional group including aliphatic lactones)[14]

The *Chemically Defined Flavourings - Group 09 (Primary aliphatic saturated or unsaturated alcohols/aldehydes/acids/acetals/esters with a second primary, secondary or tertiary oxygenated functional group including aliphatic lactones*), in this application comprises thirty substances, for which authorisation as feed additives is sought under the category "sensory additives", functional group 2(b) "flavouring compounds", according to the classification system of Annex I of Regulation (EC) No 1831/2003.

In the current application submitted according to Article 4(1) and Article 10(2) of Regulation (EC) No 1831/2003, the authorisation for all species and categories is requested. The flavouring compounds of interest have a purity ranging from 95% to 99.5%.

Mixtures of flavouring compounds are intended to be incorporated only into *feedingstuffs* or drinking *water*. The Applicant suggested no minimum or maximum levels for the different flavouring compounds in *feedingstuffs* or in *water*.

For the identification of volatile chemically defined flavouring compounds *CDG 09* in the *feed additive*, the Applicant submitted a qualitative multi-analyte gas-chromatography mass-spectrometry (GC-MS) method, using Retention Time Locking (RTL), which allows a close match of retention times on GC-MS. By making an adjustment to the inlet pressure, the retention times can be closely matched to those of a reference chromatogram. It is then possible to screen samples for the presence of target compounds using a mass spectral database of RTL spectra. The Applicant maintained two FLAVOR2 databases/libraries (for retention times and for MS spectra) containing data for more than 409 flavouring compounds. These libraries were provided to the EURL. The Applicant provided the typical chromatogram for the *CDG 09* of interest.

In order to demonstrate the transferability of the proposed analytical method (relevant for the method verification), the Applicant prepared a model mixture of flavouring compounds on a solid carrier to be identified by two independent expert laboratories. This mixture contained twenty chemically defined flavourings belonging to twenty different chemical groups to represent the whole spectrum of compounds in use as feed flavourings with respect to their volatility and polarity. Both laboratories properly identified all the flavouring compounds in all the formulations. Since the substances of *CDG 09* are within the volatility and polarity range of the model mixture tested, the Applicant concluded that the proposed analytical method is suitable to determine qualitatively the presence of the substances from *CDG 09* in the *mixture of flavouring compounds*.

Based on the satisfactory experimental evidence provided, the EURL recommends for official control for the qualitative identification in the *feed additive* of the individual (or mixture of) *flavouring compounds* of interest listed in Table 1 (*) the GC-MS-RTL (Agilent specific) method submitted by the Applicant.

As no experimental data were provided by the Applicant for the identification of the *active substance(s)* in *feedingstuffs* and *water*, no methods could be evaluated. Therefore the EURL is

[14] The full report is available on the EURL website http://irmm.jrc.ec.europa.eu/SiteCollectionDocuments/FinRep-FAD-2010-0097.pdf

unable to recommend a method for the official control to identify the *active substance(s)* of interest listed in Table 1 (*) in *feedingstuffs* or *water*.

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.

(*)Full list provided in EURL evaluation report, available from the EURL website.