Assessment of regulatory needs

Authority: ECHA

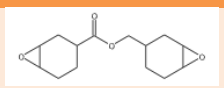
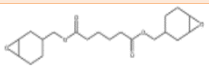
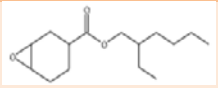
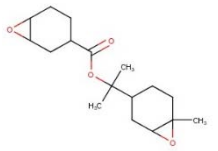
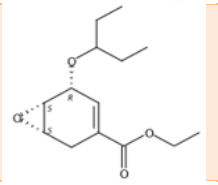
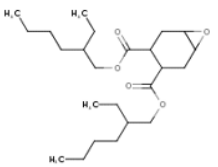
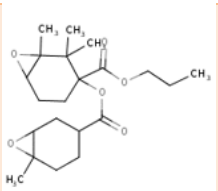
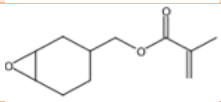
Group Name: oxabicyclo esters

General structure:

Revision history

Version	Date	Description
1.0	31 October 2023	

Substances within this group:

EC / List number	CAS number	Substance name [and / or Substance name acronyms]	Chemical structures	Registration type (full, OSII or TII, NONS), highest tonnage band among all the registrations (t/y) [1]
219-207-4	2386-87-0	7-oxabicyclo[4.1.0]hept-3-ylmethyl 7-oxabicyclo[4.1.0]heptane-3-carboxylate [ECC]		Full, 100-1000
221-518-5	3130-19-6	bis[(3,4-epoxycyclohexyl)methyl] adipate		Full, 10-100
263-471-3	62256-00-2	2-ethylhexyl 7-oxabicyclo[4.1.0]heptane-3-carboxylate		Full, not (publicly) available
428-600-1		1-[1-methyl-1-(6-methyl-7-oxabicyclo[4.1.0]hept-3-yl)ethyl]-7-oxabicyclo[4.1.0]heptane-3-carboxylate		NONS
429-020-1	204254-96-6	ethyl (1S,5R,6S)-5-(1-ethylpropoxy)-7-oxabicyclo[4.1.0]hept-3-ene-3-carboxylate		NONS
430-700-5	10138-36-0	bis(2-ethylhexyl)-4,5-epoxycyclohexane-1,2-dicarboxylate		NONS
470-140-9		[No public or meaningful name is available]		NONS
688-147-2	82428-30-6	2-Propenoic acid, 2-methyl-, 7-oxabicyclo[4.1.0]hept-3-ylmethyl ester		Full, not (publicly) available

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

[1] Note that 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 level3. 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
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 substances based on the presence of the '7-oxabicyclo[4.1.0]heptane' moieties that have a carboxyl functional group attached in position 3, creating an ester function there. These substances are with one or two oxabicyclo moieties and with altering alkyl chains. The substance with List number 688-147-2 differs from the rest of the members due to the methacrylate function.

The group consists of eight substances of which four are fully registered and four are NONS.

Based on information reported in the REACH registration dossiers, three of the group members, EC 219-207-4, EC 221-518-5 and List 688-147-2, are used as epoxy resins in formulation and other industrial uses including adhesives and sealants, coatings and paints, surface treatment and printing inks. List 688-147-2 is also used as monomer in polymerisation. EC 263-471-3 is used as a functional fluid in industrial and professional uses including as lubricant, hydraulic fluid and heat transfer fluid. EC 429-020-1 is used as an intermediate only. Three of the NONS are not currently used in the EU (EC 428-600-1, EC 430-700-5, and EC 470-140-9).

There is a potential for exposure and releases into the environment in particular for industrial and professional uses of EC 263-471-3 but also, albeit to a lesser extent, for the three epoxy resins.

For three substances in the group regulatory activities are ongoing or were completed. EC 219-207-4 was subject to a Substance Evaluation performed by Ireland, focusing on human health concerns only. Subsequently a CLH proposal for Skin Sens 1, STOT RE 2 and Muta 2 (RAC opinion available[5]) has been submitted. Two of the NONS have harmonised classifications: EC 429-020-1 for Skin Sens 1 and STOT RE 2 and EC 430-700-5 for Skin Sens 1.

[5] RAC opinion, 2.06.2022

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 number	Human Health Hazard	Environmental Hazard	Relevant use(s) & exposure potential	Suggested regulatory actions
219-207-4 **221-518-5** **688-147-2**	Known or potential hazard for mutagenicity and for skin sensitisation for all for STOT RE for ECs 219-207-4 and 221-518-5	Known or potential hazard for aquatic toxicity for ECs 219-207-4 and 221-518-5	Industrial uses as epoxy resins, with potential for workers exposure and releases to the environment	**First step:** CCH **Potential last action:** Currently no need for EU RRM <u>Justification:</u> Harmonised/self-classification require company level risk management measures (RMM) for workers to be in place. The concern related to the presence of skin sensitisers in consumer mixtures is under investigation.
263-471-3	Known or potential hazard for skin sensitisation	Known or potential hazard for aquatic toxicity	Industrial and widespread professional uses as functional fluid, with significant potential	

			for workers exposure and significant releases to the environment	
429-020-1 **430-700-5** **470-140-9** **428-600-1**	Known or potential hazard for skin sensitisation For ECs 429-020-1 and 430-700-5 for STOT RE for EC 429-020-1	Known or potential hazard for aquatic toxicity for EC 470-140-9	Intermediate uses (EC 429-020-1) No information on uses (NONS or inactive registration, ECs 430-700-5, 470-140-9, 428-600-1) where low potential for exposure and release can be assumed.	

3 Justification for the no need for regulatory risk management action at EU level (if hazards confirmed)

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

Based on currently available information, six substances of the group (EC 429-020-1 with CLH, EC 219-207-4 with ongoing CLH[5], ECs 221-518-5, 263-471-3, 430-700-5, and 470-140-9) have potential STOT RE 2 hazard.

The observed adverse effects relate to adverse ophthalmological effects (cornea) for EC 429-020-1 and degeneration in the olfactory epithelium of nasal tissues for EC 219-207-4. Other target organs noted were liver and kidney. Since no information on hormonal effects with regards to the thyroid glands were provided, no assumption on potential ED effects can be drawn.

Potential for mutagenicity hazard is observed for four substances (all three epoxy resins as well as one of the NONS, EC 470-140-9): List 688-147-2 is self-classified as Muta 2, EC 219-207-4 has a CLH as Muta 2 ongoing, for EC 221-518-5 and EC 470-140-9 the findings are based on positive *in vitro* data or read-across provided in the registration dossier.

Each member of this group has an associated skin sensitisation hazard, either known or potential. Two NONS have a harmonised classification as Skin Sens 1 (EC 429-020-1 and EC 430-700-5), three of the group members are self-classified as Skin Sens 1B (EC 219-207-4, EC 221-518-5, EC 688-147-2). Two substances in the group are not classified although the data in the registration dossiers are indicative of skin sensitising properties (EC 263-471-3, EC 428-600-1).

A CLH proposal for harmonised classification for germ cell mutation, STOT RE and skin sensitisation has been submitted for one substance (EC 219-207-4) in the group. In the opinion of RAC, the substance warrants classification as Skin Sens. 1, STOT RE 2 (H373) and Muta. 2 (H341). Other group members have experimental data indicating a skin sensitisation property and are self-classified accordingly.

EC 688-147-2 differs from the other group members as it is reported to be a methacrylate with properties favourable for absorption across the respiratory tract epithelium and may potentially be a respiratory sensitiser. No study on respiratory sensitisation is however available to confirm this. Based on physical chemical properties, vapor pressure (moderate) and no boiling up to 117C it is considered that EC 688-147-2 most likely will not be a respiratory sensitiser. However, some uncertainty remains regarding this. No respiratory sensitisation properties are expected for the other substances in the group.

Currently ecotoxicity available information in the registration dossiers does not contain any data relevant to conclude on endocrine disruption potential of any of the substances in the group.

None of the substances in the in the group is currently classified for environmental hazards or meets PBT/vPvB criteria. However, the existing data in the registration dossiers would justify classification of many group members for long-term aquatic

hazards based on surrogate approach (ECs 219-207-4, 221-518-5, 263-471-3, 470-140-9 (NONS), and List 688-147-2. The shown environmental classifications are based on available acute toxicity information, since currently there are no long-term aquatic toxicity studies available for fish and aquatic invertebrates.

No hazard is observed for the following group members: EC 429-020-1, EC 430-700-5 and EC 428-600-1, for which it can be concluded to have unlikely aquatic toxicity hazard based on the available information on other substances in the group. As there is a high uncertainty in this conclusion, their hazard potential should be reassessed if further data especially on long-term hazards in aquatic animals is generated for other substances in the group.

All the substances in this group are unlikely to fulfil the PBT/vPvB screening criteria, because all except two substances degrade > 60% in the 28-day screening tests. However, none of the substances that show > 60% degradation meet the 10-day criterion in their degradability. The two substances showing slower degradation rate are potentially persistent: EC 429-020-1 degrades 14% in 28 days and 470-140-9 degrades 1.67% in 28 days. There is no experimental test data on bioaccumulation available for any of the substances; however, all except one (EC 428-600-1) have experimental logKow values available. Two substances have logKow values above 4.5 (for EC 263-471-3 logKow is 5-5.1 and for 430-700-5 log Know is > 6.2).

In conclusion, the potentially persistent substances in the group are not bioaccumulative and there is no reason to suggest that any of the substances meet PBT or vP/vB criteria.

Compliance check is suggested, when possible, to generate information on long-term environmental effects and degradation.

The NONS substance (EC 428-600-1), for which there is no environmental fate information available to assess its PBT or vP/vB potential, is assumed to behave in the environment like other substances in the group. Based on this structural similarity there is no reason to suggest that it is both persistent and bioaccumulative and it can also be concluded to be an unlikely PBT or vP/vB substance. However, if new information showing persistence and/or bioaccumulation potential of any substance in the group becomes available, the PBT or vP/vB potential of the NONS substance(s) should also be reassessed.

It is proposed to open CCH to clarify the hazards for the substances ECs/List 219-207-4, 221-518-5, 263-471-3, 688-147-2.

It is expected that following data generation registrants would adequately self-classify the substances as relevant (as STOT RE, Muta, Skin Sens. and Aqua tox). The (self)classification will require company level risk management measures (RMM) for human health and the environment to be in place. Therefore, it is proposed that there is currently no need for EU-wide regulatory risk management.

There are uncertainties regarding potential consumer uses. Some products containing high concentrations of substances EC 219-207-4 and EC 221-518-5 seem to be available for the general public (based on SDS[6] found online), although this use is not registered. Additionally, they may be used in printing ink in food contact materials outside the EU.

Adequate product labelling should in principle provide consumers with sufficient information to manage risks arising from the use of mixtures containing the skin sensitising substance of this group (all except EC 470-140-9 and 428-600-1).

[6] https://multimedia.3m.com/mws/mediawebserver?mwsId=SSSSSuUn_zu8l00xm829582Bmv70k17zHvu9lxtD7SSSSSS--, https://www.freemansupply.com/MSDS/Combined/Huntsman/RenEpoxy/35A927E.pdf, https://docs.rs-online.com/6a14/0900766b81510b91.pdf.

However, there is a concern related to skin sensitisers (potentially) present in consumer mixtures and the need to further investigate whether further regulatory actions are needed and what would be the best options to address this concern.

Such concern has already been identified in other groups of substances and was brought for further discussion to Member States. Work is ongoing on this generic issue by both Member States and ECHA which may affect the regulatory actions on substances in this group.

Therefore, it is proposed that there is currently no need for EU-wide regulatory risk management.

Actions (including data generation) will be re-considered when the assessment will be revisited if the registration status and/or uses change.

For all substances, the need for an EU-wide worker exposure limit in air (via REACH or OSH) was also considered as a possible regulatory measure. No OELs are currently set for any substances of the group in any EU and non-EU jurisdiction[7]. However, this RRM was eventually excluded from further consideration because the substances are not volatile (except EC 688-147-2), and even if some are used in a way that can generate aerosols, the uses are not widespread and exposure is not expected to be high via inhalation.

[7] GESTIS database checked on 9 Feb 2021.

Annex 1: Overview of classifications

Data extracted on 29.01.2021

EC/ List No	Substance name	Harmonised classification	Classification in registrations
219-207-4	7-oxabicyclo[4.1.0]hept-3-ylmethyl 7-oxabicyclo[4.1.0]heptane-3-carboxylate	(RAC opinion 2.06.2022[5]) Skin sens 1, STOT RE 2 H373, Muta 2	Skin sens 1B, H317
221-518-5	bis[(3,4-epoxycyclohexyl)methyl] adipate	-	Skin sens 1B, H317
263-471-3	2-ethylhexyl 7-oxabicyclo[4.1.0]heptane-3-carboxylate	-	Not classified
428-600-1	1-[1-methyl-1-(6-methyl-7-oxabicyclo[4.1.0]hept-3-yl)ethyl]-7-oxabicyclo[4.1.0]heptane-3-carboxylate	-	Not classified
429-020-1	ethyl (1S,5R,6S)-5-(1-ethylpropoxy)-7-oxabicyclo[4.1.0]hept-3-ene-3-carboxylate	STOT RE 2, H373 Skin Sens. 1, H317	Skin Sens. 1, H317 STOT Rep. Exp. 2, affected organs Eyes, H373
430-700-5	bis(2-ethylhexyl)-4,5-epoxycyclohexane-1,2-dicarboxylate	Skin Sens. 1, H317	
470-140-9	[No public or meaningful name is available]	-	

688-147-2	2-Propenoic acid, 2-methyl-, 7-oxabicyclo[4.1.0]hept-3-ylmethyl ester	-	Eye Irrit. 2, H319 Muta. 2, H341 Skin Irrit. 2, H315 Skin Sens. 1B, H317

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

Data extracted on 15.01.2021

Main types of applications structured by product or article types	EC / List 219-207-4	EC / List 221-518-5	EC / List 688-147-2	EC / List 263-471-3	EC / List 429-020-1
PC 15: Non-metal-surface treatment products	I	I			
PC 32: Polymer preparations and compounds	I				
PC 1: Adhesives, sealants	I	I	I		
PC 9a: Coatings and paints, thinners, paint removes	F, I	F, I			
PC 18: Ink and toners		F, I			
PC 14: Metal surface treatment products	I	I			
PC 19: Intermediate	F		I		I
Unspecified PC: formulation; industrial end-use as resin in electric appliances	I		F		
PC 24: Lubricants, greases, release products				I, **P**	
PC 16: Heat transfer fluids				I, **P**	
PC 17: Hydraulic fluids				I, **P**	

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 15.01.2021

EC / List number	RMOA	Authorisation		Restriction	CLH	Actions not under REACH / CLP
		Candidate list	Annex XIV	Annex XVII	Annex VI (CLP)	
219-207-4					Yes (RAC opinion[5])	
428-600-1						NONS
429-020-1						NONS
430-700-5						NONS
470-140-9						NONS

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