Assessment of regulatory needs

Authority: European Chemicals Agency (ECHA)

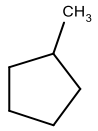
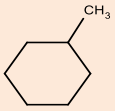
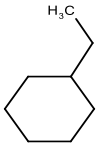
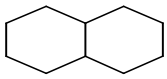
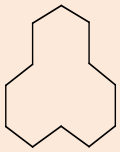
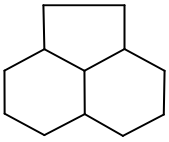
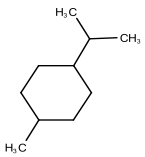
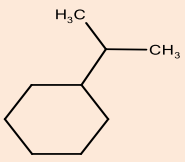
Group Name: Cycloalkanes

General structure:

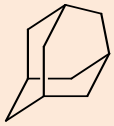
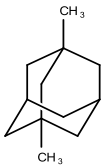
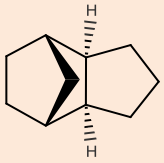
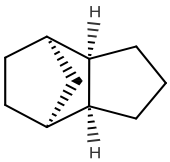
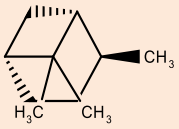
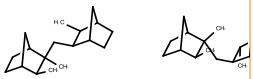
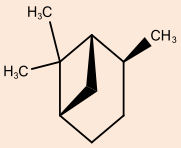
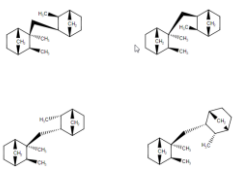
Revision history

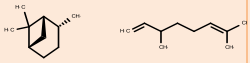
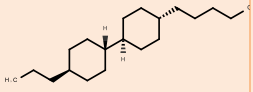
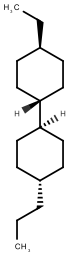
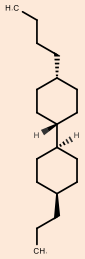
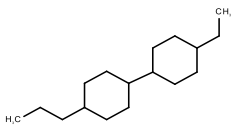
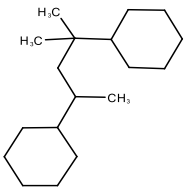
Version	*Date*	*Description*
1.0	11 December 2023	

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]
Sub-Group 1.1 Mono-cyclic rings (C5 and C6 rings)				
202-503-2	96-37-7	methylcyclopentane		Full, 10 to 100
203-624-3	108-87-2	methylcyclohexane		Full, > 1000
216-835-0	1678-91-7	ethylcyclohexane		Full, 10 to 100
Sub-Group 1.2 Fused rings and mono-cyclic rings C>6				
202-046-9	91-17-8	decahydronaphthalene		Full, >1000
206-033-9	294-62-2	cyclododecane		OSII or TII
218-412-6	2146-36-3	perhydroacenaphthene		OSII or TII
Sub group 1.3 Cyclohexane ring with isopropyl chain				
202-790-4	99-82-1	1-isopropyl-4-methylcyclohexane		Full, not (publicly) available
211-792-4	696-29-7	isopropylcyclohexane		Full, not (publicly) available

[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

Sub-Group 2 Bridged rings				
206-001-4	281-23-2	tricyclo[3.3.1.13,7]decane		OSII or TII
211-870-8	702-79-4	1,3-dimethyltricyclo[3.3.1.13,7]decane		OSII or TII
220-585-8	2825-82-3	(3aα,4β,7β,7aα)-octahydro-4,7-methano-1H-indene		Full, not (publicly) available
220-586-3	2825-83-4	(3aα,4α,7α,7aα)-octahydro-4,7-methano-1H-indene		OSII or TII
229-978-9	6876-13-7	(1α,2β,5α)-2,6,6-trimethylbicyclo[3.1.1]heptane		OSII or TII
434-420-4		exo-2-methyl-exo-3-methyl-endo-2-[(endo-3-methylbicyclo[2.2.1]hept-exo-2-yl)methyl]bicyclo[2.2.1]heptane; reaction mass of: endo-2-methyl-exo-3-methyl-exo-2-[(exo-3-methylbicyclo[2.2.1]hept-exo-2-yl)methyl]bicyclo[2.2.1]heptane		NONs
800-188-1	33626-25-4	(1S,2R,5S)-2,6,6-trimethylbicyclo[3.1.1]heptane		OSII or TII
939-299-6		Reaction mass of endo-2-methyl-exo-3-methyl-exo-2-[(endo-3-methylbicyclo[2.2.1]hept-endo-2-yl)methyl]bicyclo[2.2.1]heptane and endo-2-methyl-exo-3-methyl-exo-2-[(endo-2-methylbicyclo[2.2.1]hept-endo-3-yl)methyl]bicyclo[2.2.1]heptane and endo-2-methyl-exo-3-methyl-		Full, not (publicly) available

		exo-2-[(exo-3-methylbicyclo[2.2.1]hept-exo-2-yl)methyl]bicyclo[2.2.1]heptane and endo-2-methyl-exo-3-methyl-exo-2-[(exo-2-methylbicyclo[2.2.1]hept-exo-3-yl)methyl]bicyclo[2.2.1]heptane		
945-939-5		Reaction mass of 3,7-dimethylocta-1,6-diene and rel-(1R,2S,5R)-2,6,6-trimethylbicyclo[3.1.1]heptane		OSII or TII
Sub-group 3.1 Bi(cyclohexane) rings substituted in 4,4' position with linear alkyl chain				
618-832-3	92263-41-7	4-trans-Pentyl-4'-trans-propyl-[1,1'-bicyclohexyl]		Full, not (publicly) available
619-230-3	96624-41-8	4-trans-ethyl-4'-trans-propyl-[1,1'-bicyclohexyl]		Full, not (publicly) available
619-232-4	96624-52-1	4-trans-Butyl-4'-trans-propyl-[1,1'-bicyclohexyl]		Full, not (publicly) available
935-545-1		4-cis-ethyl-4'-trans-propyl-[1,1'-bicyclohexyl]		OSII or TII
Sub-group 3.2 Dicyclohexane with branched alkyl chain in position 1,1'				
254-227-7	38970-72-8	1,1'-(1,1,3-trimethylpropane-1,3-diyl)bis(cyclohexane)		Full, not (publicly) available

This table does not contain group members that are only notified under the CLP Regulation. Should further regulatory risk management action on one or more substances in the group be considered, ECHA may make an additional search for related C&L notified substances to be included in the group and develop an assessment of regulatory needs for them.

Contents

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The author does not accept any liability with regard to the use that may be made of the information contained in this document. Usage of the information remains under the sole responsibility of the user. Statements made or information contained in the document are without prejudice to any further regulatory work that ECHA, the Member States or other regulatory agencies may initiate at a later stage. Assessments of regulatory needs and their conclusions are compiled on the basis of available information and may change in light of newly available information or further assessment.

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.

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.

[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).

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 substances created around well-defined hydrocarbon type of substances. This cycloalkanes group (22 substances) is the third substance group of this kind. The first two groups were the well-defined linear alkanes and well-defined branched alkanes. As for the previous two groups, the cycloalkanes group only contains substances that are well-defined and in which only saturated carbon bonds are present. No heteroatoms, unsaturation or other functional groups are present.

The majority of the substances in the group are mono-constituent substances. The multi-constituent substances are all reaction masses of stereoisomers except EC 945-939-5.

The following subgroups have been created based on structural similarity and observed hazard similarity within each subgroup:

- Mono-cyclic rings (C5 and C6 rings) with linear alkyl chain, sub group 1.1,
- Fused rings and mono-cyclic rings C>6, sub group 1.2,
- Cyclohexane ring with isopropyl chain, sub group 1.3
- Bridged rings, sub group 2,
- Bi(cyclohexane) rings substituted in 4,4’ position with linear alkyl chain: sub group 3.1, and
- Dicyclohexane with branched alkyl chain in position 1,1’, sub group 3.2

The mono-cyclic substance cyclododecane EC 206-033-9 is structurally closer to a fused tri-cyclic substance and has therefore been sub-grouped with fused-ring substances in subgroup 1.2.

Some rings are substituted with saturated, linear and branched alkyl groups.

Based on information reported in the REACH registration dossiers, the main use across the group is as solvents, however other uses are also included, such as lubricant and pressure transfer agent. Almost half of the substances with full registrations (6 substances out of 13) are used by professionals and/or consumers and have a potential for releases to the environment and exposure to workers and consumers. These include uses in washing and cleaning products, lubricants/greases, inks and toners, and cosmetics. Taking also industrial uses into account, the most common uses across the whole group are in polymer preparations, lubricants and greases and as intermediates. Releases from the final articles are expected to be minimum.

EC 202-046-9 (subgroup 1.2) and EC 203-624-3 (subgroup 1.1) have been selected for substance evaluation due to suspected PBT properties. The latter was not found to be a PBT substance[5] whereas the assessment of the former is still ongoing. Furthermore, substance EC 206-033-9[6] (subgroup 1.2) has been assessed for its suspected PBT properties, but it was not identified as an SVHC due to insufficient information to conclude that the substance can be identified as a PBT/vPvB.

[5] Methylcyclohexane Substance Evaluation Conclusion

[6] Registry of SVHC intentions until outcome - ECHA (europa.eu)

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.

Subgroup name, EC/List no, substance name	Human Health Hazard	Environmental Hazard	Relevant use(s) & exposure potential	Suggested regulatory actions
Subgroup 1.3 Subgroup 1.2: EC 202-046-9	Known or potential hazard for reproductive toxicity and ED	Known or potential hazard for aquatic toxicity, PBT/vPvB and ED	Industrial uses in polymer preparations and as intermediate. Limited potential for environmental exposure.	**First step:** CCH for subgroup 1.3 Pending action for EC 202-046-9, await SEV (PBT) **Potential last action (if hazard confirmed after data generation):** CLH Justification: Harmonised classification as Repr.1 and PBT/vPvB will require company level risk management to be in place for workers and for environment (minimisation of releases.
Subgroup 1.1 Subgroup 2	Known or potential hazard for skin sensitisation for Subgroup 2: EC	Known or potential hazard for aquatic toxicity for all, and for PBT/vPvB	Subgroup 1.1: Many consumer & professional uses with exposure & release potential	**First step:** CCH (subgroup 1.1 and 3.2) No action (subgroup 2 and two subgroup 1.2 members)

Subgroup name, EC/List no, substance name	Human Health Hazard	Environmental Hazard	Relevant use(s) & exposure potential	Suggested regulatory actions
Subgroup 3.2	220-585-8, EC 220-586-3, Subgroup 3.2. Inconclusive hazard for carcinogenicity for STOT RE for reproductive toxicity for ED for Subgroups 2 and 3.2. Inconclusive hazard for mutagenicity for Subgroup 2 (except EC 434-420-4, EC 220-585-5 and EC 939-299-6) and Subgroup 3.2.	for Subgroups 2 and 3.2 Inconclusive hazard for ED for Subgroups 2 and 3.2	(e.g. washing, cosmetics, perfumes and fuels) Subgroup 2: Mainly industrial uses and intermediate registrations. EC 939-299-6 also professional uses as lubricant in vehicle maintenance & hydraulic fluids Subgroup 3.2: Industrial and professional uses in lubricants and as a pressure transfer agent	**Potential last action:** **Currently no need for EU RRM** <u>Justification</u>: It is expected that following data generation for aquatic toxicity registrants would adequately self-classify the substances. The existing harmonised classification and (appropriate) self-classification will require company level risk management measures (RMM) for environment and for workers (for skin sensitisation) to be in place. The concern related to the presence of skin sensitisers in consumer mixtures is under investigation. Regarding PBT, actions (including data generation) will be re-considered when the assessment will be revisited if the registration status changes. For substances with intermediate registrations, actions (including data generation) will be re-considered when the assessment will be revisited if the registration status changes.
Subgroup 1.2: EC 206-033-9, EC 218-412-6	Known or potential hazard for reproductive toxicity and ED	Known or potential hazard for aquatic toxicity, PBT/vPvB and ED	Intermediate registrations.	
Subgroup 3.1	Known or potential hazard	Inconclusive hazard for ED	Only industrial uses	**No action**

Subgroup name, EC/List no, substance name	Human Health Hazard	Environmental Hazard	Relevant use(s) & exposure potential	Suggested regulatory actions
	for STOT RE for subgroup 3.1. Inconclusive hazard for reproductive toxicity and ED for subgroup 3.1.			Justification: Self-classification (will) require company level risk management measures (RMM) for workers to be in place.

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

Based on currently available information, there is a need for (further) EU regulatory risk management – Harmonised classification and labelling for reproductive toxicity and PBT/vPvB hazards due to the potential for release/ exposure of all subgroup 1.3 members as well as subgroup 1.2 member EC 202-046-9 as explained below.

Based on available information, the **subgroup 1.2 and 1.3 members** have **potential reproductive toxicity** hazard. None of the substances are self-classified for this hazard. For EC 202-046-9 (subgroup 1.2) consistent and severe effects on development have been observed in both OECD TG 421 and EOGRTS[7] (both generations) studies. The effects seen may warrant classification as repro 1B for development, while for fertility the substance appears borderline between Cat 1B and 2.

Compliance check is proposed for both substances of subgroup 1.3 to further clarify their reproductive toxicity potential, for EC 202-790-4 to clarify whether the OECD TG 422 study available in the dossier is reliable and sufficient to warrant a classification as Repro 1B for sexual function and fertility. For 211-792-4 no data on reproductive toxicity is available, however based on structural similarity to EC 202-790-4, the same isopropyl group, a fertility hazard can be suspected and the CCH is to assess whether a EOGRTS study could be triggered at Annex IX level. The need for further data to also address any remaining uncertainty on neurodevelopmental toxicity potential is proposed to be investigated under the compliance checks for the subgroup 1.3 members.

The **subgroup 1.2 and 1.3 members** also have **potential PBT hazard.**

EC 202-046-9 (from subgroup 1.2) is under substance evaluation due to PBT/vPvB concern and the assessment of its PBT properties is ongoing[8].

Based on ECHA's assessment of currently available hazard information, both **subgroup 1.3** members **fulfil the PBT/vPvB screening criteria**:

- these substances are potentially persistent or very persistent (P/vP) as:
  - they are not readily biodegradable (*i.e.,* <60/70% degradation in an OECD 301F for EC 211-792-4, no reliable information for EC 202-790-4 due to a non-standard study only);
- these substances are potentially bioaccumulative or very bioaccumulative (B/vB) as:
  - they have a high potential to partition to lipid storage (*e.g.,* log K_{ow} > 4.5, for EC 211-792-4 also a calculated BCF > 2000 (ie. 4225 (QSAR) as reported in the registration dossier);
- they may meet the T criteria set in Annex XIII based on the potential for reproductive toxicity as discussed above.

[7] A EOGRTS study following a testing proposal evaluation has been submitted for EC 202-046-9 in 2022.

[8] Substance evaluation - CoRAP - ECHA (europa.eu)

The PBT properties of the subgroup 1.3 substances will be further clarified in the compliance checks proposed.

The first step of the regulatory risk management should the hazard exist, is to confirm via harmonised classification (CLH) the potential reproductive toxicity and PBT/vPvB hazards for the subgroup 1.2 and 1.3 substances as discussed above. When preparing the proposals, it may be considered what would be the best way to develop them, for instance whether to make a proposal for a subgroup of substances, to submit them individually or jointly per subgroup.

If the CLH process confirms the substances as being Repro 1B 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 (e.g restriction).

The harmonised classification as PBT/vPvB will require company level risk management measures (RMM) for environment to be in place. It will require manufacturers and importers of the substance to recommend to downstream users risk management measures that minimise exposure and emissions to humans and the environment throughout the lifecycle of the substances.

The substances are used in industrial settings as intermediates and as solvents in polymer preparations and some in inks and toners. Worker exposure resulting from industrial use as a solvent cannot be excluded. Although article service life has been reported for EC 202-790-4 (subgroup 1.3), releases from articles are not considered to be likely. EC 202-790-4 is predominantly used as a precursor in the production of 1-isopropyl-4- methylcyclohexane hydroperoxide, which is a catalyst for radical polymerization. It is therefore not the actual substance that is used in the polymerization reaction and consequently the expected releases from the article should be minimal.

Based on the uses, there is a limited potential for releases to the environment for subgroup 1.2 and 1.3 members. It is therefore considered that, with the current information, there is no need to propose further regulatory risk management on the top of the harmonised classification for the time being.

For Decahydronaphthalene, all isomers (EC 202-046-9) there are national occupational exposure limit values (OELS) available for in several countries[9]. The national values differ somewhat and it was therefore assessed whether setting up of an EU-wide exposure limit would be required, and/or whether to extend the OEL to other subgroup 1.2 and 1.3 substances due to similar uses and hazards. Based on the information provided in the registration dossiers, the substances are used mainly as solvents in industrial setting with closed batch processes with occasional controlled exposure or processes with equivalent containment conditions. Furthermore, the aggregated tonnages are not high. It is therefore considered that, as already indicated above, the CLH as repro should already require the necessary company level risk management measures (RMM) for workers to be in place and it is proposed that there is currently no need for (further) EU-wide regulatory risk management, such as an EU wide OEL in addition to the national OELs already present in several member states.

These substances in subgroups 1.2 and 1.3 also have a known or potential aquatic toxicity hazard. The substances in subgroup 1.3 have a range of aquatic self-classifications and compliance checks are proposed to obtain data on long-term

[9] GESTIS International Limit Values (dguv.de)

aquatic toxicity and to ensure appropriate self-classifications. Regarding subgroup 1.2, EC 202-046-9 is self-classified as Aquatic Acute 1 and Aquatic Chronic 1.

It is expected that following data generation for aquatic toxicity registrants of subgroup 1.3 would adequately self-classify the substances. Based on the uses, it is assumed that there is a limited potential for releases to the environment, and that ensuring adequate worker protection should be the main focus area. The self-classification (already in place for EC 202-046-9 (subgroup 1.2)) will require company level risk management measures (RMM) for environment to be in place. Therefore, it is proposed that there is currently no need for EU-wide regulatory risk management on this aspect for the subgroup 1.2 nor subgroup 1.3 members.

If the data obtained confirm the need for a CLH for human health and also for aquatic toxicity, the need for CLH for aquatic toxicity may be considered for the subgroup at the same time as developing the CLH for reprotoxicity.

Due to the identified hazard on reproductive toxicity (sexual function and/or fertility) for subgroup 1.2 and 1.3, ED potential cannot be excluded. Therefore, these substances are further flagged as potential ED for HH and ENV; however at this stage due to lack of information on specific ED mode of action in relation to the observed effects on fertility, the ED HH and ENV cannot be concluded. For EC 202-406-9 from subgroup 1.2 ED related effects were observed in both generations in the EOGRTS study (e.g., on adrenal gland, thyroid and oestrus cycle). There is an ongoing SEv for this substance and the ED hazard could be further clarified during the SEV. However, if during the CLH process for reproductive toxicity ED is further identified as hazard the regulatory strategy presented here will be revisited if needed.

For subgroup 1.2 and 1.3 substances there is **no hazard or unlikely hazard** for **skin sensitisation** (negative *in vivo* studies), for **repeated dose toxicity** (based on subacute, subchronic, chronic toxicity studies) and for mutagenicity (negative *in vitro/in vivo* studies). In addition, carcinogenicity is unlikely due to the absence of mutagenicity potential, and absence of clear evidence that hyperplasia and/or pre-neoplastic lesions can be induced after repeated exposure. For EC 202-046-9 from subgroup 1.2. there are also two carcinogenicity studies showing no relevant human health risk that can be attributed to the substance.

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

The substances in subgroup 1.1 have widespread uses with a **high potential for human exposure and releases to the environment.** The uses include washing and cleaning, fertilisers and biocidal/plant protection products, perfumes and cosmetics, fuels, polymer preparations and inks by professionals and consumer. EC 203-624-3 is a high tonnage substance (Annex X) and has the highest number of different consumer and professional uses. The substances are structurally very similar and are used as solvents, therefore a high potential for substitution among them is expected.

The substances in **subgroup 1.1**. have **known or potential hazard** for **skin irritation and narcosis** with either harmonised classification (EC 203-624-3 STOT SE 3 H336, Skin irrit. 2) or appropriate self-classification (via read-across approaches applied in registration dossiers). For industrial and professional uses, sufficient and consistent self-classification by registrants should require company level risk management measures (RMM) to be in place for workers. Adequate product labelling should in principle provide consumers with sufficient information to manage risks arising from the use of mixtures containing these substances.

Previous assessments from the OECD on methylcyclohexane (EC 203-624-3) and ethylcyclohexane (EC 216-835-0) (as part of the OECD SIDS Methyl· Ethylcyclohexane Category) also confirm the narcotic properties of these substances, however neurotoxicity potential was not confirmed. Therefore, based on structural similarity, a neurotoxicity hazard is deemed unlikely for the whole subgroup.

For **subgroup 2 substances**, there is a **known or likely skin sensitisation hazard** for EC 220-585-8 and EC 220-586-3 due to self-classification as Skin sens. 1B, while EC 254-227-7 from subgroup 3.2 is self-classified as Skin sens 1B (based on *In vivo data*). Neither of the subgroup 2 substances has widespread uses. EC 220-586-3 is registered at low tonnage (Annex VII, 1-10 tonnes) for industrial and professional uses in lubricants or as a pressure transfer agent. For industrial and professional uses, sufficient and consistent self-classification by registrants should require company level risk management measures (RMM) to be in place for workers. Adequate product labelling should in principle provide consumers with sufficient information to manage risks arising from the use of mixtures containing these substances.

For **subgroup 3.1**, based on the information available there is a **known or likely hazard for STOT RE** for all substances in this subgroup. Based on the results of oral 28 day repeated dose toxicity studies, the severity of effects at low doses, classification for STOT RE 2 appear(s) to be warranted for the substance(s) EC 619-232-4 and EC 618-832-3 and the other subgroup 3.1 members due to structural similarities. Extrapolating the hazard to the other subgroup members is justified especially since in absence of data covering longer exposures occurrence of similar effects for these structurally similar substances cannot be excluded. Such classification is however not reported in the registration dossier(s). Registrants are invited to consider the information available, self-classify the substance(s), and update their registration dossiers and Safety Data Sheets accordingly.

There is limited exposure to the subgroup 3.1 substances; i.e., worker exposure and limited releases due to manufacturing in closed processes/equivalent containment conditions and transfer at non-dedicated facilities, or intermediate use only at relatively low tonnages. The self-classification will require company level risk management (RMM) to be in place. Therefore, it is proposed that there is currently no need for EU-wide regulatory risk management. Nevertheless, as adequate classification is necessary to ensure worker protection, if the registrants do not update their self-classification to STOT RE, further action may be considered in the future.

Based on ECHA's assessment of currently available hazard information, all substances in the subgroups 2 and 3.2 **fulfil the PBT/vPvB screening criteria**[10], either based on information in their registration dossiers or for some subgroup 2 members via extrapolation from the other group members:

- these substances are potentially persistent or very persistent (P/vP) as:
    - they are not readily biodegradable (*i.e.,* <60/70% degradation in an OECD 301 study (EC 220-585-8, EC 254-227-7, EC 434-420-4 and List 939-299-6);
- these substances are potentially bioaccumulative or very bioaccumulative (B/vB) as:
    - they have a high potential to partition to lipid storage (*e.g.,* log K_{ow}

[10] As defined in REACH Annex XIII and R11 Guidance on PBT assessment (https://echa.europa.eu/documents/10162/17224/information_requirements_r11_en.pdf/a8cce23f-a65a-46d2-ac68-92fee1f9e54f

> 4.5 for the substances listed above);
- they may meet the T criteria set in Annex XIII: see discussion on aquatic toxicity above, also many human health related endpoints inconclusive

Therefore, the substances are considered as potential PBT/vPvB substances. As all of the substances in subgroups 2 and 3.2 have been registered at 1-10 t/a or as intermediates, it is not possible to request further data through compliance check. Due to these reasons, no follow-up action is proposed for the time being to obtain further information on these hazards. If the registration status changes for these substances data generation and potentially follow up actions will be re-considered when the assessment will be revisited. For EC 220-586-3 (subgroup 3.2) a PBT assessment may nevertheless be pursued later depending on the conclusions of the compliance checks of the related structurally similar substances in subgroup 1.1 and the group "Well-defined branched alkanes".

Based on ECHA's assessment of currently available information, the potential hazards for reproductive toxicity, PBT/vPvB and aquatic toxicity hazards from EC 202-046-9 (subgroup 1.2) are preliminarily extrapolated to the other two subgroup 1.2 members EC 206-033-9 and EC 218-412-6 due to similar structural features. However, as these two substances have only intermediate registrations it is not possible to clarify their hazard potential. If the registration status changes for these substances data generation and potentially follow up actions will be re-considered when the assessment will be revisited.

The substances in **subgroups 1.1, 2 and 3.2** all have **known or potential hazard for aquatic toxicity**. Regarding subgroup 1.1, EC 203-624-3 has a harmonised classification as Aquatic Chronic 2, while the self-classifications of the other substances vary from Aquatic Acute 1 and Aquatic Chronic 1 to Aquatic Chronic 4. The classifications are mainly based on short term data.. The substance EC 220-586-3 (subgroup 3.2) has an aquatic toxicity hazard based on its structural similarity with the substances of subgroup 1.1 and substances from the group "Well-defined branched alkanes". As there is no long-term data for invertebrates and the substance is poorly water soluble, a compliance check is proposed to clarify the aquatic toxicity of this substance.

In subgroup 2, EC 434-420-4 has a harmonised classification as Aquatic Acute 1 and Aquatic Chronic 1, and EC 220-585-5 the same (accurate) self-classification. EC 939-299-6 is structurally similar to EC 434-420-4, they are multi-constituent substances with different stereoisomeric composition. It is expected that EC 939-299-6 should have the same classification as EC 434-420-4, but it has been self-classified as Aquatic Chronic 4. Compliance check is suggested to clarify aquatic toxicity for EC 939-299-6.

It is expected that following data generation for aquatic toxicity registrants would adequately self-classify the substances. The existing harmonised classification and (appropriate) self-classification will require company level risk management measures (RMM) for environment to be in place and should provide adequate information to the users to limit releases to the environment as the classification triggers actions under environmental legislation in professional settings. Therefore, it is proposed that there is currently no need for EU-wide regulatory risk management on this aspect for any of these substances.

Some of the substances in subgroup 2 used only as intermediates have not been self-classified for aquatic toxicity. As there should be strictly controlled conditions in place, low potential for releases to the environment can be assumed. As the substances have been registered at 1-10 t/a or as intermediates, it is not possible to request further data through compliance check. Due to these reasons, no follow-

up action is proposed for the time being to obtain further information on these hazards. If the registration status of these substances changes data generation and potentially follow up actions will be re-considered when the assessment will be revisited.

- *Inconclusive hazards*

For **subgroup 2 and subgroup 3.2**. there are **inconclusive hazards** of all substances for **carcinogenicity, repeated dose toxicity, reproductive and developmental toxicity and endocrine disruption.** In addition, all substances apart from the three substances in subgroup 2 with full registrations (EC 434-420-4, EC 220-585-5 and EC 939-299-6) have inconclusive hazards for mutagenicity. As already indicated in the section above, it is not possible to request further data through compliance check due to low tonnage/intermediate registrations and consequently no follow-up action is proposed for the time being to obtain further information on these hazards. If the registration status changes for these substances data generation and potentially follow up actions will be re-considered when the assessment will be revisited.

Subgroup 3.1. members all have an **inconclusive hazard** for **reproductive/developmental toxicity and endocrine disruption** as there is not sufficient information to make a holistic view of available information. A negative screening study is available with EC 619-230-3, also read-across to EC 618-832-3 and EC 619-232-4 by registrants. This study showed a dose-dependent effect (increase in the mean thyroxine (T4) levels in parental males and pups) however the toxicological relevance of this finding cannot be determined in the absence of any additional findings supporting a possible endocrine disruption mode of action. Further data generation would be needed to clarify the above endpoints. However, the findings are not sufficient to trigger a PNDT or an EOGRTS study request at Annex VIII under compliance check and these substances may not be prioritised for substance evaluation since, as already discussed above, there is limited exposure.

- *No or unlikely hazards*

The substances in **subgroup 1.1** have **no or unlikely hazard for reproductive and developmental toxicity hazard** (based on screening studies and from PNDT studies in 1st species) **and endocrine disruption**. Any remaining uncertainty on neurodevelopmental toxicity potential, arising from lack of PNDT studies on second species and a EOGRTS study on the substance, will be investigated under compliance check on EC 203-624-3 (registered at Annex X). For the EOGRTS endpoint a read-across has been applied, this will also be assessed during the CCH. There is also **no or unlikely hazard for skin sensitisation** (negative *in vivo* studies), for **repeated dose toxicity** (based on subacute, subchronic, chronic toxicity studies) and for **mutagenicity** (negative *in vitro* studies) for all subgroup 1.1 substances. In addition, **carcinogenicity** is unlikely due to the absence of mutagenicity potential, and absence of clear evidence that hyperplasia and/or pre-neoplastic lesions can be induced after repeated exposure.

Regarding **subgroup 2**, the skin sensitisation hazard from EC 220-585-8 and EC 220-586-3 cannot be extrapolated to the other members of the group due to structural differences. EC 434-420-4 and EC 939-299-6 have **no or unlikely hazard for skin sensitisation** based on negative *in vivo* studies with the analogue substance EC 427-040-5. The read-across is plausible as substances only differ in the isomer ratios. The rest of the substances in the subgroup are inconclusive for skin sensitisation. The three fully registered substances EC 434-420-4, EC 220-585-5 and EC 939-299-6 of subgroup 2 also have **no or unlikely hazard for**

mutagenicity based on consistently negative in vitro and one in vivo study on EC 434-420-4. Based on structural differences, it is not possible to expand the findings to the other substances in the subgroup.

For **subgroup 3.1**. the substances have **no or unlikely hazards for skin sensitisation** (negative *in vivo* study with EC 619-232-4 and plausible read-across with the other substances), **mutagenicity** (negative *in vitro* studies on gene mutation in bacteria and chromosomal aberrations with EC 618-832-3 and EC 619-232-4) **and carcinogenity** (due to the absence of mutagenicity potential and absence of clear evidence that hyperplasia and/or pre-neoplastic lesions can be induced after repeated exposure).

The substances in the **subgroups 1.1** and **3.1** are **unlikely** to fulfil the **PBT/vPvB** screening criteria and EC 203-624-3 (subgroup 1.1) has been concluded as not PBT/vPvB in a previous Substance Evaluation. The substances in this subgroup are structurally similar. Regarding other substances in subgroup 1.1, EC 202-503-2 is readily biodegradable (via a read-across approach in the dossier) and does not screen as B/vB based on log Kow of 3.37, while EC 216-835-0 is potentially persistent or very persistent as its not readily biodegradable (ie < 60/70% degradation in OECD 301C but appears not B/vB based on experimental data from an OECD 305 fish bioaccumulation study. The subgroup 3.1. substances are potentially persistent (ie < 60/70% degradation in OECD 301 studies) but they are not B/vB based on experimental BCF values in the registration dossiers. The **subgroup 3.1** substances have also **no or unlikely hazard for aquatic toxicity**, however there is some remaining uncertainty due to lack of long-term data on aquatic invertebrates. No data generation is proposed due to low tonnage registrations, based on uses there is also limited potential for environmental exposure.

Annex 1: Overview of classifications

Data extracted on 2 March 2021.

EC/ List No	CAS No	Substance name	Harmonised classification	Classification in registrations
202-503-2	96-37-7	methylcyclopentane		*Flam. Liquid 3 H226* *Acute Tox. 3 H331* *Skin Corr. 1C H314* *Asp. Tox. 1 H304* *Aquatic Acute 1 H400, M-factor: 10.0000000000* *Aquatic Chronic 1 H410*
203-624-3	108-87-2	methylcyclohexane		*Flam. Liquid 2 H225* *Skin Irrit. 2 H315* *Asp. Tox. 1 H304* *STOT Single Exp. 3 H336*
216-835-0	1678-91-7	ethylcyclohexane		*Flam. Liquid 3 H226* *Skin Irrit. 2 H315* *Asp. Tox. 1 H304*
202-046-9	91-17-8	decahydronaphthalene	*Asp. Tox. 1 H304* *Flam. Liq. 2 H225* *Skin Irrit. 2 H315* *STOT SE 3 H336* *Aquatic Chronic 2 H411*	*Flam. Liquid 2 H225* *Skin Irrit. 2 H315* *Asp. Tox. 1 H304* *Aquatic Acute 1 H400* *STOT Single Exp. 3 H336, affected organs: Central nervous system* *Aquatic Chronic 2 H411* *Aquatic Chronic 1 H410*
206-033-9	294-62-2	cyclododecane		*Aquatic Acute 1 H400[registration, intermediate, active]*
218-412-6	2146-36-3	perhydroacenaphthene		-
202-790-4	99-82-1	1-isopropyl-4-methylcyclohexane		*Flam. Liquid 3 H226* *Asp. Tox. 1 H304* *Aquatic Chronic 4 H413*
211-792-4	696-29-7	isopropylcyclohexane		*Asp. Tox. 1 H304[registration, intermediate, active]* *Flam. Liquid 3 H226[registration, intermediate, active]*
206-001-4	281-23-2	tricyclo[3.3.1.13,7]decane		*Flam. Liquid 2 H225* *Asp. Tox. 1 H304* *STOT Single Exp. 3 H336* *Aquatic Acute 1 H400* *Aquatic Chronic 2 H411*
211-870-8	702-79-4	1,3-dimethyltricyclo[3.3.1.13,7]decane		*Asp. Tox. 1 H304[registration, intermediate, active]* *Aquatic Chronic 4 H413[registration, intermediate, active]*
220-585-8	2825-82-3	(3aα,4β,7β,7aα)-octahydro-4,7-methano-1H-indene		*Flam. Liquid 3 H226* *Skin Irrit. 2 H315* *Eye Irrit. 2 H319* *Skin Sens. 1B H317* *Asp. Tox. 1 H304*

EC/ List No	CAS No	Substance name	Harmonised classification	Classification in registrations
				Aquatic Acute 1 H400 *Aquatic Chronic 1 H410*
220-586-3	2825-83-4	(3aα,4α,7α,7aα)-octahydro-4,7-methano-1H-indene		*Skin Irrit. 2 H315[registration, intermediate, active]* *Aquatic Chronic 1 H410[registration, intermediate, active]* *Aquatic Acute 1 H400[registration, intermediate, active]* *Flam. Liquid 3 H226[registration, intermediate, active]* *Asp. Tox. 1 H304[registration, intermediate, active]* *Skin Sens. 1B H317[registration, intermediate, active]* *Eye Irrit. 2 H319[registration, intermediate, active]*
229-978-9	6876-13-7	(1α,2β,5α)-2,6,6-trimethylbicyclo[3.1.1]heptane		*Flam. Liquid 3 H226[registration, intermediate, active]* *Asp. Tox. 1 H304[registration, intermediate, active]*
434-420-4		exo-2-methyl-exo-3-methyl-endo-2-[(endo-3-methylbicyclo[2.2.1]hept-exo-2-yl)methyl]bicyclo[2.2.1]heptane; reaction mass of: endo-2-methyl-exo-3-methyl-exo-2-[(exo-3-methylbicyclo[2.2.1]hept-exo-2-yl)methyl]bicyclo[2.2.1]heptane		*Skin Sens. 1B H317*
800-188-1	33626-25-4	(1S,2R,5S)-2,6,6-trimethylbicyclo[3.1.1]heptane	*Aquatic Acute 1 H400* *Aquatic Chronic 1 H410* *Eye Dam. 1 H318* *Skin Irrit. 2 H315*	*Skin Irrit. 2 H315* *Eye Damage 1 H318* *Aquatic Acute 1 H400* *Aquatic Chronic 1 H410*
939-299-6		Reaction mass of endo-2-methyl-exo-3-methyl-exo-2-[(endo-3-methylbicyclo[2.2.1]hept-endo-2-yl)methyl]bicyclo[2.2.1]heptane and endo-2-methyl-exo-3-methyl-exo-2-[(endo-2-methylbicyclo[2.2.1]hept-endo-3-yl)methyl]bicyclo[2.2.1]heptane and endo-2-methyl-exo-3-methyl-exo-2-[(exo-3-methylbicyclo[2.2.1]hept-exo-2-		-

EC/ List No	CAS No	Substance name	Harmonised classification	Classification in registrations
		yl)methyl]bicyclo[2.2.1]heptane and endo-2-methyl-exo-3-methyl-exo-2-[(exo-2-methylbicyclo[2.2.1]hept-exo-3-yl)methyl]bicyclo[2.2.1]heptane		
945-939-5		Reaction mass of 3,7-dimethylocta-1,6-diene and rel-(1R,2S,5R)-2,6,6-trimethylbicyclo[3.1.1]heptane		-
800-188-1	33626-25-4	(1S,2R,5S)-2,6,6-trimethylbicyclo[3.1.1]heptane		-
939-299-6		Reaction mass of endo-2-methyl-exo-3-methyl-exo-2-[(endo-3-methylbicyclo[2.2.1]hept-endo-2-yl)methyl]bicyclo[2.2.1]heptane and endo-2-methyl-exo-3-methyl-exo-2-[(endo-2-methylbicyclo[2.2.1]hept-endo-3-yl)methyl]bicyclo[2.2.1]heptane and endo-2-methyl-exo-3-methyl-exo-2-[(exo-3-methylbicyclo[2.2.1]hept-exo-2-yl)methyl]bicyclo[2.2.1]heptane and endo-2-methyl-exo-3-methyl-exo-2-[(exo-2-methylbicyclo[2.2.1]hept-exo-3-yl)methyl]bicyclo[2.2.1]heptane		*Flam. Liquid 3 H226[registration, intermediate, active] Asp. Tox. 1 H304[registration, intermediate, active]*
945-939-5		Reaction mass of 3,7-dimethylocta-1,6-diene and rel-(1R,2S,5R)-2,6,6-trimethylbicyclo[3.1.1]heptane		-
618-832-3	92263-41-7	4-trans-Pentyl-4'-trans-propyl-[1,1'-bicyclohexyl]		*Flam. Liquid 3 H226[registration, intermediate, active]*
619-230-3	96624-41-8	4-trans-ethyl-4'-trans-propyl-[1,1'-bicyclohexyl]		
619-232-4	96624-52-1	4-trans-Butyl-4'-trans-propyl-[1,1'-bicyclohexyl]		
935-545-1		4-cis-ethyl-4'-trans-propyl-[1,1'-bicyclohexyl]		

EC/ List No	CAS No	Substance name	Harmonised classification	Classification in registrations
254-227-7	38970-72-8	1,1'-(1,1,3-trimethylpropane-1,3-diyl)bis(cyclohexane)		

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

Data extracted on 02 March 2021

Main types of applications structured by product or article types	203-624-3	202-790-4	216-835-0	202-503-2	254-227-7	939-299-6	202-046-9	211-792-4	220-585-8	434-420-4	618-832-3, 619-230-3, 619-232-4	206-033-9, 935-545-1
Lubricants, greases	F, I, **P, C**				I, **P**	I, **P**				I		
Washing & cleaning	F, I, **P, C**			**P**								
Polymer preparations	I, **P**	I, **A**		I			I	I				
Ink & toners, paper & board treatment	F, I, **P, C**		**C**				F, I					
Fertilisers, biocidal & plant protection	F, I, **P, C**											
Anti-freeze & de-icing	F, I, **P, C**											
Perfumes, fragrances, Cosmetics, personal care				**C**								
Air care, polishes & waxes, surface treatment	F, I, **P, C**											
Hydraulic fluids						I, **P**						

Main types of applications structured by product or article types	203-624-3	202-790-4	216-835-0	202-503-2	254-227-7	939-299-6	202-046-9	211-792-4	220-585-8	434-420-4	618-832-3, 619-230-3, 619-232-4	206-033-9, 935-545-1
Fuels				I, **P, C**					I			
Adhesives, sealants	F, I, **P, C**											
Coatings & paints, thinners, paint removes	F, I, **P, C**		I									
Textile dyes, leather treatment, welding	F, I, **P, C**											
Laboratory chemicals	F, I, **P**											
Intermediate	I	I					I	I				I
No use info, direct export											"-"	

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 05 February 2021

EC/List number	RMOA	Authorisation		Restriction*	CLH	Actions not under REACH/ CLP
		Candidate list	Annex XIV	Annex XVII	Annex VI (CLP)	
202-046-9	PBT Assessment					
203-624-3	PBT Assessment				STOT SE 3, Skin Irrit 2, Aq Ch 2	
434-420-4					Skin Irrit 2, Eye Dam 1, Aq Ac 1, Ac Ch 1	

*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.