Assessment of regulatory needs

Authority: European Chemicals Agency (ECHA)

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

General structure: -

Revision history

Version	*Date*	*Description*
1.1	18 September 2023	Reference to CLH intention for 3,5,5-trimethylhexanoic acid added

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]
267-021-7	67762-52-1	Fatty acids, C5-9, hexaesters with dipentaerythritol	Full, 100-1000T
270-470-1	68441-66-7	Decanoic acid, mixed esters with dipentaerythritol, octanoic acid and valeric acid	Full, >1000
270-560-0	68443-84-5	Triisononanoic acid, triester with 2,2'-[oxybis(methylene)]bis[2-(hydroxymethyl)propane-1,3-diol] tris(2-ethylhexanoate)	Full, not (publicly) available
271-689-5	68604-38-6	Fatty acids, C16-18 and C18-unsatd., hexaesters with dipentaerythritol	Full, 100-1000
275-019-2	70913-98-3	Fatty acids, tall-oil, esters with dipentaerythritol	Full, not (publicly) available
275-093-6	70983-72-1	Fatty acids, C5-10, esters with dipentaerythritol	C&L notification
282-775-7	84418-63-3	Isononanoic acid, mixed esters with dipentaerythritol, heptanoic acid and pentaerythritol	Full, not (publicly) available
426-590-3	187412-41-5	pentaerythritol, dipentaerythritol, fatty acids, C6-10, mixed esters with adipic acid, heptanoic acid and isostearic acid	NONS, not (publicly) available
442-200-4	not (publicly) available	2,2,6,6-tetrakis(tetradecanoyloxymethyl)-4-oxa-heptane-1,7-diyl ditetradecanoate	NONS, not (publicly) available
444-000-2	-	3-[3-(pentanoyloxy)-2,2-bis[(pantanoyloxy)methyl]propoxyl]-2,2-bis[(pentanoyloxy)methyl]propyl pentanoate 3-{3-[(3,5,5-trimethylhexanoyl)oxy]-2,2-bis({[(3,5,5-trimethylhexanoyl)oxy]methyl}propoxy)-2,2-bis({[(3,5,5-trimethylhexanoyl)oxy]methyl}propyl 3,5,5-trimethylhexanoate	Full, not (publicly) available
453-460-3	-	3-{3-[(3,5,5-trimethylhexanoyl)oxy]-2,2-	Full, 100-1000

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

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]
		bis({[(3,5,5-trimethylhexanoyl)oxy]methyl})propoxy}-2,2-bis({[(3,5,5-trimethylhexanoyl)oxy]methyl})propyl 3,5,5-trimethylhexanoate	
453-480-2	-	Decanoic acid, mixed esters with dipentaerythritol heptanoic acid and octanoic acid	Full, not (publicly) available
453-490-7	not (publicly) available	Dipentaerythritol hexaesters of 3,5,5-trimethylhexanoic, n-decanoic, n-heptanoic, and n-octanoic acids	Full, 100-1000
615-229-7	70969-57-2	2-({3-(octadecanoyloxy)-2,2-bis[[](octadecanoyloxy)methyl]propoxy}methyl)-2-[[](octadecanoyloxy)methyl]propane-1,3-diyl dioctadecanoate	Full, 10-100
700-325-4	1149346-12-2	Esterification products of 2,2'-(oxydimethanediyl)bis[2-(hydroxymethyl)propane-1,3-diol] and heptanoic acid and pentanoic acid and 3,5,5-trimethylhexanoic acid	Full, 1-10
701-334-6	-	Dipentaerythritol hexaesters of 3,5,5-trimethylhexanoic, n-decanoic, n-octanoic, and n-pentanoic acids	Full, not (publicly) available
943-730-3	-	Monopentaerythritol tetraesters and dipentaerythritol hexaesters of 2-ethylhexanoic and n-valeric acids	Full, not (publicly) available
945-883-1	1379424-11-9	3,5,5-Trimethylhexanoic acid, mixed esters with dipentaerythritol and heptanoic acid	Full, not (publicly) available
946-882-9	not (publicly) available	Fatty acids, C9, hexaesters with dipentaerythritol	Full, not (publicly) available

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

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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

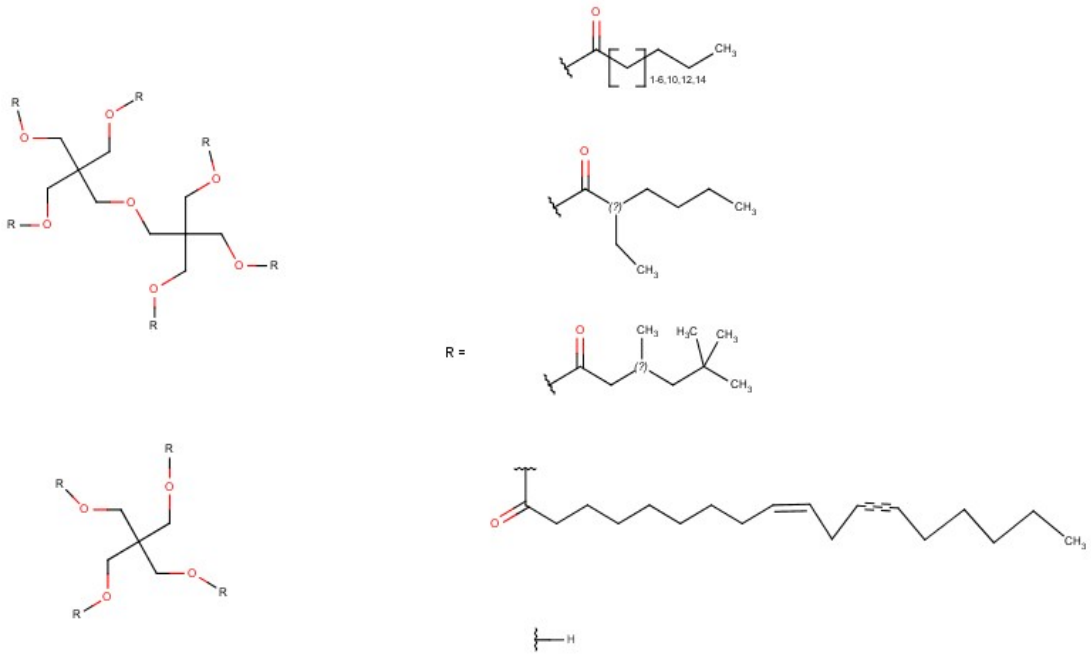
ARN	Assessment of Regulatory Needs
CCH	Compliance Check
CLH	Harmonised classification and labelling
CMR	Carcinogenic, mutagenic and/or toxic to reproduction
DEv	Dossier evaluation
ED	Endocrine disruptor
NONS	Notified new substances
OEL	Occupational exposure limit
OSII or TII	On-site isolated intermediate 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 full or partial esters of pentaerythritol and dipentaerythritol.

The substances have mostly linear and branched fatty acids with a chain length in the range between 5 and 18 carbons. In some cases also unsaturated C18 fatty acids are present among the saturated fatty acids. The branched fatty acids present are mostly 2-ethylhexanoic acids, 3,5,5-trimethylhexanoid acid (iso-nonanoic acid) and isostearic acid. Representative structures are shown in the figure below.



This group consists of 19 substances, of which 16 have full registrations. Two substances have a NONS registration and one substance is only notified to the C&L inventory. From the chemical structure perspective, these substances could potentially be used as alternatives to other substances in the group.

Based on information reported in the REACH registration dossiers, the substances that have an active registration have widespread uses in professional setting or consumer mixtures and/or articles where exposure to human health and releases to the environment can generally be expected.

The majority of substances in the group have a relatively narrow use profile. They are used as lubricating agent in lubricants and metal working fluids, as plasticiser in coatings & inks and polymers & plastics, and as emollient in cosmetics.

Seven substances in the group have a very wide use profile. They can be use by professional workers and/or consumers in washing and cleaning products, polishes and waxes, cosmetics, air care products, biocide/pest control, lubricants, metalworking fluids, construction products, polymers & plastics, textiles, etc. Article service life is consistently reported for the uses in construction products and textile & leather and reported in some cases for the use in polymers & plastics.

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

Subgroup name, EC/List no, substance name	Human Health Hazard	Environmental Hazard	Relevant use(s) & exposure potential	Suggested regulatory actions
267-021-7 **270-470-1** **270-560-0** **271-689-5** **275-019-2** **282-775-7** **444-000-2** **453-460-3** **453-480-2** **453-490-7** **615-229-7** **700-325-4** **701-334-6**	No hazard or unlikely hazard	No hazard or unlikely hazard	Widespread uses by professionals and consumers and in articles. In the case of 270-470-1, 270-560-0, 275-019-2, 444-000-2, 453-480-2, 615-229-7, 700-325-4, 701-334-6 and 943-730-3 mostly lubricants, coatings and inks. Potential for exposure for workers and consumers and release to the environment.	CCH for 267-021-7, 270-560-0, 282-775-7, 444-000-2, 453-460-3, 453-490-7, 943-730-3 and 945-883-1 **Potential last action: Currently no need for EU RRM** Justification: Overall, no or unlikely hazard that would lead to concern for the reported uses.

Subgroup name, EC/List no, substance name	Human Health Hazard	Environmental Hazard	Relevant use(s) & exposure potential	Suggested regulatory actions
943-730-3				
945-883-1 **946-882-9**			Widespread uses by professionals and consumers (in lubricating agents, cosmetics). Potential for exposure for workers and consumers and release to the environment.	
275-093-6 **426-590-3** **442-200-4**	Known or potential hazard for skin sensitisation for EC 426-590-3		No registrations/ NONS registrations.	No action <u>Justification:</u> Low potential for exposure to both human health and environment is expected. Actions may be re-considered if there is a change in the registration status when the assessment will be revisited.

3 Justification for the no need for regulatory risk management action at EU level

Currently no need to suggest (further) regulatory risk management actions for all substances

Based on currently available information, there is no need for (further) EU regulatory risk management for all substances in the group.

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.

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.

Most of the substances in this group are unlikely to fulfil the PBT/vPvB screening criteria, because they are considered to be readily biodegradable and are unlikely to fulfil the T criterion.

The substances have low water solubility (for most substances: <0.2 mg/L), the high molecular weight distribution (for most substances, 900-1900) and the central four arm structure that could increase the shielding of the molecules therefore reducing fragmentation. Reduced fragmentation may result in a lower surface area available for the inoculum to degrade the substance. The overall picture suggests that substances in this group are potentially P/vP. The substances have a low potential to bioaccumulate due to metabolisation common to all esters.

Based on the evaluations[5] from other safety bodies, group members are expected to be rapidly hydrolysed into branched carboxylic acids and alcohols by carboxylesterase enzymes found in most tissues throughout the body, including the gastrointestinal tract. The resulting linear alcohols will be oxidised to their corresponding aldehydes and linear carboxylic acids, which will in turn be metabolised to carbon dioxide via the fatty acid pathways and the tricarboxylic acid cycle. 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.

EC 426-590-3 is classified as Skin Sens 1., however, no uses are currently reported. This hazard is not extrapolated to other group members as it was not identified based on the available information on other group members.

The substances are unlikely to cause mutagenicity, carcinogenicity, reproductive and developmental toxicity, endocrine disruption or target organ toxicity. None of the substances have a classification for CMR or specific target organ toxicity properties. Regarding a potential endocrine disruption hazard, the available data does not indicate any target organ toxicity in endocrine organs such as the thyroid

[5] 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

or the reproductive organs. Therefore, there is no apparent hazard finding that could be linked to endocrine-mediated effects for any of the substances.

No studies on skin sensitisation, mutagenicity, carcinogenicity, reproductive and developmental toxicity, or repeated dose toxicity are available on the substances in the group. The information on potential health effects is based on read-across to similar substances (esters), for example esters of pentaerythritol. The data on the esters used for read-across indicates that those substances are of low toxicity.

The group members EC/List 270-560-0 and 943-730-3 contain in their moiety 2-ethylhexanoic acid that is know reproductive toxicant (Repr. 1B)[6]; for EC 943-730-3 information from a similar triester does not indicate potential reproductive toxicity.

The group members (EC/List 267-021-7, 270-560-0, 282-775-7, 444-000-2, 453-460-3, 453-490-7, 700-325-4, 701-334-6, 945-883-1 and 946-882-9) may upon enzymatic hydrolysis release 3,5,5-trimethylhexanoic acid which is intended for CLH Repr.1B[7].

The potential for enzymatic biotransformation and release of 2- ethylhexanoic acid or 3,3,5-trimethylhexanoic acid is assumed to be low taking into account the size of the parent compound.

Overall, the reproductive and developmental toxicity hazard is considered unlikely for the substances of these subgroups with remaining uncertainty. This is 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.

Applying the potential reproductive and developmental toxicity hazard for these group members would be a worst-case assumption, as it is not known whether the metabolites of concern resulting from their hydrolysis will be systemically available at concentrations sufficient to cause toxic effects. In general, it is assumed that the toxicity of the esters is expected to be lower than that of the corresponding carboxylic acids and alcohols since higher doses of the esters would be needed to reach equivalent toxic doses.

The majority of the substances in the group have widespread uses in professional settings or consumer products, with high exposure potential and release in the environment except EC 275-093-6 and EC 426-590-3 that do not have any active registration at the moment.

Due to the remaining uncertainties linked to the breakdown products and to the low data density of the information screened, further assessment and/or information is needed under CCH for EC/ List 267-021-7, 270-560-0, 282-775-7, 444-000-2, 453-460-3, 453-490-7, 943-730-3 and 945-883-1.

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

[7] https://echa.europa.eu/fi/registry-of-clh-intentions-until-outcome/-/dislist/details/0b0236e188116743

Annex 1: Overview of classifications

Data extracted on 5 October 2020.

EC/ List No	Substance name	Harmonised classification	Classification in registrations
267-021-7	Fatty acids, C5-9, hexaesters with dipentaerythritol	-	-
270-470-1	Decanoic acid, mixed esters with dipentaerythritol, octanoic acid and valeric acid	-	-
270-560-0	triisononanoic acid, triester with 2,2'-[oxybis(methylene)]bis[2-(hydroxymethyl)propane-1,3-diol] tris(2-ethylhexanoate)	-	-
271-689-5	Fatty acids, C16-18 and C18-unsatd., hexaesters with dipentaerythritol	-	-
275-019-2	Fatty acids, tall-oil, esters with dipentaerythritol	-	-
282-775-7	Isononanoic acid, mixed esters with dipentaerythritol, heptanoic acid and pentaerythritol	-	-
426-590-3	pentaerythritol, dipentaerythritol, fatty acids, C6-10, mixed esters with adipic acid, heptanoic acid and isostearic acid	Skin Sens. 1 H317	R43 (Sensitising)
442-200-4	2,2,6,6-tetrakis(tetradecanoyloxymethyl)-4-oxa-heptane-1,7-diyl ditetradecanoate	-	-
444-000-2	3-[3-(pentanoyloxy)-2,2-bis[(pantanoyloxy)methyl]propoxyl]-2,2-bis[(pentanoyloxy)methyl]propyl pentanoate 3-{3-[(3,5,5-trimethylhexanoyl)oxy]-2,2-bis({[(3,5,5-trimethylhexanoyl)oxy]methyl}propoxy)-2,2-bis({[(3,5,5-trimethylhexanoyl)oxy]methyl}propyl 3,5,5-trimethylhexanoate	-	-
453-460-3	3-{3-[(3,5,5-trimethylhexanoyl)oxy]-2,2-bis({[(3,5,5-trimethylhexanoyl)oxy]methyl})propoxy}-2,2-bis({[(3,5,5-trimethylhexanoyl)oxy]methyl})propyl 3,5,5-trimethylhexanoate	-	
453-480-2	Decanoic acid, mixed esters with dipentaerythritol heptanoic acid and octanoic acid	-	-
453-490-7	Dipentaerythritol hexaesters of 3,5,5-trimethylhexanoic, n-decanoic, n-heptanoic, and n-octanoic acids	-	-
615-229-7	2-({3-(octadecanoyloxy)-2,2-bis[[](octadecanoyloxy)methyl]propox	-	-

EC/ List No	Substance name	Harmonised classification	Classification in registrations
	y}methyl)-2-[[](octadecanoyloxy)methyl]propane-1,3-diyl dioctadecanoate		
700-325-4	Esterification products of 2,2'-(oxydimethanediyl)bis[2-(hydroxymethyl)propane-1,3-diol] and heptanoic acid and pentanoic acid and 3,5,5-trimethylhexanoic acid	-	-
943-730-3	Monopentaerythritol tetraesters and dipentaerythritol hexaesters of 2-ethylhexanoic and n-valeric acids	-	-
946-882-9	Dipentaerythritol hexaesters of n-valeric, n-heptanoic and 3,5,5-trimethylhexanoic acids	-	-

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

Data extracted on 5 October 2020 (for EC 270-560-0 and EC 444-000-2 from 7 March 2023).

Main types of applications structured by product or article types	267-021-7	270-470-1	270-560-0	271-689-5	275-019-2	282-775-7	444-000-2	453-460-3	453-480-2	453-490-7	615-229-7	700-325-4	701-334-6	943-730-3
Lubricants	F, I, **P**, **C**	F, I, **P**, **C**	F, I, **P, C**	F, I, **P**, **C**	F, I, **P**	F, I, **P**, **C**	F, I, **P, C**	F, I, **P**	F, I, **P**, **C**	F, I, **P**, **C**		I, **A**	F, I, **P**	F, I, **P**
Coatings & inks	I, **P**, **C**			I, **P**, **C**	F, I, **P**, **C**	F, I, **P**, **C**		**A**			F, I, **P**, **C**			
Fertilisers & PPP	F, I, **P**, **C**			F, **P**, **C**		F, I, **P**, **C**		F, I, **P**, **C**,		F, I, **P**, **C**,				
Oil & gas drilling	I, **P**			I, **P**		I, **P**								
Polishes & wax	**P**, **C**			**P**, **C**		**P**, **C**		**P**, **C**,		**P**, **C**,				
Washing & cleaning	F, I, **P**, **C**			F, I, **P**, **C**		F, I, **P**, **C**	F, I, **P**	F, I, **P**, **C**,		F, I, **P**, **C**,	I			
Cosmetics	F, **P**, **C**		F, **C**	F, **P**, **C**		F, **P**, **C**		F, **P**, **C**,		F, **P**, **C**,				
Biocides & pest control	F, **C**			F, **C**		F, **C**		F, I, **P**, **C**,		F, I, **P**, **C**,				
Adhesives & sealants	F, I, **P**, **C**					F, I, **C**		F, I, **P**, **C**,		F, I, **P**, **C**,				
Construction products	F, I, **P**, **C**, **A**			F, I, **P**, **C**, **A**		F, **P**, **C**, **A**								
Fuels	I, **P**, **C**			I, **P**, **C**		I, **P**, **C**		I, **P**, **C**,		I, **P**, **C**,				
Air care products	F, **C**			F, **C**		F, **C**		F, **C**		F, **C**				

Main types of applications structured by product or article types	267-021-7	270-470-1	270-560-0	271-689-5	275-019-2	282-775-7	444-000-2	453-460-3	453-480-2	453-490-7	615-229-7	700-325-4	701-334-6	943-730-3
Polymers & plastics	F, I, **A**			I, **A**		F, I, **A**		F, I, **P**, **C**,		F, I, **P**, **C**,	F, I, **P**, **A**			
Water treatment chemicals	F, I, **P**			F, I		F, I, **P**		F, I, **P**,		F, I, **P**,				
Metal working fluids	F, I, **P**			I, **P**			F, I, **P**							
Hydraulic fluids							F, I, **P**							
Textiles & leather	F, I, **A**			F, I, **A**										

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 29 September 2020.

EC / List number	RMOA	Authorisation		Restriction*	CLH	Actions not under REACH / CLP
		Candidate list	Annex XIV	Annex XVII	Annex VI (CLP)	
426-590-3					YES	

*Some of the broad restriction entries in the Annex XVII of REACH are not represented in the overview, e.g. when the scope of the restriction is defined by its classification or the substance identification is broad (e.g. entries 3, 28-30 and 40).

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