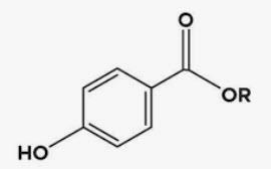
Assessment of regulatory needs

Authority: European Chemicals Agency (ECHA)

Date: 26 October 2022

Group Name: Paraben acid, salts and esters

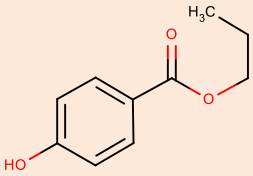
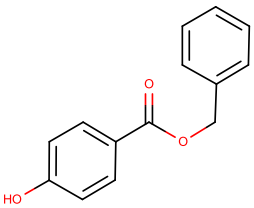
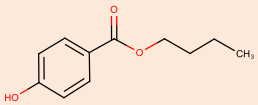
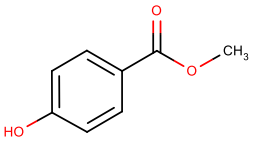
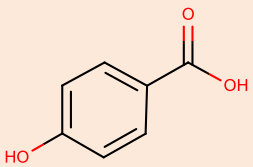
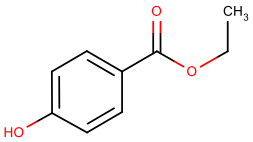
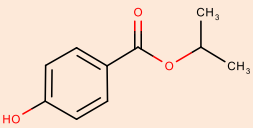
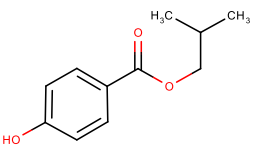
General structure:



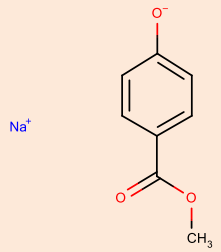
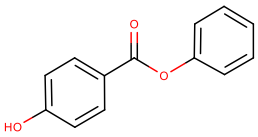
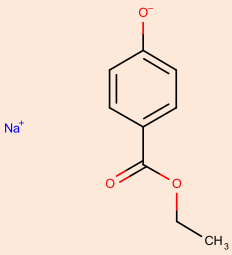
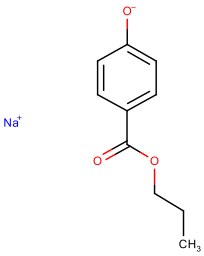
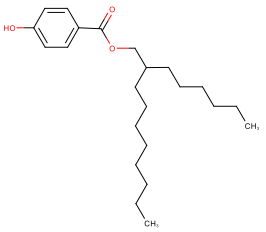
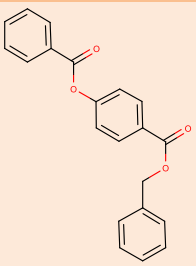
Revision history

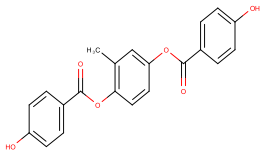
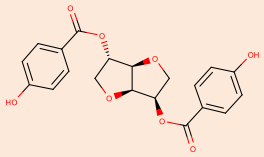
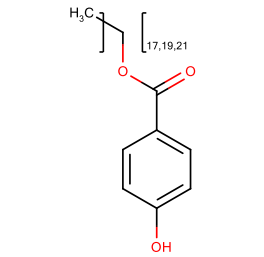
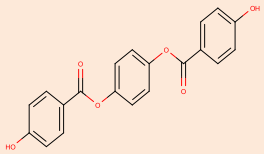
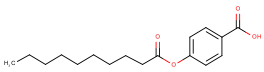
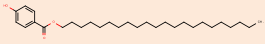
Version	*Date*	*Description*
1.0	26 October 2022	

Substances within this group:

EC/List number	CAS number	Publishable Name	Chemical Structure	Registration type (full, OSII or TII, NONS), highest tonnage band among all the registrations (t/y) [1]
202-307-7	94-13-3	Propyl 4-hydroxybenzoate		Full, 100-1000
202-311-9	94-18-8	Benzyl 4-hydroxybenzoate		Full, not (publicly) available
202-318-7	94-26-8	butyl 4-hydroxybenzoate		Cease manufacture
202-785-7	99-76-3	Methyl 4-hydroxybenzoate		Full, >1000
202-804-9	99-96-7	4-hydroxybenzoic acid		Full, >1000
204-399-4	120-47-8	Ethyl 4-hydroxybenzoate		Full, 100-1000
224-069-3	4191-73-5	Isopropyl 4-hydroxybenzoate		Full, not (publicly) available
224-208-8	4247-02-3	Isobutyl 4-hydroxybenzoate		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

EC/List number	CAS number	Publishable Name	Chemical Structure	Registration type (full, OSII or TII, NONS), highest tonnage band among all the registrations (t/y) [1]
225-714-1	5026-62-0	Sodium 4-(methoxycarbonyl)phenolate		Full, 100-1000
241-698-9	17696-62-7	Phenyl 4-hydroxybenzoate		Full, not (publicly) available
252-487-6	35285-68-8	Sodium 4-ethoxycarbonylphenoxide		Full, not (publicly) available
252-488-1	35285-69-9	Sodium 4-propoxycarbonylphenoxide		Full, 10-100
413-680-2	-	AF-394	not publicly available	NONS
415-380-7	148348-12-3	2-hexyldecyl p-hydroxybenzoate		Full, not (publicly) available
416-680-0	96682-10-9	Benzyl 4-benzoyloxybenzoate		NONS

EC/List number	CAS number	Publishable Name	Chemical Structure	Registration type (full, OSII or TII, NONS), highest tonnage band among all the registrations (t/y) [1]
601-643-5	119959-84-1	Benzoic acid, 4-hydroxy-, 1,1'-(2-methyl-1,4-phenylene) ester		OSII or TII
606-059-4	185756-31-4	D-Glucitol, 1,4:3,6-dianhydro-, bis(4-hydroxybenzoate)		OSII or TII
606-441-0	201305-16-0	Benzoic acid, 4-hydroxy-, C18-22-alkyl esters		Full, not (publicly) available
610-977-0	53201-62-0	Benzoic acid, 4-hydroxy-, 1,1'-(1,4-phenylene) ester		OSII or TII
617-941-3	86960-46-5	Benzoic acid, 4-[(1-oxodecyl)oxy]-		Full, not (publicly) available
920-338-0	109236-76-2	Benzoic acid, 4-hydroxy-, docosyl ester		Full, not (publicly) available

This table does not contain group members that are only notified under the CLP Regulation. However, the list is currently non-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

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. 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 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].

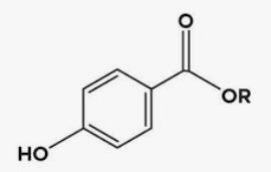
[2] https://echa.europa.eu/understanding-assessment-regulatory-needs

Glossary

ARN	Assessment of Regulatory Needs
CCH	Compliance Check
CLH	Harmonised classification and labelling
CMR	Carcinogenic, mutagenic and/or toxic to reproduction
DEv	Dossier evaluation
ED	Endocrine disruptor
NONS	Notified new substances
OEL	Occupational exposure limit
OSII or TII	On-site isolated intermediate or transported isolated intermediate
PBT/vPvB	Persistent, bioaccumulative and toxic/very persistent and very bioaccumulative
RMOA	Regulatory management options analysis
RRM	Regulatory risk management
SEv	Substance evaluation
STOT RE	Specific target organ toxicity, repeated exposure
SVHC	Substance of very high concern

1 Overview of the group

ECHA has grouped together 21 structurally similar substances based on the presence of the paraben acid moiety shown in the figure below.



The radical (R) can be in the form of an acid, salt or any aliphatic hydrocarbon group (branched and linear) or aromatic. The linear alkyl carbon chain varies in length from C1 to C22 without saturation.

Based on the information retrieved from 21 registration dossiers (of which 16 have full registration, three are intermediates and two NONs), most substances are reported as mono constituent, except of one registered as a UVCB substance.

Based on information reported in the REACH registration dossiers, half of the fully registered substances in this group are used in cosmetics. Other common uses include perfumes and pharmaceuticals. Four substances in the group have article service life for e.g., in textiles, leather, paper and photographic films. More than half of the substances in this group have at least one widespread use, leading to a high potential for exposure for workers and/or consumers, as well as a high potential for release to the environment. Additionally, for three substances which do not have widespread uses declared, potential for substitution cannot be excluded. The substances are used in the mentioned applications mostly as a preservative, but also e.g., as a colorant/pigment, intermediate, processing aid or plasticiser.

EC 202-318-7 has been identified as a SVHC for ED human health properties and placed on Candidate List (prioritised for authorisation). Denmark has submitted a proposal for another substance, EC 224-208-8, to be identified as an SVHC for the same properties. EC 415-380-7 has a harmonised classification for Aquatic Chronic 2 and EC 202-307-7 has a CLH proposal for Repr. 2 (H361fd). ED assessment under SEv is ongoing for EC 202-307-7 and 202-785-7. SEv on EC 202-804-9 (ED concern) was concluded without data generation[3] and the concern was refuted especially taking into account a limited exposure potential.

[3] SEv conclusion document for EC 202-804-9

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 ED hazards (except for List No. 601-643-5, 606-059-4, 610-977-0) due to the potential for release/exposure of most substances in the group

Based on ECHA's assessment of currently available hazard information and considerations of structural similarity and presence of common functional moiety, **all** the substances in the group have (potentially) the following human health/environmental hazards: **ED** (HH and ENV). This hazard is identified based on observed effects from a limited number of substances, including EC 202-318-7 which is already identified as an SVHC for ED human health properties and EC 224-208-8 for which there is a proposal for SVHC identification for ED HH. Based on structural similarity the findings from the (eco-)toxicity studies are extrapolated to the substances where there is limited information for this endpoint. However, it should be noted that this hypothesis bears higher uncertainty for parabens with aromatics in the side chain as (i) no higher tier studies are available on these substances and (ii) due to absence of information on the impact of aromatic side chain versus linear ones. *In silico* modelling[4] (QSAR predictions) indicates clear potential for ED for all substances in the group. The predictions are positive for the estrogen modality for all substances, generally with high or medium confidence. The potential estrogenic MoA can potentially result also in reproductive toxicity. The first step in the main metabolic pathway of parabens in human body is the hydrolysis of the ester bond by esterases. This results in the formation of 4-

[4] Integration of QSAR predictions from VEGA, OPERA with EDSP21 assays and Derek in vivo alerts

hydroxybenzoic acid, a likely common metabolite to all parabens in the group, and alkyl alcohol metabolites. The latter may potentially cause developmental toxicity.

Data (in particular OECD TG 234) has been generated under SEV for EC 202-785-7 (currently under assessment by France) and EC 202-307-7 (evaluated by Belgium and ED ENV properties were acknowledged by the ED expert group). In addition, EC 202-311-9 has a positive uterothrophic assay and, effects on VTG in fish and EC 241-698-9 is weak estrogen receptor (ER) agonist in vitro and has effects on vitellogenin (VTG) in fish. Additionally, regarding EC 202-785-7, two uterothrophic assays are positive (subcutaneous treatment) in both immature mice and rats and ovariectomized mice. The tests were also positive for EC 202-318-7, 204-399-4 and 202-307-7 (Lemini et al. 2003, 2004[5]).

Additionally, **all** the substances in the group are also suspected of having a **reproductive toxicity** hazard based on known or potential estrogenic mode of action. Reproductive toxicity-related effects have been observed with some of the substances. Based on the currently available data, the observed effects could warrant a Repr. 2 classification for some substances or no classification for others. This hypothesis is supported by an existing CLH proposal as Repr. 2 (H361fd) for EC 202-307-7 based e.g. on sperm effects, decreased anogenital distance in F1 and F2 males, and post-implantation loss. Furthermore, EOGRTS on EC 202-785-7 indicates effects on sperm counts and effects in cohorts for developmental immunotoxicity and neurotoxicity. These observations may warrant classification as Repr. 2 (H361fd).

On the basis of the above, the potential hazards for ED and reproductive toxicity need to be further clarified. For EC 202-785-7 and 202-307-7, data has already been generated under compliance check and/or substance evaluation, but ED assessment under substance evaluation is still ongoing for both substances. Data generation under compliance check is ongoing for EC 204-399-4. In 2014, EC 202-804-9 (4-hydroxybenzoic acid) has already been subjected to substance evaluation based on a concern for ED. It was concluded without data generation as the evaluating Member State regarded the concern for ED unjustified considering the limited exposure potential. However, estrogenic activity of EC 202-804-9 cannot be completely excluded considering the available QSAR predictions, *in vitro* data and the significant higher tier data gaps in the registration dossier. Especially, as EC 202-804-9 is a likely common metabolite of all substances in the group, it is important to clarify its hazard properties.

Some substances are self-classified as **Skin Sens** 1 (EC 202-311-9, 224-069-3 and 241-698-9) or Skin Sens 1B (EC 224-208-8). Potential hazard for skin sensitisation is identified for 202-318-7. The hazards for reproductive toxicity and skin sensitisation, if confirmed, are unlikely to be driving the regulatory strategy for these substances.

From the environmental side, based on ECHA's assessment of currently available hazard information, four members in the group fulfil the **PBT/vPvB** screening criteria[6] (EC 413-680-2, 415-380-7, 416-680-0, List No 606-441-0), and one

[5] Lemini C, Jaimez R, Avila ME, Franco Y, Larrea F, Lemus AE: In vivo and in vitro estrogen bioactivities of alkyl parabens. Toxicol. Ind. Health. 19:69-79, 2003.
Lemini C, Hernandez A, Jaimez R, Franco Y, Avila ME, Castell A: Morphometric analysis of mice uteri treated with the preservatives methyl, ethyl, propyl, and butylparaben. Toxicol. Ind. Health. 20:132-132, 2004.

[6] 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

substance (EC 202-311-9) is potentially **persistent/very persistent**, **mobile/very mobile and (potentially) toxic**. However, there is no possibility to request data to clarify the hazard for these substances (except for List No. 606-441-0) due to their registration status (e.g. intermediate registration). However, these environmental hazards are not driving the strategy.

Concerning the hazard for **aquatic toxicity** (seven substances with harmonised or self-classification for aquatic toxicity: EC numbers 202-307-7, 202-311-9, 202-318-7, 202-785-7, 225-714-1, 252-488-1, 415-380-7), it is expected that based on the classification registrants have implemented 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.

In terms of uses, parabens are known preservatives in a variety of cosmetics, foods, beverages and pharmaceuticals[7]. Indeed, most of the substances have, at least, one declared or assumed widespread use (e.g. in cosmetics, perfumes or pharmaceuticals) leading to a high potential for exposure for workers and/or consumers, as well as a high potential for release to the environment. Whilst many of such uses can be regulated under sector legislation, the environmental aspects are usually not addressed by that legislation (e.g. Cosmetics Regulation, Medicinal Products Regulation). Three substances do not have registered widespread uses but potential for substitution cannot be excluded (ECs 224-069-3 and 241-698-9, List 920-338-0). In the case of EC 224-069-3, it is listed in Annex I of Regulation (EU) No 10/2011 on Plastics Materials and Articles intended to come into contact with Food, therefore widespread uses can be assumed.

Based on the above considerations on hazards and uses, the first proposed action is **Compliance check**, but only for some substances and for two different reasons:

- For ECs 202-804-9 and List 606-441-0 and 617-941-3 to clarify ED HH

  The first proposed action is CCH to confirm the hazards, particularly ED for human health. The information from human health may be used to clarify ED environment. CCH will also clarify the reproductive toxicity, skin sensitisation (only for EC 202-804-9 and List 606-441-0), mutagenicity (only for EC 202-804-9 and List 606-441-0), PBT/vPvB (only for List 606-441-0), and aquatic toxicity (only for 606-441-0 and 617-941-3) concerns.

  Depending on the outcome of the ongoing and foreseen evaluation activities on higher tonnage substances, substance evaluation may be considered in the future to address the low tonnage substances (i.e., less than 10 tpa).

- For ECs/List 202-311-9, 224-069-3, 241-698-9, 920-338-0 to clarify skin sensitisation properties

  CCH is proposed to clarify hazards, including skin sensitisation, mutagenicity, and aquatic toxicity. For these low tonnage substances, CCH will not allow to clarify the ED concerns. Therefore, after CCH it is proposed to wait for the outcome of CCH for the substances above, and also the other ongoing activities (CCH and SEv/ED assessment), before deciding if further data generation is needed via substance evaluation.

For the rest of the substances, either action is ongoing at individual level, or it is proposed to wait for the outcome from the other substances. After that it will be considered whether **Substance evaluation** is still needed to clarify the concern for ED ENV/HH. For EC 224-208-8 in particular, even if CCH would allow to clarify

[7] Soni et al. 2001, 2002, 2005

the skin sensitisation, mutagenicity and aquatic toxicity hazards, there is a proposal from Denmark to identify the substance as an SVHC for ED based on a read-across from EC 202-318-7, which is already identified as SVHC based on ED properties and included in the candidate list.

If after data generation the ED hazards are concluded, for the use in cosmetics, the Commission may mandate the SCCS[8] to evaluate such substances and may take action to prohibit or restrict their use in cosmetics, if needed. Nevertheless, also because of other uses of the substances, **SVHC identification** is proposed for ED properties, both for human health (except for EC 202-318-7) and environment. 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 (in this case paper, leather, textiles, painted/coated articles, plastic/rubber articles and photographic films) contains the substance above regulatory threshold, i.e. 0.1% (w/w).

For the ED environment hazard in particular, confirmation of the hazard properties via SVHC identification is not considered sufficient to minimise potential releases of the substances in the environment. A **restriction** is seen as the most appropriate option as potential for exposure is expected from consumer uses (e.g. cosmetics), professional uses (e.g. plant protection products, biocides, cosmetics and cleaning products), industrial uses (e.g. cosmetics, pharmaceuticals) and article service life (including food contact materials). Currently, the existing sector legislation for some of the above-mentioned uses does not address the ED ENV hazard, which is the driving hazard for the regulatory strategy for the entire group.

In terms of exposure, releases to the environment from consumer uses cannot be avoided.

Widespread professional uses are typically non-contained and non-automated leading to releases to the environment.

Furthermore, potential for exposure and releases to the environment from some of the articles (e.g. tyres and general rubber goods) is likely based on available information.

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 presence of chemicals that affect the endocrine system in consumer and professional products has been recognised as an area of concern under the European Commission's Chemicals Strategy for Sustainability[9].

Moreover, **restricting substances in articles** used by professionals or consumers (reported for substance 606-441-0) is proposed for List 606-441-0 as potential for

[8] To note that some substances in this group are included in Annex V of Cosmetics Regulation – List of preservatives allowed in cosmetic products, and a maximum concentration in ready for use preparation is established (ECs 202-785-7, 204-399-4 and 225-714-1) or, additionally, cannot be used in leave-on products intended for the nappy area of children below 3 years old (ECs 202-307-7, 202-318-7 and 252-488-1). Other substances are listed in Annex II of Cosmetics Regulation – List of substances prohibited in Cosmetic Products (ECs 224-069-3, 224-208-8, 241-698-9). For EC 224-069-3 industrial uses in cosmetics are still reported in the registration dossier.

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

exposure from articles is likely. For ECs 202-311-9, 224-208-8 and Lists 413-680-2 and 415-380-7, exposure from article service life is unclear and should be further elaborated when developing a restriction of consumer/professional uses.

It is suggested to cover possibly also industrial uses as part of the restriction. However, the need for authorisation might be considered for industrial uses excluded from the scope of the restriction as it may not be proportionate to restrict all uses.

Based on currently available information, there is no need for (further) EU regulatory risk management for potential ED, reproductive toxicity and persistency, mobility and toxicity hazards of the substances 601-643-5, 606-059-4, 610-977-0

Potential hazards for ED, reproductive toxicity and persistency, mobility and toxicity (except 606-059-4) have been identified for these substances (see above). However, due to the fact that these substances are only registered as intermediates, data generation is not possible.

In terms of uses, and based on the chemical structure, no potential for substitution is envisaged.

Therefore, no EU regulatory risk management action is currently proposed for any of the aforementioned substances due to low exposure potential. It is worth noting however that the strategy may need to be revisited and need for further regulatory action reconsidered if there is a change in the registration status or reported uses for any of these substances.

Human health – unlikely hazards for all substances in the group

Based on ECHA's assessment of currently available hazard information, no potential hazards were identified for **STOT RE**, **mutagenicity** and **carcinogenicity**. However, higher uncertainty remains for the parabens with aromatics in the side chain for STOT-RE as no higher tier studies including repeated dose toxicity studies are available.

Environment – unlikely hazards for most of the substances in the group with some exceptions

Most of the substances in the group are unlikely to have the following environmental hazards: **PBT/vPvB** (except EC 413-680-2, 415-380-7, 416-680-0, List No 606-441-0) and **persistency, mobility and toxicity** (except EC 202-311-9) because they are readily biodegradable.

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
202-311-9 202-804-9 224-069-3 * 241-698-9 * 606-441-0 617-941-3 920-338-0 *	Known or potential hazard for ED Known or potential hazard for reproductive toxicity Known or potential hazard for skin sensitisation (202-311-9, 202-318-7[1)], 224-069-3 and 241-698-9)	Known or potential hazard for ED Known or potential hazard for PBT/vPvB (413-680-2, 415-380-7, 416-680-0, 606-441-0) Known or potential hazard for aquatic toxicity (202-307-7, 202-311-9, 202-318-7, 202-785-7, 225-714-1, 241-698-9, 252-488-1, 415-380-7)	Industrial uses; widespread uses (e.g. cosmetics, perfumes and pharmaceuticals), leading to a high potential for exposure for workers and/or consumers, as well as a high potential for release to the environment. Article service life, e.g. general rubber articles, tires, textile, leather or paper (only for 202-311-9, 224-208-8, 415-380-7 and 606-441-0).	**Need for EU RRM: Restriction** <u>Justification:</u> Releases to the environment from consumer and widespread professional uses cannot be avoided. Widespread professional uses are typically non-contained and non-automated leading to releases to the environment.	**First step:** CCH **Next steps (if ED hazard confirmed):** SVHC identification followed by Restriction
202-318-7 [1)] 224-208-8					**First step:** Restriction *EC 202-318-7: SVHC* *EC 224-208-8: SVHC proposal ongoing*

Subgroup name, EC number, substance name	Human Health Hazard	Environmental Hazard	Relevant use(s) & exposure potential	Last foreseen action	Action
202-307-7 202-785-7 204-399-4 225-714-1 252-487-6 252-488-1 413-680-2 415-380-7 416-680-0		Persistent, mobile, toxic/ very persistent, very mobile (202-311-9)	Potential for substitution cannot be excluded (ECs 224-069-3 and 241-698-9, List 920-338-0).	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. Restriction for use in articles to be considered together with the restriction of professional uses. Industrial uses to be considered as part of the restriction	**Pending action** *Ongoing actions described in the text*
601-643-5 606-059-4 610-977-0	Known or potential hazard for ED Known or potential hazard for reproductive toxicity	Known or potential hazard for ED Known or potential hazard for Persistent, mobile, toxic/ very persistent, very	No widespread uses. No potential for substitution envisaged.	**Currently no need for EU RRM** <u>Justification</u>: According to the reported uses, low potential for exposure to both human health and environment is	**No action**

Subgroup name, EC number, substance name	Human Health Hazard	Environmental Hazard	Relevant use(s) & exposure potential	Last foreseen action	Action
		mobile (601-643-5, 610-977-0)		expected. Actions (including data generation) will be re-considered when the assessment will be revisited if the registration status and/or uses change.	

* Potential for substitution
1) inactive registration

Annex 1: Overview of classifications

Data extracted on 21 February 2022

EC/ List No	CAS No	Substance name	Harmonised classification	Classification in registrations
202-307-7	94-13-3	propyl 4-hydroxybenzoate	-	Aquatic Chronic 3 H412
202-311-9	94-18-8	benzyl 4-hydroxybenzoate	-	Aquatic Chronic 1 H410 Skin Irrit. 2 H315 Eye Irrit. 2 H319 Skin Sens. 1 H317 Aquatic Acute 1 H400 STOT Single Exp. 3 H335, affected organs: respiratory track
202-318-7	94-26-8	butyl 4-hydroxybenzoate	-	Aquatic Chronic 3 H412 [Article 10 (inactive)] Skin Irrit. 2 H315 [Article 10 (inactive)] Eye Damage 1 H318 [Article 10 (inactive)]
202-785-7	99-76-3	methyl 4-hydroxybenzoate	-	Aquatic Chronic 2 H411
202-804-9	99-96-7	4-hydroxybenzoic acid	-	Eye Damage 1 H318 STOT Single Exp. 3 H335, affected organs: respiratory system
204-399-4	120-47-8	ethyl 4-hydroxybenzoate	-	-
224-069-3	4191-73-5	isopropyl 4-hydroxybenzoate	-	Skin Irrit. 2 H315 Eye Irrit. 2 H319 Skin Sens. 1 H317
224-208-8	4247-02-3	isobutyl 4-hydroxybenzoate	-	Skin Irrit. 2 H315 [Article 10 (inactive)] Eye Damage 1 H318 [Article 10 (inactive)] Skin Sens. 1B H317
225-714-1	5026-62-0	sodium 4-(methoxycarbonyl)phenolate	-	Skin Irrit. 2 H315 Eye Damage 1 H318 Aquatic Chronic 2 H411
241-698-9	17696-62-7	phenyl 4-hydroxybenzoate	-	Skin Irrit. 2 H315 Skin Sens. 1 H317
252-487-6	35285-68-8	sodium 4-ethoxycarbonylphenoxide	-	Eye Irrit. 2 H319
252-488-1	35285-69-9	sodium 4-propoxycarbonylphenoxide	-	Eye Damage 1 H318

EC/ List No	CAS No	Substance name	Harmonised classification	Classification in registrations
				Aquatic Chronic 3 H412
413-680-2			-	-
415-380-7	148348-12-3	2-hexyldecyl p-hydroxybenzoate	Aquatic Chronic 2 H411	Aquatic Chronic 2 H411
416-680-0	96682-10-9	Benzyl 4-benzoyloxybenzoate	-	-
601-643-5	119959-84-1	601-643-5	-	-
606-059-4	185756-31-4	606-059-4	-	-
606-441-0	201305-16-0	606-441-0	-	-
610-977-0	53201-62-0	610-977-0	-	-
617-941-3	86960-46-5	4-(decanoyloxy)benzoic acid	-	-
920-338-0	-	Benzoic acid, 4-hydroxy-, docosyl ester	-	-

(*) 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 21/02/2022.

Main types of applications structured by product or article types	202-307-7	202-311-9	202-318-7	202-785-7	202-804-9	204-399-4	224-069-3	224-208-8	225-714-1	241-698-9	252-487-6	252-488-1	415-380-7	601-643-5	606-059-4	606-441-0	610-977-0	617-941-3	920-338-0
PC 20: Products such as ph-regulators, …				i, p												f, i			
PC 36: Water softeners																c			
PC 37: Water treatment chemicals																f, i, p			
PC 2: Adsorbents																f			
PC 11: Explosives																p			
PC 12: Fertilisers																f, i, p, c			
PC 27: Plant protection products		p		p, c												p, c			
PC 4: Anti-freeze and de-icing products																p, c			
PC 35: Washing and cleaning products																f, i, p, c		i, p, c	
PC 8: Biocidal products		p		f												i, p, c			
PC 28: Perfumes, fragrances	f, c			c		f, c			f, c							f, c			
PC 3: Air care products																c			
PC 39: Cosmetics, personal care products	f, p, c		f, p, c	f, p, c		f, p, c	i		f, c		f, c	f, c				f, p, c			
PC 29: Pharmaceuticals	f, c	i	f, c	i		f, i, c	i					f, c				i, p			
PC 31: Polishes and wax blends																p, c			
PC 15: Non-metal-surface treatment products																c			

Main types of applications structured by product or article types	202-307-7	202-311-9	202-318-7	202-785-7	202-804-9	204-399-4	224-069-3	224-208-8	225-714-1	241-698-9	252-487-6	252-488-1	415-380-7	601-643-5	606-059-4	606-441-0	610-977-0	617-941-3	920-338-0
PC 24: Lubricants, greases, release products																f, i, p, c			
PC 25: Metal working fluids																i, p, c			
PC 16: Heat transfer fluids																c			
PC 17: Hydraulic fluids																i, p, c			
PC 13: Fuels																i, p, c			
PC 32: Polymer preparations and compounds					i								i, a			f, i, p, c, a			
PC 1: Adhesives, sealants				f												f, i, p, c			
PC 9c: Finger paint																c			
PC 9b: Fillers, putties, plasters, modelling clay								f, a								i, c			
PC 9a: Coatings and paints, thinners, paint removes		i						f, a								f, i, p, c			
PC 18: Ink and toners		i						f, a								f, i, p, c			
PC 26: Paper and board treatment products		i, a														i			
PC 34: Textile dyes, and impregnating products													i, a			f, i, c, a			
PC 23: Leather treatment products		i, a														f, i, p, c			
PC 14: Metal surface treatment products																i			
PC 21: Laboratory chemicals				i, p		i		i								f, i, p			

Main types of applications structured by product or article types	202-307-7	202-311-9	202-318-7	202-785-7	202-804-9	204-399-4	224-069-3	224-208-8	225-714-1	241-698-9	252-487-6	252-488-1	415-380-7	601-643-5	606-059-4	606-441-0	610-977-0	617-941-3	920-338-0
PC 19: Intermediate				i	i	i		i		i				i	i	i	i		
PC 30: Photo-chemicals	f																		

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

Additionally to the information included in the registration dossiers in relation to uses, some assumptions have been made:

- For EC 224-208-8 service life is assumed because it is a dye/pigment and declared to be used in the formulation of e.g. modelling clay, coatings and paints. Industrial uses are also assumed as it is not likely that only formulation takes place, moreover because no exported volumes are declared;
- For List 415-380-7 service life in textiles and in plastics/rubber is assumed due to its function as plasticiser;
- For List 606-441-0 service life in e.g. general rubber articles and tyres is assumed due to information retrieved from the IUCLID dossier;
- For List 617-941-3 industrial and, at least, consumer uses in cleaning products are assumed based on information from the IUCLID dossier.

Other notes on uses:

- ECs 202-307-7, 202-785-7, 202-804-9, 204-399-4 and 224-069-3 are listed in Annex I of Reg. (EU) No 10/2011 on plastics food contact materials. This use is not evident from the registration dossiers, even if some substances are indicated to be e.g. preservatives. For such substances, consumer exposure can be assumed.
- EC 224-069-3 is prohibited in cosmetics since 2014[10]. Registration data (Jan'19) declares use as preservative in cosmetics.
- For List 606-441-0 there seems to be over reporting of uses, i.e. several life cycle stages declared for almost all product categories.

[10] COMMISSION REGULATION (EU) No 358/•2014 - of 9 April 2014 - amending Annexes II and V to Regulation (EC) No 1223/•2009 of the European Parliament and of the Council on cosmetic products - (europa.eu)

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

Data extracted on 3 March 2022

EC/List number	RMOA	Authorisation		Restriction*	CLH	Actions not under REACH/ CLP
		Candidate list	Annex XIV	Annex XVII	Annex VI (CLP)	
4-HBA and parabens with short alkyl chain (C1-C4)						
202-307-7	-	-	-	-	YES	-
202-311-9	-	-	-	-	-	-
202-318-7	-	YES	-	-	-	-
202-785-7	-	-	-	-	-	-
202-804-9	-	-	-	-	-	-
204-399-4	-	-	-	-	-	-
224-069-3	-	-	-	-	-	-
224-208-8	YES	-	-	-	-	-
225-714-1	-	-	-	-	-	-
241-698-9	-	-	-	-	-	-
252-487-6	-	-	-	-	-	-
252-488-1	-	-	-	-	-	-
413-680-2	-	-	-	-	-	NONS
415-380-7	-	-	-	-	-	NONS
416-680-0	-	-	-	-	-	NONS
601-643-5	-	-	-	-	-	-
606-059-4	-	-	-	-	-	-
606-441-0	-	-	-	-	-	-
610-977-0	-	-	-	-	-	-
617-941-3	-	-	-	-	-	-
920-338-0	-	-	-	-	-	-

*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).

4 References

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