Assessment of regulatory needs

Authority: European Chemicals Agency (ECHA)

Group Name: Esters from linear and branched carboxylic acid and neopentylglycol

General structure: -

Revision history

Version	*Date*	*Description*
1.0	2 May 2023	

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]
249-060-1	28510-23-8	2,2-dimethylpropane-1,3-diyl 2-ethylhexanoate	Full, 100-1000
250-575-9	31335-74-7	2,2-dimethyl-1,3-propanediyl dioctanoate	Full, 100-1000
255-713-1	42222-50-4	2,2-dimethyl-1,3-propanediyl dioleate	Full, 100-1000
268-225-9	68038-32-4	Fatty acids, vegetable-oil, esters with neopentyl glycol	TII or OSII, not (publicly) available
272-469-1	68855-18-5	Heptanoic acid, ester with 2,2-dimethyl-1,3-propanediol	Full, 100-1000
274-764-0	70693-32-2	Decanoic acid, mixed esters with neopentyl glycol and octanoic acid	Full, 100-1000
284-957-1	85005-25-0	Fatty acids, C14-18 and C18-unsatd., branched and linear, esters with neopentyl glycol	Full, 100-1000
285-533-9	85116-81-0	Fatty acids, C14-18 and C16-18-unsatd., esters with neopentyl glycol	Full, not (publicly) available
286-072-6	85186-86-3	Fatty acids, C8-18 and C18-unsatd., esters with neopentyl glycol	Full, >1000
286-081-5	85186-95-4	Fatty acids, C12-16, esters with neopentyl glycol	Full, not (publicly) available
701-264-6	-	Fatty acids, C8-10 and C18-unsatd., diesters with neopentyl glycol	Full, not (publicly) available
807-674-2	109884-54-0	Isooctadecanoic acid, 1,1'-(2,2-dimethyl-1,3-propanediyl) ester	Full, not (publicly) available

This table does not contain group members that are only notified under the CLP Regulation.

[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

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 from linear and branched carboxylic acid and neopentyl glycol.

There are 12 substances in the group of which 11 have full registrations and one is registered as an intermediate.

Based on information reported in the REACH registration dossiers, the substances in this group are used widely in industrial processes, by professionals and by consumers in a high variety of products and applications. These include e.g, use as solvent or additive in fuels, fertilisers, plant protection products, lubricants, surface treatment, waxes, polishes, and in cosmetics. EC 268-225-9 is manufactured for intermediate use only.

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
249-060-1	Known or potential hazard for reproductive toxicity	No hazard or unlikely hazard	Industrial and professional use in lubricants, consumer use in lubricants and cosmetics. Potential for exposure for workers and consumers and release to the environment.	**First step:** Pending action **Potential next steps (if hazard confirmed after data generation):** CLH **Potential last action:** **Restriction** Justification: The harmonised classification as R 1 – would lead to generic restriction of the substance(s) in consumer mixtures by means of restriction entry 30. 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

EC/List no	Human Health Hazard	Environmental Hazard	Relevant use(s) & exposure potential	Suggested regulatory actions
				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.
250-575-9 **255-713-1** **268-225-9** **272-469-1** **274-764-0** **284-957-1** **285-533-9** **286-072-6** **286-081-5** **701-264-6** **807-674-2**	No hazard or unlikely hazard	No hazard or unlikely hazard	Industrial, professional and consumer use in fuels, fertilisers, plant protection products, paints& coatings, washing& cleaning products, lubricants, textiles and in cosmetics. Potential for exposure for workers and consumers and release to the environment. 268-225-9 only used as intermediated, low potential for exposure & release.	No action **Currently no need for EU RRM** <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 249-060-1 if reprotoxicity hazard is confirmed

Based on currently available information, there is a potential hazard for reproductive toxicity for the substance EC 249-060-1. The substance is reported to be used by industrial and professional workers and consumers in cosmetics and lubricants.

EC 249-060-1 is a diester formed from 2-ethylhexanoic acid and neopentyl glycol. It is likely that enzymatic hydrolysis of EC 249-060-1 releases 2-ethylhexanoic acid, which is a substance with harmonised classification Repr. 1B[5]. Data has been requested under compliance check (CCH).

The substance is unlikely to cause skin sensitisation, mutagenicity, carcinogenicity, endocrine disruption or target organ toxicity (see next section). An ED mode of action might be assumed for the potential reproductive toxicity; however, at this stage the strategy is based only on the hazard hypothesis of reproductive toxicity.

The substance (EC 249-060-1) in the group is (potentially) toxic to the aquatic environment. Unlike other members of the group, available aquatic toxicity studies (short-term *Daphnia*, fish and algae, long-term *Daphnia*) with EC 249-060-1 show effects on the test organisms. An enhanced biodegradation study is available to prove that it is inherently biodegradable and thus does not fulfil the P criterion. Although it has high Log K_{ow} (>6) the substance is unlikely to be PBT as it does not meet the P criterion.

The first step of the regulatory risk management action proposed, should the hazard exist, is to confirm via harmonised classification (CLH) the potential reproductive toxicity. If the CLH process confirms the substances as being R1A/B then the CLH i) 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.

CLH is also a prerequisite to restrict the presence of the substances in clothing, other textiles, and footwear articles, by means of the restriction entry 72 of REACH Annex XVII (this would require addition of the relevant substances to Appendix 12 by the Commission through Article 68(2)).

CLH will also support regulatory action under other legislations. For instance, harmonised classification as CMR cat. 1 will trigger regulatory action under the Cosmetic products regulation (EC) No 1223/2009, since CMR cat. 1 are restricted by this regulation unless specifically derogated.

The professional uses in lubricants 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.

[5] https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX%3A32023R1435&qid=1689155759608

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[6] 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.

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

None of the remaining substances in the group needs further EU regulatory risk management actions at the moment due to low potential toxicological and environmental hazard.

Many of the substances in the group have widespread uses in professional settings or consumer products, with high exposure potential and release in the environment.

Based on ECHA's assessment of currently available hazard information, no potential hazards were identified for human health. These conclusions are based on the information that both the alcohol part (neopentyl glycol) and the carboxylic acid parts of these group members are of low toxicity, it is unlikely that the group members would cause concern for human health or the environment.

For human health, no specific hazard was identified from the available data on the group. Based on the evaluations from other safety bodies[7], group members are expected to be hydrolysed into neopentyl glycol (2,2-dimethylpropane-1,3-diol) and fatty acids by carboxylesterase enzymes found in most tissues throughout the body, including the gastrointestinal tract.
The resulting branched carboxylic acids will undergo different metabolic pathways, depending on the carbon chain length and branching: beta-oxidation for short chains, omega-oxidation for long chains and alfa- and/or beta-oxidation for acids with a methyl substituent. The majority of the carboxylic acid parts of these group members have been or are being assessed by ECHA (group on fatty acids expected to be of low toxicity). Neopentyl glycol (2,2-dimethylpropane-1,3-diol) is registered under REACH. The data on this substance does not indicate any hazard for skin sensitisation, mutagenicity, carcinogenicity, reproductive toxicity, endocrine disruption or target organ toxicity.

The substances are unlikely to cause skin sensitisation, mutagenicity, carcinogenicity, reproductive and developmental toxicity, endocrine disruption or target organ toxicity. None of the substances have a classification for CMR, skin sensitisation or specific target organ toxicity properties. The data available on these

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

[7] 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

group members does not indicate any concern for human health.

In vitro mutagenicity studies are available for five of the substances (Ames studies, *in vitro* chromosomal aberration tests and *in vitro* mammalian cell gene mutation test) and are negative.
Regarding sensitisation, no functional group of concern has been identified for the group.
Information on repeated dose toxicity and developmental toxicity is based on read-across and no effects are expected for the group members.

No carcinogenicity study is available, but no carcinogenic effect is expected in view of the absence of mutagenic and repeated dose toxicity hazard.
Regarding a potential endocrine disruption hazard, the available data does not indicate any target organ toxicity in endocrine organs such as the thyroid or the reproductive organs. Therefore, there is no apparent hazard finding that could be linked to endocrine-mediated effects for any of the substances.

There is some remaining uncertainty regarding the breakdown of the esters, more specifically regarding the rate of hydrolysis, as the information available is mostly from literature sources and refers to the generic ability of carboxylesterases to breakdown the esters.

The group members are unlikely to be PBT/vPvB. All of these substances are claimed to be readily biodegradable. There are two substances which contain branched carboxylic acids (EC 284-957-1 and List 807-674-2). These are shown to be readily biodegradable. Other substances contain only liner branched carboxylic acids and ready biodegradability studies covering the shortest (C7) to longest (C18) carboxylic acids are available. Based on the available data and structural similarity across the group, it is very likely that all the substances are readily biodegradable. Although they have high Log K_{ow} (>6), they are unlikely to bioaccumulate as it is very likely that they are readily degraded in the environment and/or metabolised by organisms. Available data shows that the group members do not show any acute toxicity to aquatic organisms up to the water solubility. Most studies were performed by using water accommodated fraction, some use read-across from the group members. Only limited studies are available for long-term *Daphnia*: only two studies with EC 272-469-1, EC 255-713-1 are available. As these studies cover the shortest and longest (C7 and C18) chain carboxylic acids, and no effects were seen for other aquatic toxicity endpoints, it is very likely that all the group members are of low toxicity.

Annex 1: Overview of classifications

Data extracted on 28 February 2020.

None of the 11 substances currently has harmonised or self-classification.

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

Data extracted on 28 February 2020, for List No. 701-264-6 on 7 March 2023.

Main types of applications structured by product or article types	249-060-1	701-264-6	250-575-9	255-713-1	272-469-1	274-764-0	284-957-1	285-533-9	286-072-6	286-081-5	807-674-2
Use in washing and cleaning products, detergents, polishes, waxes		F, I, **P, C**	F, I, **P, C**								
Use in various type of coatings (paints, inks, etc)		F, I, **P, C**	F, I, **P, A**								
Use in construction materials (e.g., adhesives, coatings)		F, I, **P, C**	F, I, **P, C, A**								
Use in textiles		F, I, **C, A**	F, I, **P, C, A**								
Use in lubricants	F, I, **P, C**	F, I, **P, C**	F, I, **P, C**								
Use in cosmetics	F, **C**	F, **P, C**	F, **P, C**								
Use in plant protection products/biocides (co-formulant)		I, **P, C**	F, I, **P, C**								
Use in fuels (incl. fuel additives)		I, **P, C**	F, I, **P, C**								
Use in solvents/thinners, etc. (e.g. air freshners)		**C**	F, I, **P, C**								
De-icing		**P, C**	**P, C**								
Use in fertilizers		F, I, **P, C**	F, **P, C**								
Use in tyre and rubber			F, I, **P, C**								
Use in water treatment		F, I, **P, C**									
Use in fragrances		F, **C**									
Use in explosives		**P**									
Use in pharmaceuticals		I, **P**									
Use in surface treatment (metal, non-metal, paper & boards, leather)		F, I, **P, C**									

Main types of applications structured by product or article types	249-060-1	701-264-6	250-575-9	255-713-1	272-469-1	274-764-0	284-957-1	285-533-9	286-072-6	286-081-5	807-674-2
Metal working/ heat transfer/ hydraulic fluids		I, **P, C**									
Use in polymer preparations and compounds		F, I, **P, C**									
Use as intermediate		I									

F: formulation, I: industrial use, P: professional use, C: consumer use, A: article service life; P, C and A are highlighted in red to indicate widespread use with potential for exposure/release.

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

Data extracted on 28 February 2020.

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