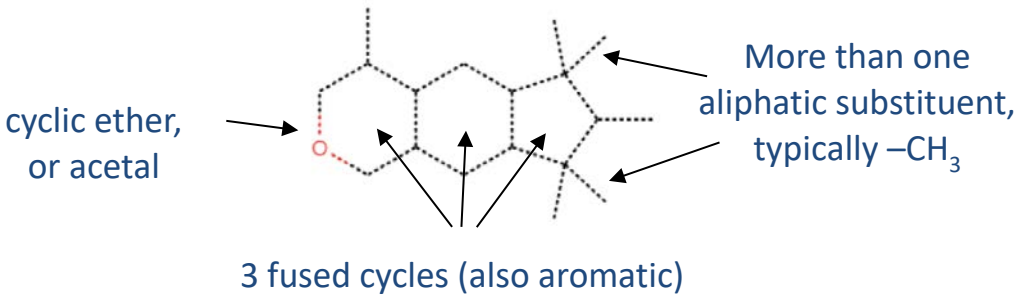
Assessment of regulatory needs

Authority: European Chemicals Agency (ECHA)

Group Name: Fused tricyclic ethers with short chain polyalkyl substituents

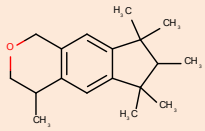
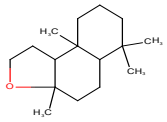
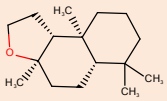
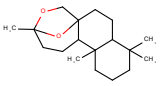
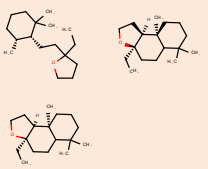
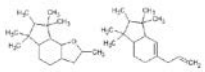
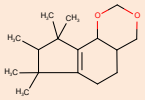
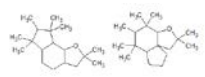
General structure:



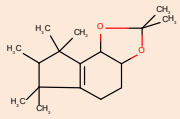
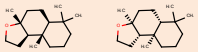
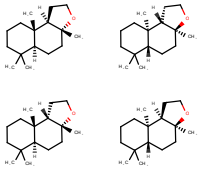
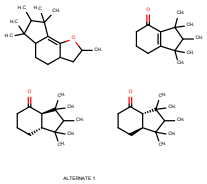
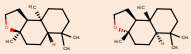
Revision history

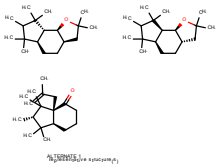
Version	*Date*	*Description*
1.0	2 May 2023	

Substances within this group:

EC/List number	CAS number	Substance name	Chemical structures	Registration type (full, OSII or TII, NONS), highest tonnage band among all the registrations (t/y) [1]
214-946-9	1222-05-5	1,3,4,6,7,8-hexahydro-4,6,6,7,8,8-hexamethylindeno[5,6-c]pyran (HHCB; Galaxolide)		Full, >1000
223-118-6	3738-00-9	Dodecahydro-3a,6,6,9a-tetramethylnaphtho[2,1-b]furan		C&L notification
229-861-2	6790-58-5	[3aR-(3aα,5aβ,9aα,9bβ)]-dodecahydro-3a,6,6,9a-tetramethylnaphtho[2,1-b]furan		Full, 10-100
260-686-4	57345-19-4	Dodecahydro-3,8,8,11a-tetramethyl-5H-3,5a-epoxynaphth[2,1-c]oxepin		Full, not (publicly) available
271-889-2	68611-23-4	3-Pentanone, 1-(2,6,6-trimethyl-2-cyclohexen-1-yl)-, reaction products with 2-propyn-1-ol		Full, not (publicly) available
440-030-5	-	Reaction mass of 6-allyl-1,1,2,3,3-pentamethyl-2,3,3a,4,5,7a-hexahydro-1H-indene and 2,6,6,7,8,8-hexamethyldecahydro-2H-indeno[4,5-b]furan		Full, not (publicly) available
446-220-4	365411-50-3	Indeno[4,5-d]-1,3-dioxin, 4,4a,5,6,7,8,9,9b-octahydro-7,7,8,9,9-pentamethyl-		Full, not (publicly) available
449-360-4	-	Reaction mass of 2,2,7,7,8,9,9-heptamethyldecahydroindeno[4,3a-b]furan and 2,2,6,6,7,8,8-heptamethyldecahydro-2H-indeno[4,5-b]furan		NONS

[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

EC/List number	CAS number	Substance name	Chemical structures	Registration type (full, OSII or TII, NONS), highest tonnage band among all the registrations (t/y) [1]
457-070-4	823178-41-2	4H-Indeno[4,5-d]-1,3-dioxole, 3a,5,6,7,8,8b-hexahydro-2,2,6,6,7,8,8-heptamethyl-		Full, not (publicly) available
481-920-3	-	[No public or meaningful name is available]		NONS
701-326-2	-	Reaction mass of (3aR,5aS,9aS,9bR)-3a,6,6,9a-Tetramethyldodecahydronaphtho[2,1-b]furan and (3aS,5aR,9aR,9bS)-3a,6,6,9a-Tetramethyldodecahydronaphtho[2,1-b]furan		Full, 100-1000
942-754-1	-	Reaction mass of (3aR*,5aS*,9aS*,9bR*)-3a,6,6,9a-Tetramethyldodecahydronaphtho[2,1-b]furan and (3aR*,5aS*,9aS*,9bS*)-3a,6,6,9a-Tetramethyldodecahydronaphtho[2,1-b]furan		Full, not (publicly) available
944-675-8	-	Reaction products of 3-methyl-5-[(1S,4aS,8aS)-5,5,8a-trimethyl-2-methylenedecahydro-1-naphthalenyl]-1-penten-3-ol, cyclized		Full, not (publicly) available
946-273-8	-	2,6,6,7,8,8-hexamethyl-3,3a,4,5,5a,6,7,8-octahydro-2H-indeno[4,5-b]furan, 1,1,2,3,3-pentamethyl-1,2,3,5,6,7-hexahydro-4H-inden-4-one and rel-(3aR,7aR)-1,1,2,3,3-pentamethyloctahydro-4H-inden-4-one		OSII or TII
948-069-4	-	(+/-)-(3aRS,5aSR,9aSR,9bSR)-3a,6,6,9a-Tetramethyldodecahydronaphtho[2,1-b]furan		Full, not (publicly) available

EC/List number	CAS number	Substance name	Chemical structures	Registration type (full, OSII or TII, NONS), highest tonnage band among all the registrations (t/y) [1]
954-347-6	-	Reaction mass of rel-(3aR,5aR,8aR,8bS)-2,2,6,6,7,8,8-heptamethyldecahydro-2H-indeno[4,5-b]furan and rel-(3aS,5aR,8aS,8bS)-2,2,6,6,7,8,8-heptamethyldecahydro-2H-indeno[4,5-b]furan and rel-(2R,3aR,7aS)-1,1,2,3,3-pentamethyl-3a-(2-methylallyl)octahydro-4H-inden-4-one		OSII or TII

This table contains also group members that are only notified under the CLP Regulation. However, the list is not necessarily exhaustive. 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. Assessment 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 purpose of the assessment of regulatory needs of a group of substances is to help authorities conclude on the most appropriate way to address the identified concerns for a group of substances or a single substance, i.e., the combination of the regulatory risk management instruments to be used and any intermediate steps, such as data generation, needed to initiate and introduce these regulatory measures.

An assessment of regulatory needs can conclude that regulatory risk management at EU level is required for a (group of) substance(s) (e.g., harmonised classification and labelling, Candidate List inclusion, restriction, other EU legislation) or that no regulatory action is required at EU level. While the assessment is done for a group of substances, the (no) need for regulatory action can be identified for the whole group, a subgroup or for single substance(s).

The assessment of regulatory needs is an important step under ECHA's Integrated Regulatory Strategy. However, it is not part of the formal processes defined in the legislation but aims to support them.

The assessment of regulatory needs can be applied to any group of substances or single substance, i.e., any type of hazards or uses and regardless of the previous regulatory history or lack of such. It can be done based on a different level of information. A Member State or ECHA can carry out this case-by-case analysis. The starting point is available information in the REACH registrations and any other REACH and CLP information. However, a more extensive set of information can be available, e.g., assessment done under REACH/CLP or other EU legislation, or can be generated in some cases (e.g., further hazard information under dossier evaluation). Uncertainties associated to the level of information used should be reflected in the documentation. It will be revisited when necessary. For example, after further information is generated and the hazard has been clarified or when new insights on uses are available. It can be revisited by the same or another authority.

The responsibility for the content of this assessment rests with the authority that developed it. It is possible that other authorities do not have the same view and may develop further assessment of regulatory needs. The assessment of regulatory needs does not yet initiate any regulatory process, but any authority can consequently do so and should indicate this by appropriate means, such as the Registry of Intentions.

For more information on Assessment of regulatory needs please consult ECHA website[2].

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

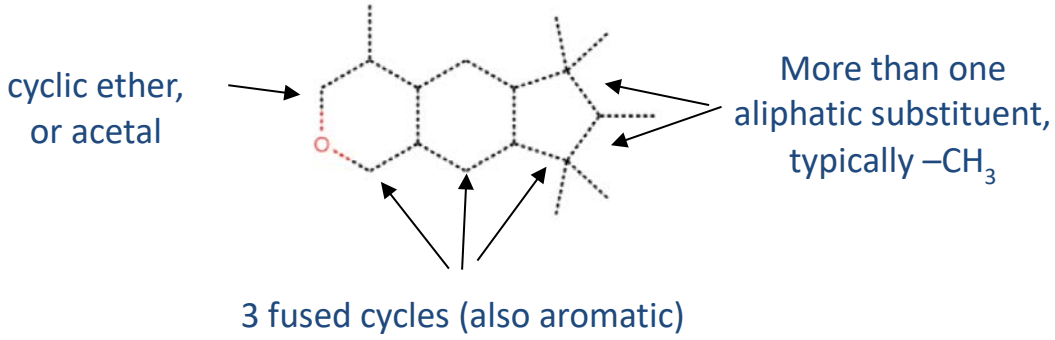
Glossary

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
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

1 Overview of the group

ECHA has grouped together 16 substances based on the presence of :

- 3 fused cycles (aromatic and/or aliphatic)
- a cyclic ether (or acetal)
- more than one aliphatic substituent, typically –CH_3



and on the common property of the substances of having a “musk scent”.

The status of the 16 substances is as such:

- **11** substances with full registrations
- **2** intermediates
- **2** not updated NONS
- **1** not registered

The substances in the group were sub-grouped based on similarities in structure and hazardous properties:

Aromatic ethers	Non-aromatic ethers 1	Non-aromatic ethers 2	Acetals	Bridged acetals
214-946-9	223-118-6	271-889-2	446-220-4	260-686-4
481-920-3	229-861-2	440-030-5	457-070-4	944-675-8
	701-326-2	449-360-4		
	942-754-1	946-273-8		
	948-069-4	954-347-6		

Non-aromatic ethers were further sub-grouped due to additional structural differences.

Based on the information reported in the REACH registration dossiers, the substances are used as fragrances in a variety of consumer and professional uses, and occasionally also industrial uses. The substances are used in the formulation of fragrance oils that are in turn used in products with high potential for exposure

(including from articles) to both humans and the environment such as perfumes, air care products, cosmetics, personal care products, washing and cleaning products, biocidal products and polishes and wax blends.

Substance EC 214-946-9 (HHCB, Galaxolide) is used in a particularly wide range of applications that also include water treatment chemicals, fertilisers, textile dyes, leather treatment products and pharmaceuticals in addition to those mentioned above. This substance is currently under substance evaluation including PBT and ED assessment and has a harmonised classification for aquatic toxicity. Substance 440-030-5 also has a harmonised classification for aquatic toxicity.

Note on the scope of ECHA's assessment of regulatory needs

Regarding hazards, the focus of ECHA's assessment is 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 table in section 3. This does not mean that the substances do not have other known or potential hazards. In some specific cases, where ECHA identifies a need for regulatory risk management action at EU level for other hazards (e.g., neurotoxicity, STOT RE), such additional hazards may be addressed in the assessment. An overview of classification is presented in Annex 1.

On the exposure side, ECHA is mainly using the information on uses reported in the registration dossiers (IUCLID) as a proxy for assessing the potential for exposure to humans and releases to the environment. The potential for release/exposure is generally considered high for "widespread" uses, i.e., professional and consumer uses and uses in articles. For these uses, normally happening at many places, the expected level of control is *à priori* considered limited. The chemical safety reports are not necessarily consulted, and no quantitative exposure assessment is performed at this stage.

2 Justification for the need for regulatory risk management action at EU level

Based on currently available information, there is a need for (further) EU regulatory risk management – restriction for the potential PBT/vPvB, or potential ED HH/ENV hazards, or both, and due to the potential for release/exposure. This applies to aromatic ethers (EC 214-946-9 and 481-920-3), non-aromatic ethers 1 (EC/List nr. 229-861-2, 701-326-2, 942-754-1, and 948-069-4) and acetals (EC 446-220-4 and 457-070-4).

Based on ECHA's assessment of currently available hazard information, four members in the subgroup (EC 214-946-9 and 481-920-3 – aromatic ethers 1, and 446-220-4 and 457-070-4 - acetals) fulfil the PBT/vPvB screening criteria[3]:

- these substances are potentially persistent or very persistent (P/vP) as:
    - EC 214-946-9, 446-220-4, and 457-070-4 are not readily

[3] 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

biodegradable (*i.e.,* <60/70% degradation in OECD 301 studies);
    - Indication for potential persistency is extrapolated to EC 481-920-3, based on structural similarity (within the group aromatic ethers), supported by internal predictions with PBT profiler indicating that these substances contain structures which can be persistent.
- these substances are potentially bioaccumulative or very bioaccumulative (B/vB) as:
    - EC 214-946-9, 481-920-3, and 457-070-4 have a high potential to partition to lipid storage (*e.g.,* log K_{ow} > 4.5);
    - they (and EC 446-220-4 in addition) have a high potential for bioaccumulation in air-breathing organisms (log K_{ow} >2 and log K_{oa} >5)
    - EC 214-946-9 is widely detected in biota (including mammals and birds) and human placenta, umbilical cord, maternal milk.
- EC 214-946-9 may meet the T criteria set in Annex XIII: based on available data, classification as toxic to reproduction cat. 2 could be envisaged (see section 3). This hazard can be extrapolated to EC 481-920-3 (aromatic ethers).

Therefore, these four substances are considered as potential PBT/vPvB substances. Acetals EC 446-220-4 and 457-070-4 that screen for PBT/vPvB also screen for PMT/vPvM[4].

Based on ECHA's assessment of currently available hazard information, potential hazards were also identified for human health. The available information indicates potential for endocrine disrupting properties due to ED indications (EAS modality, hypertrophy of thyroid gland, T4/TSH effects) during the substance evaluation for EC 214-946-9 (aromatic ether) as well as thyroid effects found in repeated dose toxicity studies at relatively high doses for List nr. 701-326-2 (non-aromatic ethers 1) and EC 446-220-4 and 457-070-4 (acetals). Due to structural similarity, the findings were extrapolated to all substances in the subgroups affected, namely aromatic ethers, non-aromatic ethers 1 and acetals.

Based on the limited available data a general concern for developmental toxicity in relation to these substances cannot be excluded. This is underpinned by findings of skeletal and visceral abnormalities observed in data available for EC 214-946-9 (aromatic ether) and List nr. 701-326-2 (non-aromatic ethers 1). A potential developmental toxicity hazard was therefore extrapolated to aromatic ethers and non-aromatic ethers 1. Unlike the ED hazard, developmental toxicity was not extrapolated to EC 446-220-4 and 457-070-4 (acetals) because negative and no data on reprotoxicity was available, respectively.

Overall, there are some substances in the group with either a potential PBT/vPvB (non-aromatic ethers 2) or a potential endocrine disrupting property (non-aromatic ethers 1), but not both. It should be noted that hazard data is only available for a small number of substances with read-across performed by registrants to other group members. In addition, all substances have known, or potential, aquatic toxicity and sufficient harmonised and self-classification are in place regarding this particular hazard.

Substance evaluation is proposed for all the substances in the non-aromatic ethers 1 subgroup to confirm ED. The outcome of the screening suggests that these

[4] Screening of the logKow versus logKoc creates an overlap of B and M for some of these substances. Furthermore, some substance with logKow <4 screen for B in air-breathing organisms. Further data generation would be beneficial but in practice not justified for most of the substances due to low registration tonnage.

substances should be evaluated as a group rather than individually. Similarly, compliance check is proposed for EC 446-220-4 to clarify ED property.

The first step of the regulatory risk management action proposed, should the hazard(s) exist, is the confirmation of hazard(s) via SVHC identification and inclusion on the Candidate List as PBT/vPvB/ED (HH and ENV)/PMT/vPvM.

SVHC identification is highly recommended as a step prior to restriction. In addition, SVHC identification brings immediate obligations for suppliers of the substances such as (i) supplying a safety data sheet and communicating on the safe use of the substances, (ii) responding to consumer requests within 45 days and (iii) notifying ECHA if the article they produce contains the substance above regulatory threshold.

Confirmation of the hazard properties via SVHC identification is not considered sufficient to minimise potential releases of the substances in the environment and exposure to humans. A restriction is seen as the most appropriate option as potential for exposure is expected from consumer uses, professional uses, article service life and potentially also industrial uses.

Neither releases to the environment from consumer uses nor human exposure can be avoided for fragrances. Widespread professional uses are typically non-contained and non-automated leading to releases to the environment. Furthermore, exposure to general population and the environment is already demonstrated for EC 214-946-9 which is widely detected in biota (including mammals and birds)[5] and human placenta, cordon umbilical, maternal milk[6].

Therefore, a restriction of the substances as such or in mixtures (concentration limit in mixtures) used by consumers, professional workers and industrial workers is suggested after SVHC identification, with the aim to minimise exposures and emissions to humans and the environment.

The use of PBT/vPvB and ED substances by consumers and professional workers has been recognised as an area of concern under the European Commission's Chemicals Strategy for Sustainability[7].

In addition, EC/List nr. 214-946-9, 481-920-3, 229-861-2, 701-326-2, 942-754-1, and 948-069-4 might qualify for potential developmental toxicity and the regulatory risk management action proposed is the confirmation of this hazard via harmonised classification (CLH) as possibly Reprotoxic cat. 2.

CLH in itself will require company level risk management measures (RMM) under the OSH legislation for workers to be in place. In addition, a harmonised classification as Reprotoxic cat. 2 will prohibit the substance(s) under the Cosmetic Products Regulation (EC) No 1223/2009 unless an exemption is granted upon assessment of safe use of the substances in cosmetic products by the Scientific Committee on Consumer Safety (SCCS). CLH has the potential to be in place before

[5] Norman database, Lange et al., 2015, Zeng et al., 2005, Sumner et al., 2010, Nakata, 2005, Kannan et al. 2005, Nakata et al. 2007, Moon et al. 2012

[6] Duedahl-Olesen et al., 2005, Lignell et al., 2008, Lee et al. 2015, Zhou et al., 2012, Kang et al., 2010, Zhang et al., 2015, Schlumpf et al., 2010

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

the proposed restriction and thus control the risk from developmental toxicity in a timelier manner.

In addition, 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 (EC 446-220-4, 948-069-4, 449-360-4).

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 regarding skin sensitisation concerns in general. It is however proposed to also confirm skin sensitisation via harmonised classification (CLH) for substance List nr. 948-069-4 along with CLH for reprotoxicity (see above).

Based on currently available information, it is not possible to assess the need for regulatory risk management for bridged acetals EC/List nr. 260-686-4 and 944-675-8 (the only two substances for which neither potential ED nor PBT hazards were determined) as information on hazards is not sufficient to conclude on ED human health and environment, and due to the registration status, it is not possible to clarify the inconclusive ED hazards of these two substances. If the registration status changes, data generation and potentially follow up actions will be re-considered when the assessment will be revisited.

It is expected that following data generation (under CCH) for aquatic toxicity registrants would adequately self-classify the substances and implement necessary RMMs to ensure safe use. Therefore, it is proposed that there is currently no need for EU-wide regulatory risk management to address aquatic toxicity.

Based on currently available information, there is no need for (further) EU regulatory risk management for PBT/vPvB, PMT/vPvM and aquatic toxicity hazards of EC/List nr. 271-889-2, 440-030-5, 449-360-4, 946-273-8, and 954-347-6 in the non-aromatic ethers 2 subgroup.

Based on ECHA's assessment of currently available hazard information, all five members in the subgroup fulfil the PBT/vPvB screening criteria[8]:

- these substances are potentially persistent or very persistent (P/vP) as:
    - EC 271-889-2, 440-030-5, and 449-360-4 are not readily biodegradable (*i.e.,* <60/70% degradation in OECD 301 studies);
    - Indication for potential persistency is extrapolated to List nr. 946-273-8 and 954-347-6 based on structural similarity, supported by internal predictions with PBT profiler indicating that these substances contain structures which can be persistent.
- these substances are potentially bioaccumulative or very bioaccumulative (B/vB) as:

[8] 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

- EC 271-889-2 and 440-030-5 have a high potential to partition to lipid storage (*e.g.,* log K_{ow} > 4.5);
- they (and EC/List nr. 449-360-4, 946-273-8, and 954-347-6 in addition) have a high potential for bioaccumulation in air-breathing organisms (log K_{ow} >2 and log K_{oa} >5).

Therefore, the substances are considered as potential PBT/vPvB substances. Three of the substances (EC/List nr. 449-360-4, 946-273-8, and 954-347-6) that screen for PBT/vPvB also screen for PMT/vPvM[9].

Due to due to the registration status (e.g., low tonnage, intermediate registrations or not updated NONS status), it is not possible to clarify the potential PBT/vPvB and PMT/vPvM hazards of the substances in this subgroup, i.e., via compliance check. Therefore, it is proposed that there is currently no need for EU RRM action on these substances. If the registration status changes, data generation and potentially follow up actions will be re-considered when the assessment will be revisited.

Similar to above, it is expected that for aquatic toxicity registrants already adequately self-classify the substances and implement necessary RMMs to ensure safe use. In addition, EC 440-030-5 already has a harmonised classification for aquatic toxicity and RMMs and OCs are assumed to be in place. Therefore, it is proposed that there is currently no need for EU-wide regulatory risk management.

[9] Screening of the logKow versus logKoc creates an overlap of B and M for some of these substances. Furthermore, some substance with logKow <4 screen for B in air-breathing organisms. Further data generation would be beneficial but in practice not justified for most of the substances due to low registration tonnage.

3 Conclusions and actions

The conclusions and actions proposed in the table below are based on the REACH and CLP information available at the time of the assessment by ECHA. 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 will be updated, and conclusions and actions revisited.

Subgroup name, EC number, substance name	Human Health Hazard	Environmental Hazard	Relevant use(s) & exposure potential	Last foreseen action	Action
All except bridged acetals (EC/List nr. 260-686-4 and 944-675-8) and non-aromatic ethers 2 (EC/List nr. 271-889-2, 440-030-5, 449-360-4, 946-273-8, and 954-347-6)	*Aromatic ethers (*EC *214-946-9, and 481-920-3), Non-aromatic ethers 1 (*EC/List nr. *223-118-6, 229-861-2, 701-326-2, 942-754-1, and 948-069-4), Acetals (EC 446-220-4 and 457-070-4):* Known or potential hazard for ED *Aromatic ethers (*EC *214-946-9 and 481-920-3), Non-aromatic ethers 1 (*EC/List nr. *223-118-6, 229-861-2, 701-326-2, 942-754-1, and 948-069-4):* Known or potential hazard for reproductive toxicity EC/List nr. *446-220-4, 449-360-4, 948-069-4:* Known or potential hazard for skin sensitisation	*All:*Known or potential hazard for aquatic toxicity *Aromatic ethers (*EC *214-946-9 and 481-920-3), Acetals (EC 446-220-4 and 457-070-4):* Known or potential hazard for PBT/vPvB *Aromatic ethers (*EC *214-946-9 and 481-920-3), Non-aromatic ethers 1 (*EC/List nr. *223-118-6, 229-861-2, 701-326-2, 942-754-1, and 948-069-4), Acetals (EC 446-220-4 and 457-070-4):* Known or potential hazard for ED *Acetals (EC 446-220-4 and 457-070-4):* Known or potential hazard for PMT/vPvM	Widespread and high tonnage professional and consumer uses as fragrance with high environmental and human exposure potential.	**Need for EU RRM: Restriction** <u>Justification</u>: Releases to the environment and exposure to humans from consumer and widespread professional uses cannot be avoided for fragrances. Widespread professional uses are typically non-contained and non-automated leading to exposure and releases to the environment. Restriction of professional uses is preferred over authorisation as it is considered to be more efficient and effective to introduce controls at the level of placing on the market rather than at the level of uses. Specific restriction for use in articles is proposed as potential exposure from articles is likely. Industrial uses to be considered as part of the restriction	**First step:** *EC 214-946-9:* Pending Action (under SEv and CCH) *EC 446-220-4:* CCH *Aromatic ethers (*EC *214-946-9 and 481-920-3), Non-aromatic ethers 1 (*EC/List nr. *223-118-6, 229-861-2, 701-326-2, 942-754-1, and 948-069-4):* CLH (possibly Repro cat.2) *List nr. 948-069-4:* *CLH (Skin sens)* *Non-aromatic ethers 1 (*EC/List nr. *223-118-6, 229-861-2, 701-326-2, 942-754-1, and 948-069-4):* Substance evaluation (group entry) **Next steps (if hazard confirmed):**

Subgroup name, EC number, substance name	Human Health Hazard	Environmental Hazard	Relevant use(s) & exposure potential	Last foreseen action	Action
				Skin Sens: Harmonised/self-classification followed by implementation of necessary RRMs should be sufficient to ensure safe use at the workplace. The concern related to the presence of skin sensitisers in consumer mixtures is under investigation.	SVHC identification Restriction
Bridged acetals (EC/List nr. 260-686-4 and 944-675-8)	Inconclusive hazard for ED	Known or potential hazard for aquatic toxicity Inconclusive hazard for ED	Widespread and high tonnage professional and consumer uses as fragrant with high environmental and human exposure potential.	**Currently not possible to assess the regulatory needs** <u>Justification</u>: No data generation is possible to clarify the hazard Self-classification for aquatic toxicity followed by implementation of necessary RRMs should be sufficient to ensure safe use for environment	**First step:** CCH
Non-aromatic ethers 2 (*EC/List nr. 271-889-2, 440-030-5, 449-360-4, 946-273-8, and 954-347-6*)	Inconclusive hazard for ED	Known or potential hazard for PBT/vPvB Known or potential hazard for PMT/vPvM (EC 449-360-4, 946-273-8, 954-347-6) Inconclusive hazard for ED	Widespread professional and consumer uses as fragrance with high environmental and human exposure potential.	**Currently no need for EU RRM** <u>Justification:</u> Due to either low tonnage, NONs, or intermediate registrations no data generation is possible to clarify the hazards currently. Actions (including data generation) will be re-considered when the assessment will be revisited if the registration status and/or uses change.	**First step:** No action

Annex 1: Overview of classifications

Data extracted on 28.09.2022.

EC/List number	CAS No	Substance name	Harmonised classification	Classification in registrations	Classification in C&L notifications (*)
223-118-6	3738-00-9	Dodecahydro-3a,6,6,9a-tetramethylnaphtho[2,1-b]furan	-	-	Aquatic Chronic 2 H411 [1 out of 31]
260-686-4	57345-19-4	Dodecahydro-3,8,8,11a-tetramethyl-5H-3,5a-epoxynaphth[2,1-c]oxepin	-	Aquatic Chronic 4 H413	Skin Irrit. 2 H315 [2 out of 16] Eye Irrit. 2 H319 [1 out of 16] STOT Single Exp. 3 H335, affected organs: respiratory tract [1 out of 16]
449-360-4	-	Reaction mass of 2,2,7,7,8,9,9-heptamethyldecahydroindeno[4,3a-b]furan and 2,2,6,6,7,8,8-heptamethyldecahydro-2H-indeno[4,5-b]furan	-	-	Skin Sens. 1 H317 [2 out of 3] Aquatic Chronic 4 H413 [1 out of 3] Aquatic Chronic 1 H410 [2 out of 3] Skin Irrit. 2 H315 [1 out of 3] Aquatic Acute 1 H400 [1 out of 3] Skin Sens. 1B H317 [1 out of 3]
942-754-1	-	Reaction mass of (3aR*,5aS*,9aS*,9bR*)-3a,6,6,9a-Tetramethyldodecahydronaphtho[2,1-b]furan and (3aR*,5aS*,9aS*,9bS*)-3a,6,6,9a-Tetramethyldodecahydronaphtho[2,1-b]furan	-	Aquatic Chronic 2 H411	-
944-675-8	-	Reaction products of 3-methyl-5-[(1S,4aS,8aS)-5,5,8a-trimethyl-2-methylenedecahydro-1-naphthalenyl]-1-penten-3-ol, cyclized	-	Skin Irrit. 2 H315	-
229-861-2	6790-58-5	[3aR-(3aα,5aβ,9aα,9bβ)]-dodecahydro-3a,6,6,9a-tetramethylnaphtho[2,1-b]furan	-	-	-
214-946-9	1222-05-5	1,3,4,6,7,8-hexahydro-4,6,6,7,8,8-hexamethylindeno[5,6-c]pyran	Index number: 603-212-00-7 Aquatic Acute 1 Statement: H400 Aquatic Chronic 1 Statement: H410	Aquatic Acute 1 H400 Aquatic Chronic 1 H410	Skin Irrit. 2 H315 [1 out of 177] Repr. 2 H361 [1 out of 177]
946-273-8	-	2,6,6,7,8,8-hexamethyl-3,3a,4,5,5a,6,7,8-octahydro-2H-indeno[4,5-b]furan, 1,1,2,3,3-pentamethyl-1,2,3,5,6,7-hexahydro-4H-inden-4-one and rel-(3aR,7aR)-1,1,2,3,3-pentamethyloctahydro-4H-inden-4-one	-	-	-

EC/List number	CAS No	Substance name	Harmonised classification	Classification in registrations	Classification in C&L notifications (*)
948-069-4	-	(+-)-(3aRS,5aSR,9aSR,9bSR)-3a,6,6,9a-Tetramethyldodecahydronaphtho[2,1-b]furan	-	Skin Irrit. 2 H315 Skin Sens. 1B H317 Aquatic Chronic 2 H411	-
457-070-4	823178-41-2	4H-Indeno[4,5-d]-1,3-dioxole, 3a,5,6,7,8,8b-hexahydro-2,2,6,6,7,8,8-heptamethyl-	-	Aquatic Chronic 2 H411	-
954-347-6	-	Reaction mass of rel-(3aR,5aR,8aR,8bS)-2,2,6,6,7,8,8-heptamethyldecahydro-2H-indeno[4,5-b]furan and rel-(3aS,5aR,8aS,8bS)-2,2,6,6,7,8,8-heptamethyldecahydro-2H-indeno[4,5-b]furan and rel-(2R,3aR,7aS)-1,1,2,3,3-pentamethyl-3a-(2-methylallyl)octahydro-4H-inden-4-one	-	Aquatic Chronic 1 H410 Skin Sens. 1B H317	-
701-326-2	-	Reaction mass of (3aR,5aS,9aS,9bR)-3a,6,6,9a-Tetramethyldodecahydronaphtho[2,1-b]furan and (3aS,5aR,9aR,9bS)-3a,6,6,9a-Tetramethyldodecahydronaphtho[2,1-b]furan	-	Aquatic Chronic 3 H412	-
271-889-2	68611-23-4	3-Pentanone, 1-(2,6,6-trimethyl-2-cyclohexen-1-yl)-, reaction products with 2-propyn-1-ol	-	Aquatic Chronic 1 H410	-
446-220-4	365411-50-3	Indeno[4,5-d]-1,3-dioxin, 4,4a,5,6,7,8,9,9b-octahydro-7,7,8,9,9-pentamethyl-	-	Skin Sens. 1B H317 Aquatic Chronic 2 H411	-
440-030-5	-	Reaction mass of 6-allyl-1,1,2,3,3-pentamethyl-2,3,3a,4,5,7a-hexahydro-1H-indene and 2,6,6,7,8,8-hexamethyldecahydro-2H-indeno[4,5-b]furan	Index number: 603-230-00-5 Skin Irrit. 2 (Hazard Statement: H315); Eye Dam. 1 (Hazard Statement: H318); Aquatic Chronic 4 (Statement: H413)		

(*) the number in brackets indicates the number of notifications received. Each notification can represent a group of notifiers; therefore, the number may differ from the C&L inventory which displays number of notifiers.

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

Data extracted on 28.09.2022.

EC / List number	214-946-9	229-861-2	260-686-4	271-889-2	440-030-5	446-220-4	457-070-4	701-326-2	942-754-1	948-069-4
PC 20: Products such as pH-regulators, flocculants, precipitants, neutralisation agents	C	I								
PC 36: Water softeners	C									
PC 37: Water treatment chemicals	C	I								
PC 2: Adsorbents	C									
PC 12: Fertilisers	C									
PC 27: Plant protection products	C									
PC 4: Anti-freeze and de-icing products	C									
PC 35: Washing and cleaning products	F, I, P, C	I, P, C	F, I, P, C	I, P, C	P, C	I, P, C	I, P, C	I, P, C	I, P, C	I, P, C
PC 8: Biocidal products (e.g., disinfectants, pest control)	C	I, P, C	F, I, P, C	C	C	C	C	C	C	
PC 28: Perfumes, fragrances	F, C	F, I, C	F, C	F, C	F, C	F, C	F, C	F, C	F, C	F, C
PC 3: Air care products	C	I, C	F, C	C	C	C	C	C	C	C
PC 39: Cosmetics, personal care products	F, C	C	P, C	P, C	C	C	P, C	P, C	C	C

PC 29: Pharmaceuticals	**C**									
PC 31: Polishes and wax blends	**P, C**	**I, P, C**	**F, P, C**	**P, C**	**C**	**P, C**	**P, C**	**P, C**	**P, C**	**P, C**
PC 24: Lubricants, greases, release products	**C**									
PC 13: Fuels	**C**									
PC 32: Polymer preparations and compounds	**C**				**A**					
PC 1: Adhesives, sealants	**C**									
PC 9b: Fillers, putties, plasters, modelling clay	**C**									
PC 9a: Coatings and paints, thinners, paint removes	**C**									
PC 18: Ink and toners	**C**									
PC: 26: Paper and board treatment products					**A**					
PC 34: Textile dyes, and impregnating products	**C**									
PC 23: Leather treatment products	**C**									
PC 14: Metal surface treatment products			**I**							
PC 21: Laboratory chemicals	**C**	**I**								
PC 19: Intermediate		**I**								
PC 30: Photo-chemicals	**C**									

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

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

Data extracted on 28.09.2022.

EC/List number	RMOA	Authorisation		Restriction*	CLH	Actions not under REACH/ CLP
		Candidate list	Annex XIV	Annex XVII	Annex VI (CLP)	
214-946-9	Yes				Yes	ESR
440-030-5					Yes	NONS, claimed, updated under REACH
446-220-4						NONS, tpa upgraded
449-360-4						NONS, claimed
457-070-4						NONS, claimed, updated under REACH
481-920-3						NONS, claimed

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

*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).