CATEGORY 2 - 'Rosin Esters'

UVCB CATEGORY JUSTIFICATION DOCUMENT

1 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 (Table 1) includes three sub-categories: Simple esters, Linear esters and Bulky esters. The composition ranges for these sub-categories are detailed in Table 2 to Table 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
	8050-25-7	232-478-3	Resin acids and Rosin acids, esters with triethylene glycol
	68648-53-3	271-996-4	Resin acids and Rosin acids, hydrogenated, esters with triethylene glycol
Bulky Esters	8050-31-5	232-482-5	Resin acids and Rosin acids, esters with glycerol
	84776-83-0	284-009-7	Resin acids and Rosin acids, esters with trimethylolpropane
	8050-26-8	232-479-9	Resin acids and Rosin acids, esters with pentaerythritol
	65997-13-9	266-042-9	Resin acids and Rosin acids, hydrogenated, esters with glycerol
	64365-17-9	264-848-5	Resin acids and Rosin acids, hydrogenated, esters with pentaerythritol

[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

	68475-37-6	614-523-2	Resin acids and Rosin acids, polymd., esters with glycerol
	65997-12-8	613-868-6	Resin acids and Rosin acids, polymd., esters with pentaerythritol

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, trimethylolpropane, 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 reactivity of resin acids, dimers can be produced. These rosin dimers are also known as oligomers or by the trivial name of polymerised rosin.

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 and trimethylolpropane 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.

Due to the UVCB nature of rosin, the combination of multiple different resin acid species with alcohols to form di-, tri- and tetra-esters can result in each individual ester species being present at very low level (<10%).

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 a UVCB sub-type 3, where the source is biological (family: *pinaceae*, genus: *pinus*), with subsequent refinement. This process can be either distillation, fractional distillation, or extraction and solvent refining or purification. A batch/continuous process is used, in a partially closed system with a process temperature between 160 and 275 °C and under reduced pressure. The category of Rosin Esters, is comprised of rosins which have been esterified with alcohols, typically methanol, diethylene glycol, triethylene glycol, glycerol, trimethylpropane, 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

Constituent Type		Resin acids and Rosin acids, Me esters	Resin acids and Rosin acids, hydrogenated, Me esters	Category Boundary Condition
Ester type	Mono	80 – 100	80 – 100	80 – 100
	Poly	0 – 10	0 – 10	0 – 10
Non-esterified acids		0 – 10	0 – 10	0 – 10
Neutral fraction		0 – 10	0 – 10	0 – 10

Table 3 Category Constituents – Linear Esters

Constituent Type		Resin acids and Rosin acids, esters with ethylene glycol	Resin acids and Rosin acids, esters with diethylene glycol	Resin acids and Rosin acids, esters with triethylene glycol	Resin acids and Rosin acids, hydrogenated, esters with triethylene glycol	Category Boundary Condition
Ester type	Mono	20 – 50	10 – 35	5 – 40	10 – 40	5 – 50
	Di	40 – 50	45 – 90	20 – 80	50 – 70	20 – 90
	Poly	0 – 10	0 – 22	5 – 40	0 – 10	0 – 40
Non-esterified acids		20 – 50	0 – 15	0 – 25	0 – 10	0 – 50
Neutral fraction		0 – 5	0 – 10	0 – 10	0 – 10	0 – 10

Table 4 Category Constituents – Bulky esters

Constituent types		Resin acids and Rosin acids, esters with glycerol	Resin acids and Rosin acids, esters with trimethylolpropane	Resin acids and Rosin acids, hydrogenated, esters with glycerol	Resin acids and Rosin acids, polymd., 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, polymd., esters with pentaerythritol	Category Boundary Condition
Ester type	Mono	0 – 10	0 – 15	0 -7	0 – 10	0 – 10	0 – 7	0 – 10	0 – 15
	Di	1 – 35	5 – 25	0 – 30	2 – 15	0 – 15	0 – 20	0 – 10	0 – 35
	Tri	35 – 80	40 – 90	40 – 80	15 – 75	0 – 50	10 – 50	10 – 25	0 – 90
	Tetra	-	-	-	-	20 – 92	20 – 80	10 – 25	0 - 92
	Poly	0 – 25	0 – 45	0 – 25	15 – 80	5 – 25	0 – 25	40 – 70	0 – 80
Non-esterified acids		0 – 25	0 – 15	0 – 15	0 – 15	0 – 15	0 – 15	0 – 15	0 – 25
Neutral fraction		0 – 10	0 – 10	0 – 10	0 – 10	0 – 10	0 – 10	0 – 10	0 – 10

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).

In an OECD 414 key study with "Resin acids and rosin acids, esters with ethylene glycol" (CAS 68512-65-2), there were foetal findings at the 8750 ppm dietary exposure level. These data are sufficient 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 this study are not used for Read-Across within the category Rosin, esters. Instead, 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. The results of this study clearly show that the appropriate Read-Across for the linear esters is 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, Me esters" and "Resin acids and rosin acids, hydrogenated, Me esters". These substances are classified as Aquatic Chronic Category 3 based on the EC_{50} result from an acute study with *Daphnia magna*, with the test item "Resin acids and rosin acids, Me 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, except for 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). In an OECD 414 study with another member of the linear esters sub-category, "Resin acids and rosin acids, esters with triethylene glycol", foetal effects were not seen.

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 various members of the Rosin Esters category. The only Category 2 member in which classifiable effects were seen was "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 CATEGORY JUSTIFICATION

2.1 Composition

See Table 2 to Table 4.

2.2 Physico-Chemical

The molecular weight of the alcohol used in the esterification reaction varies, as does its potential for esterification. Therefore, it is expected to find 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

2.3.1 Biodegradation

Ready biodegradation studies have been conducted for several 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
- Resin acids and rosin acids, hydrogenated, esters with pentaerythritol,

All studies were conducted in accordance with 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, whose potential for biodegradation varies, due, for example, to differences in molecular size and water solubility.

Therefore, a screening assessment involving QSAR predictions using BIOWIN models (part of EPISuite, US EPA 2000), was carried out on the ester components of rosin ester substances. QSAR predictions were 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. In response to a Final Decision Letter (FDL) received from ECHA on the 09th February 2017, a ready biodegradation OECD 310 study was conducted using a mono-ester fraction prepared from “Resin acids and Rosin acids, hydrogenated, esters with glycerol”. This study confirmed that primary degradation of mono-ester constituents was high and that they were therefore to be considered not persistent. ECHA, in a FDL dated 17th December 2020, have requested an additional ready biodegradation OECD 310 study using a mono-ester fraction prepared from “Resin acids and Rosin acids, hydrogenated, esters with pentaerythritol”. Work on this study is currently underway.

2.3.2 Bioaccumulation

No experimental bioaccumulation data is available for rosin ester substances. Although measured K_{ow} values are available for rosin ester substances, results are variable due to difficulties with testing these substances, with log K_{ow} values ranging from 2.44 - >6.5. BCF values are known to increase with increasing K_{ow}, however at very high K_{ow} values a decrease in BCF is observed, due to reduced uptake based on the size of the molecule.

Due to the difficulties with measuring K_{ow} for these substances and the fact that a single measured K_{ow} is unlikely to be representative of the constituents in the UVCB, as well as the problems with

assessing unbounded K_{ow} values, a screening assessment for bioaccumulation potential was carried out for the ester components of rosin ester substances.

To this end, QSAR predictions were run for representative structures of mono-, di-, tri- and tetra-esters in order to assess the bioaccumulation potential of the individual constituents. Predictions were 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 K_{ow} 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 K_{ow} values of between 4.66 and 6.42 and therefore bioaccumulation of these constituents cannot be ruled out based on log K_{ow} alone. For those mono-ester constituents with predicted log K_{ow} 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 K_{ow} 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.

2.3.3 Ecotoxicity

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)
- Resin acids and rosin acids, esters with ethylene glycol (fish, Daphnia, algae).

A 48-hour EL_{50} 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 EL_{50} 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 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

In a key guideline (OECD 414) pre-natal developmental toxicity study with "Resin acids and Rosin acids, esters with ethylene glycol", the foetal findings at the 8750 ppm dietary exposure level are considered to satisfy the CLP classification criteria for Rep Cat 2. This substance is the only category member in which classifiable effects were seen. 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 the OECD 414 study with the ethylene glycol esters 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 (EC_{50} of 27 mg/L), for "Resin acids and Rosin acids, hydrogenated, Me esters". This result is read across to "Resin acids and Rosin acids, Me esters" and is used to derive the PNECs for these substances. As this EC_{50} 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 EC_{50} is >10 and <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 category, 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, ready biodegradation testing of the mono-ester fraction for "Resin acids and Rosin acids, hydrogenated, esters with glycerol" was performed and confirmed that the fraction is to be considered not persistent. Similarly, the mono-ester fraction of "Resin acids and Rosin acids, hydrogenated, esters with pentaerythritol" is currently ongoing ready biodegradation testing to further clarify the persistence assessment for these constituents.

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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