Assessment of regulatory needs

Authority: European Chemicals Agency (ECHA)

Group Name: Esters from linear and branched carboxylic acids and short chain diols

General structure: "-"

Revision history

Version	*Date*	*Description*
1.0	20 Dec 2020	
1.1	16 March 2023	Reference to RAC opinion added for EC 285-503-5

Substances within this group:

EC/List no	CAS no	Substance name	Registration type (full, OSII or TII, NONS, cease manufacture), highest tonnage band among all the registrations (t/y) [1]
203-315-3	105-62-4	1-methyl-1,2-ethanediyl dioleate	Full, 100-1000
210-817-6	623-84-7	Propane-1,2-diyl diacetate	Full, >1000
210-826-5	624-03-3	Ethane-1,2-diyl palmitate	Full, >1000
211-014-3	627-83-8	Ethylene distearate	Full, 100-1000
214-244-2	1117-31-3	1,3-butylene glycol diacetate	Full, not (publicly) available
215-549-3	1330-80-9	Oleic acid, monoester with propane-1,2-diol	Full, 1-10
269-905-8	68390-58-9	Fatty acids, tall-oil, 1-methyl-1,2-ethanediyl esters	Full, not (publicly) available
271-516-3	68583-51-7	Decanoic acid, mixed diesters with octanoic acid and propylene glycol	Full, 100-1000
284-864-6	84988-75-0	Fatty acids, C14-18 and C16-18-unsatd., esters with propylene glycol	Full, 100-1000
285-503-5	85114-00-7	2-ethylhexanoic acid, monoester with propane-1,2-diol	Full, not (publicly) available
292-927-4	91031-27-5	Fatty acids, C6-18, 2,2-dimethyl-1,3-propanediyl esters	Full, 100-1000
292-932-1	91031-31-1	Fatty acids, C16-18, esters with ethylene glycol	Full, >1000
306-522-8	97281-23-7	Fatty acids, C16-18, 2-hydroxyethyl esters	Full, 10-100
424-180-9	-	A mixture of: but-1,3-diyl didecanoate; but-1,3-diyl dioctanoate; but-1,3-diyl 1-decanoate-3-octanoate; but-1,3-diyl 1-octanoate-3-decanoate	Full, not (publicly) available
700-003-3	56519-71-2	Octanoic acid, 1,1'-(1,3-propanediyl) ester	Full, not (publicly) available
943-011-4	-	Fatty acids, C16-18 (even numbered), esters with 1,2-propanediol	Full, 10- 100

This table does not contain group members that are only notified under the CLP Regulation, however, the list is not necessarily exhaustive.

[1] The total aggregated tonnage band may be available on ECHA's webpage at https://echa.europa.eu/information-on-chemicals/registered-substances

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Foreword

The assessment of regulatory needs of a group of substances is an iterative, informal process to help authorities consider the most appropriate way to address an identified concern for a group of substances or a single substance and decide whether further regulatory risk management activities are necessary.

The grouping is mainly based on structural similarity and associations made by the registrants between substances through read-across and category approaches as well as category associations from external sources (e.g. OECD categories)[2]. These methods are different from grouping as defined in Section 1.5 of Annex XI to REACH because the scope and intended use of ECHA's grouping is different. Thus, in this context, grouping does not aim to validate read-across and category approaches according to the Annex XI requirements but rather to support a faster and more consistent approach for regulating chemicals and avoid regrettable substitution.

The focus of the assessment is largely based on information available in the registration dossiers and on properties requiring regulatory risk management action at EU level[3]. The information reported on uses is from the registration dossiers (IUCLID) and is used as a proxy for assessing how widespread uses are and whether potential for exposure to humans and releases to the environment can be expected. The chemical safety reports are not necessarily consulted and no quantitative exposure assessment is performed at this stage.

The outcome of these assessments are proposals for immediate (the first action) and subsequent regulatory action(s), including the foreseen ultimate regulatory action (last foreseen regulatory action) to address the identified concern(s) in case the potential hazards are confirmed. For example, further data generation through compliance check is suggested as a first action, to confirm the identified hazard.

Where hazards are confirmed, regulatory risk management actions could be considered for the whole group, for a subgroup or for individual substances within the group. The robustness of the group depends on the stage of assessment and the level of certainty this stage requires. For example, the needs for grouping under restriction may differ from the needs for grouping for the purpose of harmonised classification. Group membership is reconsidered accordingly throughout the iterative assessment of regulatory needs, for example, after further information is generated and the hazard has been clarified or when new insights on uses and risks are available.

The assessment of regulatory needs in itself does not represent a regulatory action, but rather a preparatory step to consider further possible regulatory actions at the level of individual substances or groups/subgroups of substances.

[2] Working with Groups - ECHA (europa.eu)

[3] Regarding hazard properties the focus is for instance on CMR (carcinogenic, mutagenic and/or toxic to reproduction), sensitiser, ED (endocrine disruptor), PBT/vPvB or equivalent (e.g. substances being persistent, mobile and toxic), aquatic toxicity hazard endpoints and therefore only those are reflected in the report. This does not mean that the substances do not have other known or potential hazards. In some specific cases, ECHA may consider additional hazards (e.g. neurotoxicity, STOT RE).

Publication of ARNs makes it easier for companies to follow the latest status of their substances of interest, anticipate potential regulatory actions and make strategic choices in their chemicals portfolio.

For more information on assessments of regulatory needs please consult ECHA's website[4].

[4] https://echa.europa.eu/understanding-assessment-regulatory-needs

Glossary

ARN	Assessment of Regulatory Needs
CCH	Compliance Check
CLH	Harmonised classification and labelling
CMR	Carcinogenic, mutagenic and/or toxic to reproduction
DEv	Dossier evaluation
ED	Endocrine disruptor
NONS	Notified new substances
OEL	Occupational exposure limit
OSII or TII	On-site isolated intermediate or transported isolated intermediate
PBT/vPvB	Persistent, bioaccumulative and toxic / very persistent and very bioaccumulative
PMT/vPvM	Persistent, mobile, and toxic / very persistent and very mobile
RDT	Repeated dose toxicity
RMOA	Regulatory management options analysis
RRM	Regulatory risk management
SEv	Substance evaluation
STOT RE	Specific target organ toxicity, repeated exposure
SVHC	Substance of very high concern
TPE	Testing proposal evaluation
UVCB	Substances of unknown or variable composition, complex reaction products or biological materials

1 Overview of the group

Explanations on the scope of this assessment is available in the foreword to this document. Please read it carefully before going through the report.

ECHA has grouped together structurally similar esters of carboxylic acids and polyols. Generally, the group can be described as esters or diesters of glycols (i.e. ethylene glycol and propylene glycol) or butane-1,3-diol with varying chain lengths from C6 to C18, saturated and/or with a double bond, linear and branched.

The subcategorization for the linear aliphatic esters takes into account the alcohol alkyl chain length. It follows previous experience on aliphatic type of substances considering the impact of the alkyl chain length in the (eco)toxicological properties. In most of the cases, the carboxylic acid moiety is a fatty acid.

Most of the substances are defined UVCBs due to variability of fatty acid and/or the polyol ether. A few of the substances, which contain only a fatty acid, could be considered as well-defined multi-constituent substances. Also, five substances are registered as mono-constituent.

All 16 substances have full registrations.

For EC EC 285-503-5[5] there is a RAC Opinion for harmonised classification as Repr. 1B.

Based on information reported in the REACH registration dossiers, the substances have a very wide variety of uses, including uses by workers and consumers with high exposure potential. They are used in coatings and paints, adhesives and sealants, lubricant and greases, fuels, construction applications, plastic and rubber articles, personal care and cosmetic products, air fresheners, washing/cleaning products, inks/toners/textile dyes, etc.

[5] https://echa.europa.eu/documents/10162/1d73eb33-d8ee-3d5b-1003-45304642bec6

2 Conclusions and proposed actions

The conclusions and actions proposed in the table below are based mainly on the REACH and CLP information available at the time of the assessment by ECHA. The conclusions are preliminary suggestions from a screening-level assessment done by ECHA with the aim to propose the next steps for further work (e.g., strengthening of the hazard conclusions, clarification of the uses and/or potential for exposure). The main source of information is the registration dossiers. Relevant public assessments may also be considered. When new information (e.g., on hazards through evaluation processes, or on uses) will become available, the document may be updated, and conclusions and actions revisited.

Table 1: Conclusions and proposed actions

EC/List no	Human Health Hazard	Environmental Hazard	Relevant use(s) & exposure potential	Suggested regulatory actions
285-503-5	Known or potential hazard for reproductive toxicity	No hazard or unlikely hazard	Industrial, professional and consumer uses in coatings and inks. Potential for exposure for workers and consumers and release to the environment.	**First step:** Restriction Justification: The reported professional uses are widespread (at many sites and many users) with relatively low levels of operational controls and risk management measures but with often frequent exposures with a long duration. Restriction of professional uses is preferred over authorisation as it is considered to be more efficient and effective to introduce controls at the level of placing on the market rather than at the level of uses. The harmonised classification as R 1 – would lead to generic restriction of the

EC/List no	Human Health Hazard	Environmental Hazard	Relevant use(s) & exposure potential	Suggested regulatory actions
				substance(s) in consumer mixtures by means of restriction entry 30.
203-315-3 210-817-6 210-826-5 211-014-3 214-244-2 215-549-3 269-905-8 271-516-3 284-864-6 292-927-4 292-932-1 306-522-8 424-180-9 700-003-3 943-011-4	No hazard or unlikely hazard	Inconclusive hazard for aquatic toxicity for all except for EC 210-817-6 & EC 214-244-2	Industrial, professional and consumer uses in personal care and cosmetic products, air fresheners, washing/cleaning products, coatings& paints, adhesives & sealants, lubricant & greases, fuels, plastic and rubber articles, coatings and inks. 210-817-6 is also used in polishes& waxes, fertilisers & plant protection products, biocides, anti-freeze and de-icing products, non-metal surface treatment products, leather treatment products. Potential for exposure for workers and consumers and release to the environment. EC 214-244-2 has only industrial/professional use as intermediate/laboratory agent reported, potential for exposure is low.	No action for EC 210-817-6, 214-244-2, 215-549-3, 292-927-4, 306-522-8 Ongoing CCH for remaining group members <u>Justification</u>: Overall, no or unlikely hazard that would lead to concern for the reported uses.

3 Justification for the need for regulatory risk management action at EU level (if hazards confirmed)

Suggested regulatory risk management action for EC 285-503-5

Based on currently available information, there is a potential for reproductive developmental toxicity for EC 285-503-5 based on the effects seen in PNDT studies (rats, mice) and potential classification as Repro. 1B was proposed by RAC in 2023[6]. The substance is an ester of 2-ethylhexanoic acid that is also harmonised classified for Repr. 1B. No other group members are esters of 2-ethylhexanoic acid, therefore this hazard is not extrapolated to other group members.

The substance is not considered PBT/vPvB or PMT/vPvM based on the available data that show that the substance is readily biodegradable. The substance is not hazardous for the aquatic environment based on the available experimental data.

Industrial, professional and consumer uses in coatings and inks is reported for the substance.

The harmonised classification (CLH) as Repr. 1B will require company level risk management measures (RMM) for workers to be in place; ii) is needed or highly recommended in support of further regulatory processes under REACH; and iii) would lead to generic restriction of the substance(s) in consumer mixtures by means of restriction entry 30.

The professional uses in coatings and inks are expected to be widespread (at many sites and by many users). Professional use is often widespread with relatively low levels of operational controls and risk management measures but with often frequent exposures with a long duration. In addition, professional users may be self-employed and therefore not covered by occupational safety and health (OSH) legislation.

Consumers may be co-exposed to the substances used by professionals.

Therefore, a **restriction of the substance as such or in mixtures (concentration limit in mixtures) used by professionals** is suggested after CLH.

Restriction of professional uses is preferred over authorisation as it is considered to be more efficient and effective to introduce controls at the level of placing on the market rather than at the level of uses.

Moreover, the use of the most harmful substances by professional workers has been recognised as an area of concern under the European Commission's Chemicals Strategy for Sustainability[7] which aims to extend to professional users under REACH the level of protection granted to consumers.

Furthermore, potential exposure from articles needs further investigation. The need for restricting substances in articles used by professionals or consumers should be considered in the context of the restriction of professional uses.

[6] https://echa.europa.eu/documents/10162/1d73eb33-d8ee-3d5b-1003-45304642bec6

[7] European Commission, *Chemical Strategy for Sustainability Towards a Toxic-Free Environment*, available at https://ec.europa.eu/environment/pdf/chemicals/2020/10/Strategy.pdf

Currently no need to suggest (further) regulatory risk management actions for the remaining substances in the group.

The substances in the group have widespread uses in professional settings or consumer products, with high exposure potential and release in the environment, however, none of the registered substances in the group needs further EU regulatory risk management actions at the moment due to low potential toxicological and environmental hazard.

No potential hazards are identified for human health for the remaining substances. These conclusions are based on the available data on the registered substances, the hypothesis of enzymatic hydrolysis and available information on the metabolites as well as extrapolation of hazard hypothesis due to structural similarity. Based on the evaluations[8] from other safety bodies, group members are expected to be rapidly hydrolysed into corresponding carboxylic acids and alcohols by carboxylesterase enzymes found in most tissues throughout the body, including the gastrointestinal tract.

The group members are diesters of fatty acids with short chain diols and some degree of hydrolysis to the corresponding acid and alcohol can be expected. The available experimental data from the group members covers all substances that are expected to release propylene glycol, ethylene glycol or 1,3 butylene glycol as well as the majority of fatty acids following potential enzymatic hydrolysis. The majority of the carboxylic acid parts of these group members have been or are being assessed by ECHA (group on fatty acids and group on branched carboxylic acids) and are expected to be of low toxicity. Furthermore, the assessment of regulatory needs (ARN) of the group of 1, 2 ethanediols and their carbonates covers the majority of the expected alcohol metabolites which are expected to be of potential low toxicity.

No systemic toxicity has been observed in the available repeated-dose toxicity studies with ECs 424-180-9, 271-516-3, 269-905-8 and 210-817-6 at the highest doses tested. There is no hazard observed in the available PNDT and screening reproductive studies with ECs 271-516-3, 292-932-1, 424-180-9, 269-905-8 and 210-817-6. Experimental data for mutagenicity and skin sensitisation for some group members are also negative. No hazard for carcinogenicity is expected for the group members as they are not likely to be mutagenic and no specific target organ toxicity has been seen in the systemic toxicity studies. The group members are also unlikely endocrine disrupters since no effects in endocrine organs have been observed.

Overall, group members are unlikely to have CMR/ED properties but there is remaining uncertainty due to the potential breakdown of the esters, more specifically regarding the rate of hydrolysis, the information available is mostly from literature sources and refers to the generic ability of carboxylesterases to breakdown the esters.

None of the group members is considered PBT/vPvB or PMT/vPvM based on the available data that show that the substance is readily biodegradable. There is no difference between the branched and unbranched substances in term of biodegradability, this is probably due to the low degree of branching. The majority

[8] JECFA, 1999 http://onlinelibrary.wiley.com/doi/10.2903/j.efsa.2013.3169/epdf; COM, 2003 https://ec.europa.eu/food/sites/food/files/safety/docs/sci-com_scf_out158_en.pdf; EFSA, 2013 http://onlinelibrary.wiley.com/doi/10.2903/j.efsa.2013.3169/epdf

of the substances has high Log KOW (> 5), which indicates a potential of bioaccumulation except for ECs 285-503-5, 210-817-6 and 214-244-2. However, based on their structure and the literature data, all of them are expected to metabolise to fatty acids and diols which are likely not biodegradable . Therefore, there is a low likelihood that these substances would meet the B/vB criteria.

EC 210-817-6 and EC 214-244-2, which are highly soluble and are considered as non-hazardous for aquatic environment, whereas the rest of the group members are poorly water soluble. Therefore, the short-term data are not relevant to conclude the aquatic toxicity and are all inconclusive for this hazard.

There is ongoing CCH for group members; depending on the outcome the strategy might be revisited.

Annex 1: Overview of classifications

Data extracted on 16 January 2020.

There are no self-classifications by the REACH registrants and no harmonised classifications exist.

For EC 285-503-5[9] there is a RAC Opinion for harmonised classification as Repr. 1B.

[9] https://echa.europa.eu/documents/10162/1d73eb33-d8ee-3d5b-1003-45304642bec6

Annex 2: Overview of uses based on information available in registration dossiers

Data extracted on 16 January 2020 and 7 March 2023 (EC 210-817-6, EC 214-244-2)

The substances are used by workers and/or consumers as intermediate and e.g. solvent, additive and degreaser in polymer in coatings & paints, adhesives & sealants, lubricant & greases, fuels, construction applications, plastic and rubber articles, personal care and cosmetic products, air fresheners, washing/ cleaning products, inks/toners/textile dyes, polishes& waxes, fertilisers & plant protection products, biocides, anti-freeze and de-icing products, non-metal surface treatment products, leather treatment products etc.

For EC 285-503-5 there are limited uses compared to all the other substances. Its registered uses in coatings, printing inks and laboratory uses (for industrial and professional workers), and coatings and printing inks for consumers.

EC 214-244-2 has only industrial use as intermediate and professional use as laboratory reagent reported.

Annex 3: Overview of completed or ongoing regulatory risk management activities

Data extracted on 16 January 2020.

There are no relevant completed or ongoing regulatory risk management activities for any of the substances.

For EC 285-503-5[10] there is a RAC Opinion for harmonised classification as Repr. 1B.

[10] https://echa.europa.eu/documents/10162/1d73eb33-d8ee-3d5b-1003-45304642bec6