CATEGORY 2 - 'Rosin Esters'

UVCB CATEGORY JUSTIFICATION DOCUMENT

1.0 CATEGORY DEFINITION AND ITS MEMBERS

This document describes the Rosins Esters category and its members as per ECHA guidance R6: QSARs and grouping of chemicals (2008) the ECHA Read-Across Assessment Framework[1] and the specific guidance for UVCBs[2]. Although this format is more applicable to analogue or chemical categories the main headings of the guidance are included for this UVCB category to ensure consistency in reporting.

The category includes three sub-categories: Simple esters, Linear esters and Bulky esters. These sub-categories and their composition ranges are detailed in Tables 2, 3 and 4.

Table 1: Category UVCB Members

	CAS Number	EC Number	Registered Substance Name
Simple Esters	68186-14-1	269-035-9	Resin acids and Rosin acids, Me esters
	8050-15-5	232-476-2	Resin acids and Rosin acids, hydrogenated, Me esters
Linear Esters	68512-65-2	270-986-7	Resin acids and Rosin acids, esters with ethylene glycol
	68153-38-8	268-884-2	Resin acids and Rosin acids, esters with diethylene glycol
	68648-53-3	271-996-4	Resin acids and Rosin acids, hydrogenated, esters with triethylene glycol
	8050-25-7	232-478-3	Resin acids and Rosin acids, esters with triethylene glycol
Bulky Esters	8050-31-5	232-482-5	Resin acids and Rosin acids, esters with glycerol
	65997-13-9	266-042-9	Resin acids and Rosin acids, hydrogenated, esters with glycerol
	8050-26-8	232-479-9	Resin acids and Rosin acids, esters with pentaerythritol
	64365-17-9	264-848-5	Resin acids and Rosin acids, hydrogenated, esters with pentaerythritol
	68475-37-6	614-523-2	Resin acids and Rosin acids, polymerized, esters with glycerol
	65997-12-8	613-868-6	Resin acids and Rosin acids, polymerized, esters with pentaerythritol
	84776-83-0	284-009-7	Resin acids and rosin acids, esters with trimethylolpropane

1.1 Category Definition

1.1.1 Category Hypothesis

The category of Rosin Esters consists of rosin which has been esterified with alcohols, typically methanol, ethylene glycol, diethylene glycol, triethylene glycol, glycerol and pentaerythritol. Resin acids are the predominant components of rosin (>85%) and, due to the acid functionality, the primary species for esterification reaction. Resin acids are composed of three skeletal classes of tricyclic carboxylic acids which share similar structure, but vary in the position and number of the double bonds, alkyl side and methyl groups. Hydrogenated rosin is implicitly included in the definition of rosin as is disproportionated rosin which is a combination of hydrogenated and dehydrogenated rosin naturally produced when rosin is heated.

Due to the UVCB nature of the acids, the combination of multiple examples to form di-, tri- and tetra-esters can result in each individual species being present at very low level (<10%).

The category therefore also includes the hydrogenated rosin forms of these substances. Due to the reactivity of resin acids, dimers can be manufactured. These rosin dimers are also known as oligomers or by the trivial name of polymerised rosin.

[1] https://echa.europa.eu/documents/10162/13628/raaf_en.pdf

[2] https://echa.europa.eu/documents/10162/13630/raaf_uvcb_report_en.pdf/3f79684d-07a5-e439-16c3-d2c8da96a316

As each member of this category is a UVCB, the resin acid components will vary in type and proportion.

The number of ester bonds that can be formed is driven by the alcohol. Methanol can form mono-esters, ethylene glycol, diethylene glycol and triethylene glycol can form mono- and di- esters, glycerol can form mono-, di- and tri-esters and pentaerythritol can form mono-, di-, tri- and tetra-esters. In each case, the esterification reaction results in a UVCB containing esters with varying numbers of ester bonds formed by the reaction of the various resin acids with the alcohol.

All substances in the category contain ester constituents with different levels of esterification and non-esterified resin acids. Properties of Category 2 substances change in a consistent manner depending on the level of esterification.

1.1.1.1 Brief Manufacturing Process Description

Rosin is the resinous constituent of the oleo-resin exuded by various species of pine. The separation of the oleo-resin into the essential oil (spirit of turpentine) and common rosin is accomplished by distillation. The essential oil is taken leaving fluid rosin, which is run off and purified. The category of Rosin Esters, is comprised of rosins which have been esterified with alcohols, typically methanol, diethylene glycol, triethylene glycol, glycerol and pentaerythritol.

1.1.2 Applicability domain (AD) of the category

The chemistry of Rosin and its derivatives is highly complex. H4R has produced a reference document on analytical aspects. It also provides an insight into this chemistry. A copy is also given in the registration dossier.

Table 2: Category Constituents – Simple esters

Simple Esters				
Constituent types		Resin acids and Rosin acids, Me esters	Resin acids and Rosin acids, hydrogenated, Me esters	Category Boundary Conditions
Ester Type	Mono	80-100	80-100	0-100
	Di			0-90
	Tri			0-80
	Tetra			0-90
	Poly			0-80
Non-esterified acids		≤10	≤10	0-50
Neutral Fraction		≤10	≤10	0-20
Heavy Ends		≤10	≤10	0-45

Table 3: Category Constituents – Linear esters

Linear						
Constituent types		Resin acids and Rosin acids, esters with ethylene glycol	Resin acids and Rosin acids, esters with diethylene glycol	Resin acids and Rosin acids, hydrogenated, esters with triethylene	Resin acids and Rosin acids, esters with triethylene glycol	Category Boundary Conditions
Ester	Mono	40-50	10-35	10-30	15-40	0-100
	Di	40-50	45-90	50-70	25-80	0-90
	Tri					0-80
	Tetra					0-90
	Poly	0-10	≤15		0-30	0-80
Non-esterified		40-50	≤15	0-10	0-20	0-50
Neutral Fraction		0-5	≤10	0-10	0-10	0-20
Heavy Ends			≤15	0-10	0-20	0-45

Table 4: Category Constituents – Bulky esters

Bulky esters									
Constituent types		Resin acids and Rosin acids, esters with glycerol	Resin acids and Rosin acids, hydrogenated , esters with glycerol	Resin acids and Rosin acids, esters with pentaerythritol	Resin acids and Rosin acids, hydrogenated, esters with pentaerythritol	Resin acids and Rosin acids, polymerized, esters with glycerol	Resin acids and Rosin acids, polymerized, esters with pentaerythritol	Resin acids and rosin acids, esters with trimethylolpropane	Category Boundary Conditions
Ester Type	Mono	0 - 3	0-10	0-10	0-10	≤10	≤10	<15	0-100
	Di	4 - 25	0-30	0 - 15	0-10	2 - 15	≤10	5 - 25	0-90
	Tri	45-80	40-80	5 - 50	10 -50	15-30	10 - 25	40-90	0-80
	Tetra			20-90	20-80		10 -25		0-90
	Poly	0-25		5 -25		50-80	40-70	<45	0-80
Non-esterified acids		0-25	0-15	0-15	0-15	≤15	≤15	≤15	0-50
Neutral Fractions		0-10	0-10	0-10	0-10	≤10	≤10		0 -20
Heavy Ends		3 - 45	3 - 45	0-45	0-25				0-45

1.2 Purity / Impurities

The substances in this category are UVCBs and as such are considered to be 100% pure. The term impurity is not relevant for UVCBs. Often, substances will be described by known constituents present at 10% or greater identified by IUPAC name and EC number/CAS number, indicating typical concentrations and/or concentration ranges. However, there are no individual constituents at concentrations > 10%. Consequently, these substances are characterised by their constituent types.

1.2.1 Substances with CLP Implications

All member of Category 2 with the exception of Resin acids and rosin acids, esters with ethylene glycol (CAS# 68512-65-2) are not classified for reproductive or developmental toxicity according to EU Classification, Labelling and Packaging of Substances and Mixtures (CLP) Regulation (EC) No.

1272/2008 or UN Globally Harmonized System of Classification and Labelling of Chemicals (GHS).

Rosin, esters with ethylene glycol (CAS# 68512-65-2): In a key guideline (OECD 414) pre-natal developmental toxicity study with, the No Observed Adverse Effect Level (NOAEL) for the pregnant rat was considered to be 8750 ppm and the NOAEL for developmental toxicity was considered to be 3250 ppm (equivalent to 266.7 mg/kg bw/day). The foetal findings at the 8750 ppm dietary exposure level are considered to satisfy the CLP classification criteria for Rep Cat 2.

In an OECD 414 study with Resin acids and rosin acids, esters with ethylene glycol (CAS 68512-65-

2), based on the observation of foetal developmental toxicity at dietary exposure levels below those that resulted in maternal toxicity. This OECD 414 key study provides data to trigger Reproductive Category 2 Classification for Resin acids and rosin acids, esters with ethylene glycol (CAS 68512-65-

2) under EU CLP. However, the results of the OECD 414 with Resin acids and rosin acids, esters with ethylene glycol (CAS 68512-65-2) will not be used for read across within the category Rosin,

esters. H4R commissioned a study to assess and compare the in vitro gut absorption and chemistry of the Ethylene Glycol (EG), Diethylene Glycol (DEG), and Triethylene Glycol (TEG) esters and results shows that the appropriate read across for the linear esters developmental toxicity will be from

the TEG to the DEG ester. Additionally, there is only one registration of Resin acids and rosin acids, esters with ethylene glycol (CAS 68512-65-2) and the registrant had ceased production/sale of this substance in the EU in quarter 4 of 2016.

Two substances in the category are classified for environmental endpoints, Resin acids and rosin acids, methyl esters and Resin acids and rosin acids, hydrogenated, methyl esters. These substances are classified as Aquatic Chronic Category 3 based on the EC50 result from an acute study with *Daphnia magna*, with the test item Resin acids and rosin acids, methyl esters. No other substances within the category have an environmental classification.

1.2.2 Toxicity Classification Overview

The available toxicity data demonstrate that there are no significant or classifiable toxicological effects identified across the whole of Category 2, with the exception of foetal effects at a sub-maternally toxic dose in an OECD 414 study with Resin acids and rosin acids, esters with ethylene glycol (CAS# 68512-65-2). No similar findings were observed in an OECD 414 study with another

member of the linear esters sub-category, Resin acids and rosin acids, esters with triethylene glycol. Furthermore, five key guideline (OECD 414) pre-natal toxicity studies and two combined reproductive / developmental toxicity screening tests (OECD 421 and OECD 422) are available to evaluate the developmental toxicity potential of the Rosin Esters category.

The only Category 2 member in which classifiable effects were seen is Resin acids and rosin acids, esters with ethylene glycol. Consequently, the foetal findings in this OECD 414 study are not considered to be representative of the developmental toxicity of the UVCB substances in Category 2.

2.0 CATEGORY JUSTIFICATION

2.1 Composition

See Tables 2, 3 and 4.

2.2 Physico-Chemical

The molecular weight of the alcohol to form the ester varies, and so does the potential for esterification, therefore it would be expected that there would some differences in physico-chemical properties.

	Substance / CAS No.	Physical state	Melting point °C)	Boiling point (°C)	Density (kg/m³)	Vapour pressure (Pa)	Partition coefficient (log Pow)	Water Solubility (mg/L)
Simple Esters	Resin acids and Rosin acids, Me esters (68186-14-1)	Liquid	6	360 - 430	1040 (at 20°C)	0.0031 (at 25°C)	>6.5	≤11 Loading 10,000 ≤3.1 Loading 1,000
	Resin acids and Rosin acids, hydrogenated, Me esters (8050-15-5)	Liquid	-5.5	386	1050 (at 20°C)	0.026 (at 25°C)	>6.5	≤6.3 Loading 10,000 ≤1 Loading 1,000
Linear Esters	Resin acids and Rosin acids, esters withethylene glycol (68512-65-2)	Solid	66 - 88	384	1080 (at 21.4°C)	0.0031	5.65 - >6.5	≤3.3 Loading 10,000 ≤3.7 Loading 1,000
	Resin acids and Rosin acids, esters with diethylene glycol (68153-38-8)	Liquid	8.9	131 (decomposition temperature)	1064	$3.3x10^{-9}$ - <248	>3.1 <7.3	<3.47 (at 20°C ± 0.5°C)
	Resin acids and Rosin acids, hydrogenated,esters with triethylene glycol (68648-53-3)	Liquid	27	367	1060 (at 20.0°C)	0.00061	>6.5	≤32.3 Loading 10,000 ≤4.347 Loading 1,000
	Resin acids and Rosin acids, esters with triethylene glycol (8050-25-7)	Liquid	< -20	300	1038 (at 20°C)	8	2.44	8
	Resin acids and Rosin acids, esters with glycerol (8050-31-5)	Solid	62.1 - 87.1	228 (decomposition temperature)	1063 (at 20°C)	< 4 (at 20°C)	3.97	<0.43 (at 20°C)
	Resin acids and Rosin acids, hydrogenated, esters with glycerol (65997-13-9)	Solid	63.5 - 83.3	240 (decomposition temperature)	1004	< 100 (at 20°C)	4.7 - 5.8	0.15 (at 20°C)

Bulky Esters	Resin acids and Rosin acids, esters with pentaerythritol (8050-26-8)	Solid	77.8 - 96.8	275 (decomposition temperature)	1021 (at 20°C)	< 75 (at 20°C)	>1.5 - 3.62	<0.63 (at 20°C)
	Resin acids and Rosin acids, hydrogenated, esters with pentaerythritol (64365-17-9)	Solid	81.3 - 92.2	> 300	1005 (at 22°C)	< 100 (at 20°C)	4.6 - >6	< 0.22 (at 20°C)
	Resin acids and Rosin acids, polymerized, ester with glycerol (68475-37-6)	Solid	93 - 105	393 and 450	1080 (at 21.5°C)	<0.003	>6.5	≤1.24 Loading 10,000 ≤0. 879 Loading 1,000
	Resin acids and Rosin acids, polymerized, esters with pentaerythritol (65997-12-8)	Solid	68 - 125	380 - 450	1090	<0.00038	>6.5	≤2.1 Loading 10,000 ≤1 Loading 1,000
	Resin acids and rosin acids, esters with trimethylolpropane (CAS 84776-83-0)	Solid	24.2 - 51.2 ± 0.5°C (297 to 324 ± 0.5°K)	418 ± 0.5°C (691 ± 0.5 K) at 100.9 kPa	1070 kg/m3 at 19.8 ± 0.5 °C	1.4 x10 ^-3 Pa at 25°C	Pow= 1.06 to 297 Log10 Pow= 2.71x10^-2 to 4.47	6.09E-4 g/L (at 20°C)

2.3 Environmental

Ready biodegradation studies have been conducted for the following members of the rosin esters category: Resin acids and rosin acids, Me esters; Resin acids and rosin acids, hydrogenated, Me esters; Resin acids and rosin acids, esters with diethylene glycol; Resin acids and rosin acids, esters with glycerol; Resin acids and rosin acids, hydrogenated esters with glycerol; Resin acids and rosin acids, esters with pentaerythritol; and Resin acids and rosin acids, hydrogenated, esters with pentaerythritol, all following the OECD 301B guideline (Inveresk 2002, Notox 1988a,b, Harlan 2012).

None of the rosin ester substances could be considered to be readily biodegradable on the basis of these results, with percentage biodegradation determined in the studies ranging from 0 – 50.7% after 28 days. However, rosin ester substances are made up of different constituents and the biodegradation potential varies between constituents, due, for example, to differences in the size of the molecule and differences in water solubility.

A screening assessment, using QSAR predictions using the BIOWIN models (part of EPISuite, US EPA 2000), has been carried out for the ester components of rosin ester substances. QSAR predictions have been run for representative structures of mono-, di-, tri- and tetra-esters in order to assess the biodegradation potential of the individual constituents. Although some of these constituents are outside the domain of the QSAR model, the QSAR approach is considered to be appropriate as a screening assessment in order to identify any constituents that may require further assessment.

The QSAR results show that di-, tri- and tetra-esters are potentially persistent. However, some of the mono-esters are likely to biodegrade and therefore would not be persistent in the environment. Further biodegradation testing of the mono-ester fraction is currently ongoing to clarify the persistence assessment for these constituents. This testing was requested in Final Decision letters received from ECHA on 9 February 2017 for the category members resin acids and rosin acids, hydrogenated, esters with glycerol and resin acids and rosin acids, hydrogenated, esters with pentaerythritol.

No measured bioaccumulation data is available for rosin ester substances. Measured Kow values are available for rosin ester substances, however results are variable due to the difficulties with testing these substances, with log Kow values ranging from 2.44 - >6.5. BCF values are known to increase with increasing Kow, however at very high Kow values a decrease in BCF is observed, due to reduced uptake based on the size of the molecule. Due to the difficulties with measuring Kow for these substances and the fact that a single measured Kow is unlikely to be representative of the constituents in the UVCB, as well as the problems with assessing unbounded Kow values, bioaccumulation potential is assessed based on QSAR predictions for representative structures in the UVCB substances.

A screening assessment has been carried out for the ester components of rosin ester substances. QSAR predictions have been run for representative structures of mono-, di-, tri- and tetra-esters in order to assess the bioaccumulation potential of the individual constituents. Predictions have been conducted using the US EPA's EPISuite models, KOWWIN and BCFBAF (regression-based estimates).

Although some of these constituents are outside the domain of the QSAR model, the QSAR approach is considered to be appropriate as a screening assessment in order to identify any constituents that may require further assessment.

The bioaccumulation screening assessment shows that di-, tri- and tetra-ester constituents are predicted to have log Kow values >10. Based on this, these constituents are unlikely to be taken up due to the large molecular size of the constituents and are therefore considered not to be bioaccumulative or very bioaccumulative.

Mono-ester constituents have predicted log Kow values of between 4.66 and 6.42 and therefore bioaccumulation of these constituents cannot be ruled out based on log Kow alone. For those mono-ester constituents with predicted log Kow values between 4.66 and 5.3, the predicted BCF values are less than 2000 L/kg. On this basis, these substances are considered to be unlikely to bioaccumulate and these constituents are not considered to be bioaccumulative or very bioaccumulative.

Mono-ester constituents with higher predicted log Kow values (between 5.67 and 6.42) have predicted BCF values greater than 2000 L/kg or 5000 L/kg. Based on these predicted BCF values, bioaccumulation of these constituents cannot be ruled out and they are considered to be potentially bioaccumulative or very bioaccumulative.

Acute ecotoxicity studies are available for the following members of the rosin esters category: Resin acids and rosin acids, hydrogenated, Me esters (fish, Daphnia and algae); Resin acids and rosin acids, esters with pentaerythritol (fish, Daphnia and algae); Resin acids and rosin acids, esters with glycerol (Daphnia); and Resin acids and rosin acids, esters with ethylene glycol (fish, Daphnia, algae).

A 48-hour EL50 of 27 mg/L was determined for resin acids and rosin acids, hydrogenated, Me esters and this was the most sensitive result for this substance. For all category members with higher molecular weights than the Me ester substances, the EL50 values in all studies were determined to be above the highest loading rate tested.

2.4 Mammalian Toxicology

The available data demonstrate that no significant or classifiable toxicological effects occurred within the category, with the exception of foetal effects in an OECD 414 study with Rosin, esters with ethylene glycol (CAS# 68512-65-2).

In a key guideline (OECD 414) pre-natal developmental toxicity study with Rosin, esters with ethylene glycol (CAS# 68512-65-2), the No Observed Adverse Effect Level (NOAEL) for the pregnant rat was considered to be 8750 ppm (equivalent to 715 mg/kg bw/day) and the NOAEL for developmental toxicity was considered to be 3250 ppm (equivalent to 266.7 mg/kg bw/day). At the highest exposure

level (18750 ppm), external examination of the foetuses and detailed skeletal evaluation did not indicate any effect of maternal exposure on foetal development. However, there was a cluster of visceral findings (kinked ureters, dilated ureters, increased renal pelvic cavitation, absent renal papilla misshapen kidneys and absent renal medulla) that indicated a treatment-related disturbance of the normal development of the kidneys and ureters. At the middle exposure level (8750 ppm), the incidence of foetuses/litters with kinked ureters, dilated ureters, increased renal pelvic cavitation and absent renal papilla was higher than control and the historical control range, indicating a treatment-related effect on the normal development of the kidneys and ureters. Since 8750 ppm was the NOAEL for maternal toxicity, the foetal findings in this OECD 414 study at the 8750 ppm dietary exposure level are considered to satisfy the CLP classification criteria for Rep Cat 2.

However, it should be noted that five key guideline (OECD 414) pre-natal toxicity studies and two combined reproductive / developmental toxicity screening tests (OECD 421 and OECD 422) are available to evaluate the developmental toxicity potential of the Rosin Esters category. The only category member in which classifiable effects were seen is Rosin, esters with ethylene glycol. Furthermore, no similar findings were observed in an OECD 414 study with another member of the linear esters sub-category, Resin acids and Rosin acids, esters with triethylene glycol.

Consequently, the foetal findings in this OECD 414 study are not considered to be representative of the developmental toxicity of the UVCB substances in Category 2.

3.0 CONCLUSIONS FOR CLASSIFICATION & LABELLING, PBT/vPvB

3.1 Classification & Labelling

3.1.1 Physico-chemical Hazard Assessment

There are no hazardous properties.

3.1.2 Human Health Hazard Assessment

Rosin, esters with ethylene glycol (CAS# 68512-65-2): In a key guideline (OECD 414) pre-natal developmental toxicity study with, the foetal findings at the 8750 ppm dietary exposure level are considered to satisfy the CLP classification criteria for Rep Cat 2. The only category member in which classifiable effects were seen is Rosin, esters with ethylene glycol. No similar findings were observed in an OECD 414 study with another member of the linear esters sub-category, Resin acids and Rosin acids, esters with triethylene glycol. Consequently, the foetal findings in this OECD 414 study are not considered to be representative of the developmental toxicity of the UVCB substances in Category 2. Additionally, there is only one registration of Resin acids and rosin acids, esters with ethylene glycol (CAS 68512-65-2) and the registrant had ceased production/sale of this substance in the EU in quarter

4 of 2016.

3.1.3 Environmental Hazard Assessment

Resin acids and Rosin acids, hydrogenated, Me esters (8050-15-5) and Resin acids and Rosin acids, Me esters (68186-14-1) are both classified as Aquatic Chronic 3.

At the low molecular weight end of the category, effects were seen in an acute Daphnia study (EC50 of 27 mg/L), for resin acids and rosin acids, hydrogenated, methyl esters. This result is read across to resin acids and rosin acids, methyl esters and is used to derive the PNECs for these substances. As this EC50 is > 1 mg/L an acute environmental classification is not appropriate. Neither Resin acids and rosin acids, Me esters or Resin acids and rosin acids hydrogenated Me esters are readily biodegradable therefore, as the lowest EC50 is >10 <100 mg/L a chronic classification of Chronic Category 3 is applied for both substances in accordance with the CLP regulation.

For higher molecular weight esters (with molecular weights higher than for the Methyl esters), no effects were seen at the limit of solubility in acute ecotoxicity studies and therefore no environmental classification is assigned.

3.2 Conclusion for PBT/vPVB

The PBT assessment of rosin ester substances has been conducted by assessing the PBT potential of different constituents within the UVCB, as constituents will behave differently in the environment and have different potential for toxicity. As the substances contain too many constituents to assess each one individually, representative structures have been assessed in order to screen the potential for persistence and bioaccumulation of different fractions within the UVCBs.

Some mono-ester constituents exceed the screening criterion for bioaccumulation based on QSAR predictions, and biodegradation predictions are borderline for persistence. As the QSAR results show some uncertainty, direct ready biodegradation testing of the mono-ester fraction is currently ongoing to clarify the persistence assessment for these constituents. This testing was requested in Final Decision letters received from ECHA on 9 February 2017 for the category members resin acids and rosin acids, hydrogenated, esters with glycerol and resin acids and rosin acids, hydrogenated, esters with pentaerythritol.

Based on the results of the QSAR screening assessment, di, tri and tetra esters are not considered to be bioaccumulative and are therefore not PBT / vPvB. Free resin acids within the UVCBs are not considered to be persistent or bioaccumulative based on measured data, and are therefore not PBT / vPvB.

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