Assessment of regulatory needs

Authority: European Chemicals Agency

Date: 12 August 2021

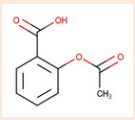
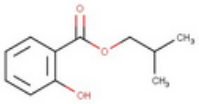
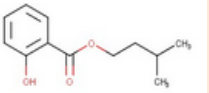
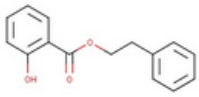
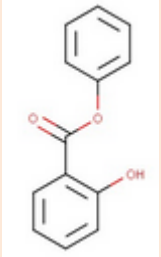
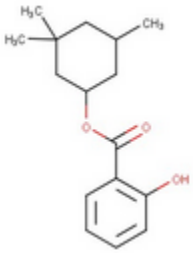
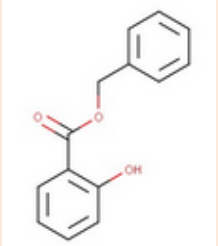
Group Name: Salicylate esters

Chemical structure: -

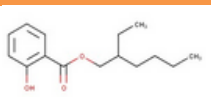
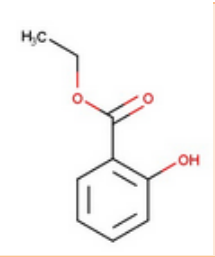
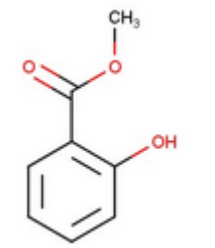
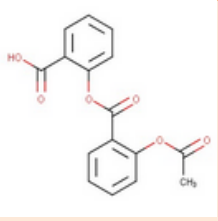
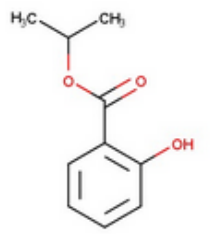
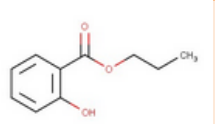
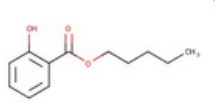
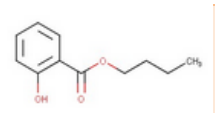
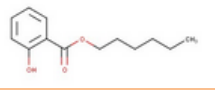
Revision history

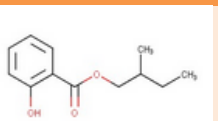
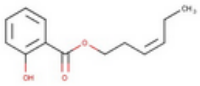
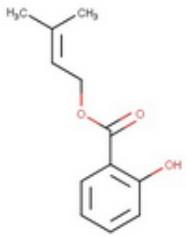
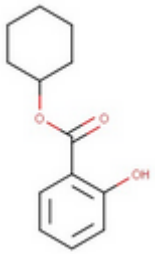
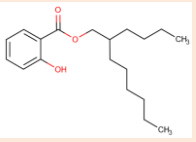
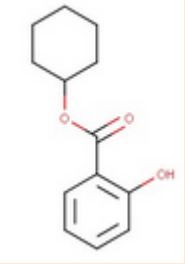
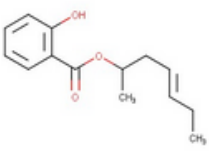
Version	*Date*	*Description*
1	12/08/2021	

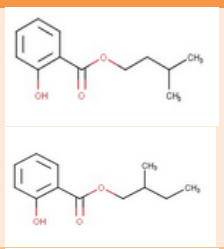
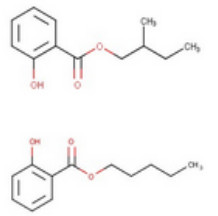
Substances within this group:

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]
200-064-1	50-78-2	O-acetylsalicylic acid		Not (publicly) available
201-729-9	87-19-4	isobutyl salicylate		Full, 1-10
201-730-4	87-20-7	isopentyl salicylate		Full, 1-10
201-732-5	87-22-9	phenethyl salicylate		Not (publicly) available
204-259-2	118-55-8	phenyl salicylate		Not (publicly) available
204-260-8	118-56-9	homosalate		Full, 100-1000
204-262-9	118-58-1	benzyl salicylate		Full, 100-1000

[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]
204-263-4	118-60-5	2-ethylhexyl salicylate		Full, 100-1000
204-265-5	118-61-6	ethyl salicylate		Full, 1-10
204-317-7	119-36-8	methyl salicylate		Full, >1000
208-493-6	530-75-6	2-carboxyphenyl o-acetylsalicylate		C&L notification
210-143-2	607-85-2	isopropyl salicylate		
210-145-3	607-90-9	propyl salicylate		
218-080-2	2050-08-0	pentyl salicylate		Not (publicly) available
218-142-9	2052-14-4	butyl salicylate		C&L notification
228-408-6	6259-76-3	hexyl salicylate		Full, >1000

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]
256-972-3	51115-63-0	2-methylbutyl salicylate		C&L notification
265-745-8	65405-77-8	(Z)-3-hexenyl salicylate		Full, 100-1000
271-434-8	68555-58-8	3-methyl-2-butenyl salicylate		Not (publicly) available
400-410-3 (607-733-0)	25485-88-5	cyclohexyl salicylate (cyclohexyl 2-hydroxybenzoate)		Full, 10-100
431-090-3	190085-41-7	2-hydroxybenzoic acid, 2-butyloctyl ester		Not (publicly) available
453-440-4	610271-60-8	Not (publicly) available	Not (publicly) available	Not (publicly) available
607-733-0 (400-410-3)	25485-88-5	cyclohexyl 2-hydroxybenzoate (cyclohexyl salicylate)		C&L notification
700-488-1	873888-84-7	(4Z)-hept-4-en-2-yl salicylate		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]
904-908-6	-	reaction mass of 2-methylbutyl salicylate and isopentyl salicylate		Full, 10-100
911-280-7	-	reaction mass of 2-methylbutyl salicylate and pentyl salicylate		Full, 100-1000
Not (publicly available)	-	Keratoplast; TDS; BTN, Edesal; Keratoplast-ITS.	Not (publicly) available	Not (publicly) available

The group includes also a non-registered substance with no publicly available identifier(s). This table contains also group members that are not registered (yet) but have a C&L notification under the CLP Regulation. However, the list is currently non-exhaustive. Once further regulatory risk management action on one or more registered substances is being considered, ECHA will make an additional search for related C&L notified substances to be included in the group and develop a regulatory strategy for them.

Contents

DISCLAIMER

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 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 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 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, 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

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

1 Overview of the group

ECHA has grouped together structurally similar substances based on the presence of the carboxylic group moiety shown in the figure below.

-C(=O)-O-

The group "Salicylate esters" consists of 27 substances where salicylic acid is reacted with either aliphatic (linear or (mono or multi)-branched, saturated or unsaturated) alcohol(s) with carbon number ranging from C1 to C16 as well as cyclic and aromatic alcohols by esterification. The group includes 25 well-defined (mono- and multi-constituent) substances and two UVCB substances, all sharing the same functional carboxylic group (-C(=O)-O-).

One substance, namely methyl salicylate (EC 204-317-7) contains several impurities that may impact the classification (e.g. phenol and limonene).

RAC adopted a harmonised classification as Acute Tox. 4; Skin Sens. 1B; Repr. 2, Aquatic Chronic 3 for EC 204-317-7 (methyl salicylate)[3]. A CLH proposal has been submitted by French Competent Authority (FR CA) for EC 228-408-6 (hexyl salicylate) proposing Skin Sens.1; Repr. 2, based on read-across from data on salicylic acid (SA), sodium salicylate (NaS) and methyl salicylate (MeS).

ECHA assessed the needs for regulatory action of the related group of "salicylic acid, its salts and derivatives". In addition, the groups "benzoates", "branched primary alkyl alcohols" and "branched secondary and tertiary alkyl alcohols" have also been assessed and may have some relevance to this group of "salicylate esters".

Based on information reported in the REACH registration dossiers, the substances are mainly used as fragrances/odour agents. A total of fourteen group members are used to confer an odour to a wide range of products, primarily cosmetics, perfumes, air care products, washing/cleaning products and biocidal formulations; hexyl salicylate (EC 228-408-6) stands out as the substance with the widest range of uses in this field. Notable exceptions to the use of substances as odour agents include the presence of two UV filters and three emollients/moisturisers for cosmetics. With the exception of two substances, all other substances have several uses that are likely to be associated with high potential for human exposure as they include professional and consumer uses. Article service life is relevant to scented products (candles, erasers, textiles, paper products) made with two group members (see also Annex 3).

[3] https://echa.europa.eu/documents/10162/ea33d742-d73f-a7a7-8bca-be3679b713e0

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

Note that salicylic acid (EC 200-712-3) in the group 'salicylic acid, its salts and alkyl derivatives' is currently under approval as an active substance under the Biocidal Products Regulation and it is proposed to await the outcome of the ED assessment in that context before considering the need for additional regulatory risk management based on ED properties for the whole group. The actions proposed below for the different sub-groups may need to be revisited if based on this assessment the substances are considered to have ED properties.

Based on currently available information, there is a need for further EU regulatory risk management – namely restriction for reprotoxicity and skin sensitisation hazards due to the potential for exposure of most substances in the group (excluding ECs 200-064-1, 431-090-3 and 208-493-6).

Need for restriction for skin sensitisation and reprotoxicity is due to potential for prolonged consumer exposure during scented article service life. Only two substances, ECs 201-732-5 and 228-408-6 are reported to be used for this purpose, however it is suggested to cover all salicylates in the proposed restriction due to structural similarity of the substances and potential for substitution.

Developmental toxicity is a known or potential hazard for most group members; for hexyl salicylate (EC 228-408-6) there is a CLH proposal for Repr. 2 based on methyl salicylate (EC 204-317-7) data (developmental effects) for which a RAC opinion for Repr. 2 has also been adopted. A third substance (phenyl salicylate, EC 204-259-2) has a self-classification of Repr. 2. Although several group members are lacking data, a group-wide pattern emerges around the formation of the same metabolite, salicylic acid, thus classification as Repr. 2 seems warranted for all substances in the group.

Based on similarity in structures of substances in this group it is expected that all substances would have potential skin sensitisation. However, there exist some uncertainty since there have been some negative test results (for EC/List Nos 204-265-5, 911-280-7, Keratoplast and one substance without publicly available identifiers) which are ambiguous or uncertain. To gain a better group overview on skin sensitisation potential , it is proposed to open a compliance check for some substances (ECs 204-265-5, Keratoplast and one substance without publicly available identifiers).

Finally, for environmental hazards, the substances in the group are toxic to aquatic organisms but are unlikely to be PBT/vPvB. In few cases a classification more stringent than existing self-classification could apply and for several cases the adequacy of the data submitted would need to be further assessed in a compliance check. Note that two substances, Keratoplast and one substance without publicly available identifiers, fulfils the screening PBT criteria[4] however due to low tonnage no data generation is possible to clarify the hazards currently. In addition, this substance is expected to have a low exposure potential.

The first step of the regulatory risk management action proposed, should the hazard exist, is the confirmation of hazard via harmonised classification (CLH) as Repr. (possibly category 2) (excluding ECs 228-408-6 and 204-317-7 for which CLHs are already under consideration).

Based on currently available information it seems that the substances in this subgroup would benefit from harmonised classification as repro 2. Due to the widespread uses of the group members and the commonality in their functions and uses, which could indicate a potential for substitutability, harmonised classification would add value by ensuring proper classification in the context of the use of these substances by workers and proper description of RMMs in exposure scenarios and supply chain communication.

The harmonised classification as repro 2 would support actions under the Cosmetic Products Regulation for most of the substances. For action under the Cosmetics Products Regulation to be triggered, harmonised classification as CMR 1/2 is required (NB. the Scientific Committee on Consumer Safety (SCCS) would have to assess whether the use of the reprotoxic substance is safe). Furthermore the CLH will facilitate the elimination of CMR category 2 substances from toys under the Toy Safety Directive (2009/48/EC) in addition to existing restrictions that apply to three group members (benzyl salicylate (EC 204-262-9) is banned, while methyl salicylate (EC 204-317-7) and pentyl salicylate (EC 218-080-2) must be listed on the label if they exceed a concentration of 100 mg/kg in the toy or components, according to the directive's Annex II, Sec II on allergenic substances). In addition, CLH can facilitate conformity assessment and declaration, particularly when the toy manufacturer bearing obligations is located outside the EU and therefore self-classification in registration dossiers is not applicable to them. As regards skin sensitisation, it is proposed to consider this hazard endpoint when the harmonised classification for toxic to reproduction is proposed; this would be in line with methyl salicylate and benzyl salicylate (where RAC has adopted a proposal for a harmonised classification of Skin Sens 1B), and hexyl salicylate (it has been proposed for harmonised classification as Skin Sens 1), and four more group members having self-classification as Skin Sens 1. It is also suggested to consider

4

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

at the same time aquatic toxicity when developing the harmonised classification proposal.

A restriction under REACH would be appropriate to prohibit the use of the reprotoxic and skin sensitising members of the group in articles which may lead to prolonged consumer exposure. Registration dossiers reveal the presence of two group members (phenethyl salicylate (EC 201-732-5) and hexyl salicylate (EC 228-408-6)) in articles with relevant service life in the EU. These substances are used as fragrances/odour agents in scented articles such as clothes, candles, paper products, CDs, toys and erasers. Some of these articles may be associated with prolonged consumer exposure through the skin (for example, clothing) in addition to inhalation exposure, or, depending on the article type (for example, scented erasers) may even be ingested by children.

Harmonised classification, as discussed previously, would prevent the use of these salicylates in toys but not in other article types, e.g., childcare articles.

It is noted that the SEv conclusion document for methyl salicylate (EC 204-317-7)[5] proposes that a RMOA be undertaken to properly manage the skin sensitisation risks to workers and consumers from exposure to the substance and it further confirms that this is an issue relevant to other salicylates too. It is thus considered appropriate to first wait for the results of the RMOA, and duly take those into account in confirming the appropriateness and scope of a restriction proposal for members of this group.

For environment it is expected that following the harmonised classification the necessary RMMs would be implemented and would be sufficient to ensure safe use in accordance with environmental legislation. However, it is proposed that in the CLH planned for toxicity to reproduction consideration could be given also to aquatic toxicity, this would strengthen the RMM measures. Until such harmonised classification is developed it is expected that after compliance check, registrants would adequately self-classify the substances and then implement similar necessary RMMs.

As regulatory risk management is proposed for this group, a closer look has been taken at five C&L notified substances originally included in the group:

- EC 208-493-6, 2-carboxyphenyl o-acetylsalicylate;
- EC 210-143-2, isopropyl salicylate;
- EC 210-145-3, propyl salicylate;
- EC 218-142-9, butyl salicylate; and
- EC 256-972-3, 2-methylbutyl salicylate.

The structure of these substances would support the theory of their hydrolysis to salicylic acid, the common metabolite for all salicylates, and as such reprotoxic effect is considered to be relevant for these too. Additionally, the skin sensitisation hazard that has been identified as relevant across the group is also deemed likely to apply to these substances too. As such, the five substances are included in the assessment of regulatory needs presented below; they are proposed for inclusion in the proposed harmonised classification for reprotoxicity and skin sensitisation

[5] https://echa.europa.eu/information-on-chemicals/evaluation/community-rolling-action-plan/corap-table/-/dislist/details/0b0236e1807e9072

and the restriction on use in scented consumer articles, with the exception of EC 208-493-6 which is addressed below.

Based on currently available information, there is a need for further EU regulatory risk management – CLH for potential reprotoxicity, skin sensitisation and potentially aquatic toxicity hazards due to the potential for exposure of the remaining substances in the group (ECs 200-064-1, 431-090-3 and 208-493-6).

The potential need for restriction applies to all substances with the exception of the following ones for which only the CLH is considered needed:

- o-acetylsalicylic acid (EC 200-064-1) which is only used in applications very different to the rest of the group (as a dental device disinfectant additive and a binder for resins);

- 2-hydroxybenzoic acid, 2-butyloctyl ester (EC 431-090-3), which is reprotoxic but unlikely to be a skin sensitiser based on available data and only used as cosmetic emollient; and

- 2-carboxyphenyl o-acetylsalicylate (EC 208-493-6), which has only C&L notification and is used/present in pharmaceutical products.

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
201-729-9 201-730-4 201-732-5 204-259-2 204-260-8 204-262-9 204-263-4 204-265-5 204-317-7 210-143-2 (C&L) 210-145-3 (C&L) 218-080-2	Known or potential hazard for reproductive toxicity and for skin sensitisation Inconclusive hazard for ED (assessment ongoing under BPR)	Known or potential hazard for aquatic toxicity	Fragrances, UV filters and cosmetic emollients in several product types (cosmetics, perfumes, cleaning products, etc.). Widespread professional and consumer uses for all substances except Keratoplast (industrial only) and 204-259-2 (intermediate)	**Need for EU RRM: Restriction of use in scented articles** <u>Justification</u>: Restriction of use in scented articles with prolonged consumer exposure. Some of these articles may be associated with prolonged consumer exposure through the skin (for example, clothing) in addition to inhalation exposure, or, depending on the article type (for	CCH for 218-080-2, 228-408-6, 271-434-8, 400-410-3, 904-908-6, 911-280-7, 201-732-5, 204-262-9, 265-745-8, 700-488-1, 204-265-5, 947-975-7, 950-068-9 CLH for all except 204-262-9, 204-317-7 and 228-408-6, as already proposed for CLH and Restriction for toxicity to reproduction

Subgroup name, EC number, substance name	Human Health Hazard	Environmental Hazard	Relevant use(s) & exposure potential	Last foreseen action	Action
218-142-9 (C&L) 228-408-6 256-972-3 (C&L) 265-745-8 271-434-8 400-410-3 453-440-4 700-488-1 904-908-6 911-280-7 Keratoplast Substance without publicly available identifiers				example, scented erasers) may even be ingested by children. Two substances reported the specific use in scented articles, however most salicylates across the group have a common function as fragrances and as such there is significant potential for substitution among these substances. It is proposed to await the French RMOA for EC 204-317-7 addressing risks to workers due to skin sensitisation and based on that decide the scope of the restriction, including whether relevant for all salicylates.	

Subgroup name, EC number, substance name	Human Health Hazard	Environmental Hazard	Relevant use(s) & exposure potential	Last foreseen action	Action
200-064-1 208-493-6 (C&L)	Known or potential hazard for reproductive toxicity (all) and for skin sensitisation (not 431-090-3) Inconclusive hazard for ED (assessment ongoing under BPR)	Known or potential hazard for aquatic toxicity	200-064-1: dental device disinfectant additive (professional use); binder for resins (industrial use). 208-493-6: pharmaceutical substance	**Need for EU RRM: CLH for reprotoxicity, skin sensitisation (not 431-090-3) and potential aquatic toxicity** Justification: CLH would ensure proper classification in the context of the use of these substances by workers and proper description of RMMs in exposure scenarios.	CCH CLH (without generation of data (human health))
431-090-3			Cosmetic emollient with widespread use		

Annex 1: Harmonised classifications and self-classifications reported by registrants

Data extracted on 22 December 2020.

EC/List No	Substance name		Self-classification	
		Harmonised classification	**Self-classification in registration dossier**	**Additional classification in C&L notifications**
204-265-5	ethyl salicylate	*Not included in Annex VI*	Acute Tox. 4 H302 Skin Irrit. 2 H315	Eye Irrit. 2 H319
204-262-9	benzyl salicylate	*Proposed classfication by RAC: Skin Sens. 1B* (RAC/M/48/2019)	Eye Irrit. 2 H319 Skin Sens. 1B H317 Aquatic Chronic 3 H412	Aquatic Chronic 1 H410 STOT Single Exp. 3 H335, affected organs: respiratory tract Skin Irrit. 2 H315 STOT Single Exp. 2 H371, affected organs: Not precised Aquatic Chronic 2 H411 STOT Single Exp. 3 H335, affected organs: respiratory tract STOT Single Exp. 2 H371, affected organs: Damage to organs Aquatic Acute 1 H400 STOT Single Exp. 2 H371, affected organs: Rate Skin Sens. 1 H317 STOT Single Exp. 3 H335 STOT Single Exp. 2 H371
256-972-3	2-methylbutyl salicylate	*Not included in Annex VI*	-	Skin Sens. 1B H317 Acute Tox. 4 H302 Eye Irrit. 2 H319 Aquatic Chronic 2 H411 Skin Irrit. 2 H315

EC/List No	Substance name		Self-classification	
		Harmonised classification	**Self-classification in registration dossier**	**Additional classification in C&L notifications**
204-263-4	2-ethylhexyl salicylate	*Not included in Annex VI*	-	Skin Irrit. 2 H315 Aquatic Chronic 4 H413 Eye Irrit. 2 H319
204-260-8	homosalate	*Not included in Annex VI*	-	Eye Irrit. 2 H319 Aquatic Chronic 4 H413 Skin Irrit. 2 H315STOT Single Exp. 3 H335
201-732-5	phenethyl salicylate	*Not included in Annex VI*	Skin Irrit. 2 H315 Skin Sens. 1 H317 Aquatic Chronic 2 H411	Skin Sens. 1B H317 STOT Single Exp. 3 H335 Eye Irrit. 2 H319
Not (publicly) available	Not (publicly) available	*Not included in Annex VI*	Aquatic Acute 1 H400 Aquatic Chronic 2 H411	-
265-745-8	(Z)-3-hexenyl salicylate	*Not included in Annex VI*	Aquatic Acute 1 H400	Aquatic Chronic 2 H411 Aquatic Chronic 1 H410 Skin Sens. 1 H317 Eye Irrit. 2 H319Skin Irrit. 2 H315 STOT Single Exp. 3 H335 Aquatic Chronic 3 H412

EC/List No	Substance name	Harmonised classification	Self-classification	
			Self-classification in registration dossier	Additional classification in C&L notifications
400-410-3	cyclohexyl salicylate	*Not included in Annex VI*	Aquatic Chronic 3 H412[registration, Article 10, inactive] Aquatic Chronic 2 H411	Aquatic Chronic 1 H410 Aquatic Acute 1 H400
Not (publicly available)	Keratoplast; TDS; BTN, Edesal; Keratoplast-ITS	*Not included in Annex VI*	-	-
453-440-4	No public or meaningful name is available	*Not included in Annex VI*	-	Skin Sens. 1B H317
201-730-4	isopentyl salicylate	*Not included in Annex VI*	Acute Tox. 4 H302 Aquatic Chronic 2 H411	Acute Tox. 5 H303 Skin Irrit. 2 H315Eye Irrit. 2 H319Aquatic Chronic 1 H410Aquatic Acute 1 H400
204-259-2	phenyl salicylate	*Not included in Annex VI*	Skin Sens. 1 H317[registration, intermediate, active] Skin Irrit. 2 H315[registration, intermediate, active] Aquatic Chronic 2 H411[registration, intermediate, active]	Eye Irrit. 2A H319 STOT Single Exp. 3 H335 Acute Tox. 4 H302Eye Irrit. 2 H319 STOT Single Exp. 3 H335, affected organs: Respiratory system STOT Single Exp. 3 H335, affected organs: Respiratory tract

EC/List No	Substance name	Harmonised classification	Self-classification	
			Self-classification in registration dossier	**Additional classification in C&L notifications**
			Repr. 2 H361, specific effect:H361fd: Suspected of damaging fertility. Suspected of damaging the unborn child.[registration, intermediate, active]	STOT Single Exp. 3 H335, affected organs: respiratory tract
271-434-8	3-methyl-2-butenyl salicylate	*Not included in Annex VI*	Aquatic Acute 1 H400 Aquatic Chronic 2 H411	Aquatic Chronic 2 H411
904-908-6	Reaction mass of 2-methylbutyl salicylate and isopentyl salicylate	*Not included in Annex VI*	Skin Sens. 1 H317 Aquatic Acute 1 H400 Aquatic Chronic 3 H412	Aquatic Chronic 2 H411
911-280-7	Reaction mass of 2-methylbutyl salicylate and pentyl salicylate	*Not included in Annex VI*	Acute Tox. 4 H302 Aquatic Acute 1 H400 Aquatic Chronic 2 H411	Aquatic Chronic 1 H410
200-064-1	O-acetylsalicylic acid	*Not included in Annex VI*	STOT Single Exp. 3 H335, affected organs: Not determined[registration, intermediate, active] Eye Irrit. 2 H319[registration,	Repr. 1B H360, specific effect: May damage the unborn child Skin Sens. 1 H317 Repr. 1B H360

EC/List No	Substance name	Harmonised classification	Self-classification	
			Self-classification in registration dossier	**Additional classification in C&L notifications**
			intermediate, active] Skin Irrit. 2 H315[registration, intermediate, active] Acute Tox. 4 H302	STOT Rep. Exp. 2 H373, affected organs: Liver, Blood (System), Central Nervous System, Auditory System Acute Tox. 3 H301 STOT Single Exp. 2 H371, affected organs: Stomach, Kidney, Lung STOT Single Exp. 3 H335, affected organs: Atemwege Resp. Sens. 1 H334 Repr. 2 H361] STOT Single Exp. 3 H335 Repr. 1A H360
607-733-0	Cyclohexyl 2-hydroxybenzoate	*Not included in Annex VI*	-	Aquatic Acute 1 H400 , Aquatic Chronic 1 H410, Aquatic Chronic 2 H411
218-142-9	butyl salicylate	*Not included in Annex VI*	-	Eye Irrit. 2 H319 Skin Irrit. 2 H315 Acute Tox. 4 H302 STOT Single Exp. 3 H335

EC/List No	Substance name	Harmonised classification	Self-classification	
			Self-classification in registration dossier	**Additional classification in C&L notifications**
204-317-7	methyl salicylate	*Proposed classification by RAC as* Skin Sens. 1B (RAC/M/50/2019)	Acute Tox. 4 H302 Eye Damage 1 H318	STOT Single Exp. 3 H335, affected organs: respiratory tract Eye Irrit. 2 H319 Skin Irrit. 2 H315 Repr. 2 H361 Repr. 2 H361, specific effect:d STOT Single Exp. 3 H335 Repr. 1B H360, specific effect: Unborn child Aquatic Chronic 3 H412 Skin Sens. 1B H317 Effect on or via lactation H362 Eye Irrit. 2A H319
431-090-3	2-hydroxybenzoic acid, 2-butyloctyl ester	Aquatic Chronic 4, H413	Aquatic Chronic 4 H413	-
700-488-1	(4Z)-hept-4-en-2-yl salicylate	*Not included in Annex VI*	-	-
218-080-2	pentyl salicylate	*Not included in Annex VI*	Acute Tox. 4 H302 Aquatic Acute 1 H400 Aquatic Chronic 1 H410	Aquatic Chronic 2 H411Aquatic Chronic 1 H411Skin Irrit. 2 H315Eye Irrit. 2 H319

EC/List No	Substance name		Self-classification	
		Harmonised classification	Self-classification in registration dossier	Additional classification in C&L notifications
228-408-6	hexyl salicylate	*RAC proposed harmonised classfication as Repr. 2; H361d and Skin Sens. 1B*	Skin Sens. 1B H317 Aquatic Chronic 1 H410	STOT Single Exp. 3 H335Eye Irrit. 2 H319Aquatic Chronic 2 H411Skin Irrit. 2 H315Aquatic Acute 1 H400Skin Sens. 1 H317
201-729-9	isobutyl salicylate	*Not included in Annex VI*	Acute Tox. 4 H302 Aquatic Acute 1 H400 Aquatic Chronic 2 H411	Eye Irrit. 2 H319Skin Irrit. 2 H315

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

Data extracted in January 2021.

Main types of applications structured by product or article types	228-408-6	700-488-1	204-317-7	400-410-3	201-732-5	265-745-8	911-280-7	201-729-9	201-730-4	204-262-9	204-265-5	218-080-2	271-434-8	904-908-6	200-064-1	204-260-8	204-263-4	431-090-3	Not (publicly) available	Keratoplast	204-259-2
Cosmetics, personal care products	P, C	P, C	F, I, P, C	P, C	I, P, C, **A**	F, P, C	F, I, P, C	C	C	F, I, P, C	C	F, I, C	C	C		F, P, C	F, I, P, C	F, P, C	F, C	F, I	
Perfumes, Fragrances	F, I, P, C, **A**	F, P, C	F, I, P, C	F, I, P, C	F, I, C, **A**	F, C	F, I, P, C	C	C	F, I, P, C	C	F, I, P, C	C	F, P, C			C				
Air care products	C, **A**	F, C	F, I, P, C	F, C	C, **A**	F, P, C	F, I, P, C	C	C	F, I, P, C	C	F, I, P, C	C	C							
Washing and cleaning products	I, P, C, **A**	P, C	F, I, P, C	F, I, P, C	I, P, C	F, I, P, C	F, I, P, C	I, P, C	I, P, C	F, I, P, C	I, P, C	F, I, P, C	I, P, C	I, P, C	P						
Polishes and wax blends	P, C	P, C	F, I, P, C	F, P, C	P, C	F, P, C	F, I, P, C	P, C	P, C	F, I, P, C	P, C	F, I, P, C	P, C	P, C							
Biocidal products	C	P, C	F, I, P, C	F, I, P, C	C	F, I, P, C	F, I, P, C	C	C	F, I, P, C	C	F, I, P, C	C	C	F, P						
Pharmaceuticals	C		F, I, P		I, C																
Fuel additives	C	P, C	F, I, P																		

Main types of applications structured by product or article types	228-408-6	700-488-1	204-317-7	400-410-3	201-732-5	265-745-8	911-280-7	201-729-9	201-730-4	204-262-9	204-265-5	218-080-2	271-434-8	904-908-6	200-064-1	204-260-8	204-263-4	431-090-3	Not (publicly) available	Keratoplast	204-259-2
Coatings and paints, thinners, paint removes	C	P, C		C																	
Fillers, putties, plasters, modelling clay	C	P, C																			
Finger paint		C																			
Photo-chemicals	C		I																		
Anti-freeze and de-icing products	C					P															
Lubricants, greases, release products	C					P															
Products such as pH-regulators, flocculants, precipitants, neutralisation agents	C																				
Water softeners	C																				
Water treatment chemicals	C																				
Adsorbents	C																				

Main types of applications structured by product or article types	228-408-6	700-488-1	204-317-7	400-410-3	201-732-5	265-745-8	911-280-7	201-729-9	201-730-4	204-262-9	204-265-5	218-080-2	271-434-8	904-908-6	200-064-1	204-260-8	204-263-4	431-090-3	Not (publicly) available	Keratoplast	204-259-2
Extraction agents															I						
Fertilisers	C																				
Plant protection products	C																				
Polymer preparations and compounds	C, **A**																				
Adhesives, sealants	C																				
Ink and toners	C																				
Paper and board treatment products	**A**																				
Textile dyes, and impregnating products	C																				
Leather treatment products	C																				
Welding and soldering products, flux products							P			P		P					F				
Metal surface treatment products				I		I	I														

Main types of applications structured by product or article types	228-408-6	700-488-1	204-317-7	400-410-3	201-732-5	265-745-8	911-280-7	201-729-9	201-730-4	204-262-9	204-265-5	218-080-2	271-434-8	904-908-6	200-064-1	204-260-8	204-263-4	431-090-3	Not (publicly) available	Keratoplast	204-259-2
Intermediate			F, I		F, I										I						I
Laboratory chemicals	C		F, I, P		I																

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

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

Data extracted on 29 January 2021.

EC/List number	RMOA	Authorisation		Restriction*	CLH	Actions not under REACH/ CLP
		Candidate list	Annex XIV	Annex XVII	Annex VI (CLP)	
204-260-8	YES					
204-262-9					YES	
204-263-4						
204-317-7					YES	
228-408-6					YES	

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

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