Assessment of regulatory needs

Authority: European Chemicals Agency (ECHA)

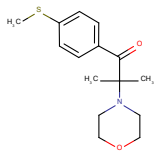
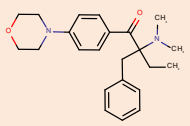
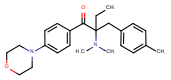
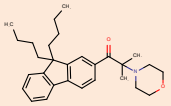
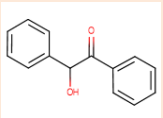
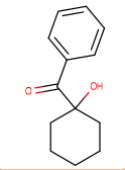
Group Name: Photoinitiators (benzoyl radical precursor type)

General structure: -

Revision history

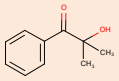
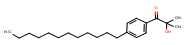
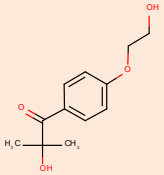
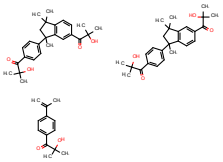
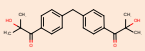
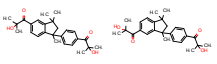
Version	*Date*	*Description*
1.0	5 July 2023	

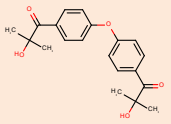
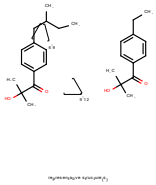
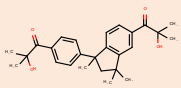
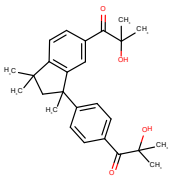
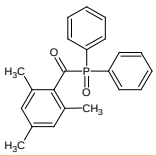
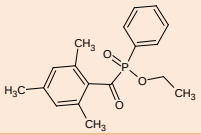
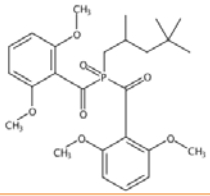
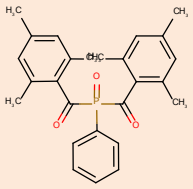
Substances within this group:

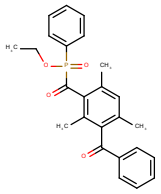
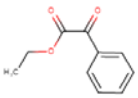
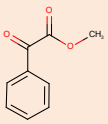
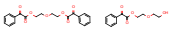
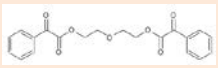
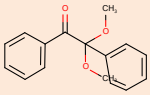
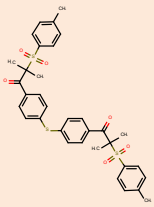
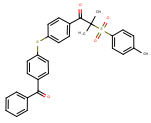
EC/List number	CAS number	Substance name	Chemical structure	Registration type (full, OSII or TII, NONS), highest tonnage band among all the registrations (t/y) [1]
Alpha-amino acetophenones				
400-600-6	71868-10-5	2-methyl-1-(4-methylthiophenyl)-2-morpholinopropan-1-one		Full, >1000
404-360-3	119313-12-1	2-benzyl-2-dimethylamino-4'-morpholinobutyrophenone		Full, 10-100
438-340-0	119344-86-4	2-(dimethylamino)-2-[(4-methylphenyl)methyl]-1-[4-(morpholin-4-yl)phenyl]butan-1-one		Full, 10-100 (full)
819-558-9	2020359-04-8	1-(9,9-dibutyl-9H-fluoren-2-yl)-2-methyl-2-(morpholin-4-yl)propan-1-one		Full, not (publicly) available
Alpha-hydroxy acetophenone				
204-331-3 [2]	119-53-9	benzoin		Full, 100-1000
213-426-9	947-19-3	hydroxycyclohexyl phenyl ketone		Full, >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

[2] EC 209-441-5 is only notified under the CLP Regulation and is considered a duplicate entry of EC 204-331-3. When ECHA is receiving a submission (e.g. Registration, C&L notification, etc.) without EC/List number, a new or existing EC/List number will be assigned to the substance. Sometimes, due to IT technical limitations, duplicate EC/List numbers are created during this submission process.

EC/List number	CAS number	Substance name	Chemical structure	Registration type (full, OSII or TII, NONS), highest tonnage band among all the registrations (t/y) [1]
231-272-0	7473-98-5	2-hydroxy-2-methylpropiophenone		Full, >1000
274-071-3	69673-80-9	1-(4-dodecylphenyl)-2-hydroxy-2-methylpropan-1-one		not registered
402-670-3	106797-53-9	2-hydroxy-4'-hydroxyethoxy-2-methylpropiophenone		Full, 10-100)
402-990-3	163702-01-0	A mixture mainly based on: 2,3-dihydro-6-(2-hydroxy-2-methyl-1-oxopropyl)-1,1,3-trimethyl-3-[4-(2-hydroxy-2-methyl-1-oxopropyl)phenyl]-1H-indene; 2,3-dihydro-5-(2-hydroxy-2-methyl-1-oxopropyl)-1,1,3-trimethyl-3-[4-(2-hydroxy-2-methyl-1-oxopropyl)phenyl]-1H-indene		10-100 tpa (full)
444-860-9	474510-57-1	2-hydroxy-1-(4-(4-(2-hydroxy-2-methylpropionyl) benzyl)phenyl)-2-methylpropan-1-one		Full, not (publicly) available
445-510-8	-	Reaction mass of 2-hydroxy-1-{3-[4-(2-hydroxy-2-methylpropanoyl) phenyl]-1,1,3-trimethyl-2,3-dihydro-1H-inden-5-yl}-2-methylpropan-1-one and 2-hydroxy-1-{1-[4-(2-hydroxy-2-methylpropanoyl)phenyl]-1,3,3-trimethyl-2,3-dihydro-1H-inden-5-yl}-2-methylpropan-1-one		Full, not (publicly) available

EC/List number	CAS number	Substance name	Chemical structure	Registration type (full, OSII or TII, NONS), highest tonnage band among all the registrations (t/y) [1]
472-110-0	71868-15-0	2-hydroxy-1-[4-[4-(2-hydroxy-2-methylpropanoyl)phenoxy]phenyl]-2-methylpropan-1-one		Full, 10-100
600-033-6	1001416-18-7	1-Propanone, 2-hydroxy-2-methyl-, 1-(4-C10-13-alkylphenyl) derivs.		Full, not (publicly) available
696-038-6	135452-43-6	1-Propanone, 1-[2,3-dihydro-1-[4-(2-hydroxy-2-methyl-1-oxopropyl)phenyl]-1,3,3-trimethyl-1H-inden-5-yl]-2-hydroxy-2-methyl-		Full, not (publicly) available
700-676-3	135452-42-5	2-Hydroxy-1-{3-[4-(2-hydroxy-2-methylpropanoyl)phenyl]-1,1,3-trimethyl-2,3-dihydro-1H-inden-5-yl}-2-methylpropan-1-one		Full, not (publicly) available
Phosphine oxides				
278-355-8	75980-60-8	diphenyl(2,4,6-trimethylbenzoyl) phosphine oxide		Full, 100-1000
282-810-6	84434-11-7	ethyl phenyl(2,4,6-trimethylbenzoyl) phosphinate		Full, 100-1000
412-010-6	145052-34-2	bis(2,6-dimethoxybenzoyl)-2,4,4-trimethylpentylphosphino xide		Cease manufacture
423-340-5	162881-26-7	phenyl bis(2,4,6-trimethylbenzoyl)-phosphine oxide		Full, 100-1000

EC/List number	CAS number	Substance name	Chemical structure	Registration type (full, OSII or TII, NONS), highest tonnage band among all the registrations (t/y) [1]
806-801-9	1539267-56-5	ethyl (3-benzoyl-2,4,6-trimethylbenzoyl)phenyl phosphinate		Full, not (publicly) available
Phenylglyoxylates				
216-504-0	1603-79-8	ethyl phenylglyoxylate		OSII or TII
239-263-3	15206-55-0	methyl benzoylformate		Full, 10-100
442-300-8	-	(2-(2-hydroxyethoxy)ethyl) oxo(phenyl)acetate;reaction mass of: 2-(2-((oxo(phenyl)acetyl)oxy)ethoxy)ethyl oxo(phenyl)acetate		Full, not (publicly) available
689-353-5	211510-16-6	Benzeneacetic acid, .alpha.-oxo-, 1,1'-(oxydi-2,1- ethanediyl)		not registered
Alpha-acetal ketones				
246-386-6	24650-42-8	2,2-dimethoxy-1,2-diphenylethan-1-one		Full, 100-1000
Alpha-sulfo acetophenones				
415-410-9	-	4,4'-bis(2-methyl-2-(4-methylphenyl)-1-propionyl)diphenylsulfide		NONS
429-040-0	272460-97-6	1-{4-[(4-benzoylphenyl)sulfanyl]phenyl}-2-methyl-2-[(4-methylphenyl)sulfonyl]propan-1-one		Full, not (publicly) available

This table does not contain 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[3].

[3] 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 substances that function as photoinitiators with a benzoyl radical releasing mode of action.

Photoinitiators are substances that convert absorbed light energy into chemical energy in the form of free radicals or cations. Based on the presence of key structural features the group members can be split into the six following sub-groups:

- Alpha-amino acetophenones
- Alpha-hydroxy acetophenones
- Phosphine oxides
- Phenylglyoxylates
- Alpha-acetal ketones
- Alpha-sulfo acetophenones

However, the structural similarity between members of some sub-groups is limited.

The group consists of 27 substances, out of which 23 have a full registration within REACH, 1 is intermediate, 1 is NONS, 1 is not registered and for 1 the manufacture has ceased.

Based on information reported in the REACH registration dossiers, the substances of the group are typically used as processing aids for curing/polymerisation of relatively thin films. The relative concentration of photoinitiators in the mixture to be cured/polymerised can be between 1 and 10 %. The uses include mainly industrial and professional uses in ink and toners, such as one of the components for 3D printing. For one substance (EC 278-355-8) consumer use of ink and toners is reported and for several substances article service life is reported in the registration dossiers (mainly in coatings and paints, thinners, paint removes, ink and toners, paper and board treatment products, but also in adhesives and polymer preparations and compounds). Considering that almost all registered substances of the group are used in ink and toners, article service life could be expected for all substances and the use of articles by consumers might be anticipated. However, since this type of photoinitiators is cleaved to reactive metabolites (radicals) to initiate the polymerisation, it is unclear if unreacted photoinitiators are still present in the final article and at which concentration. Based on the information available, exposure of workers and consumers and release into the environment can be assumed for most substances in the group.

The alpha-amino acetophenones ECs 400-600-6, 404-360-3, 438-340-0[4] and the phosphine oxide EC 278-355-8[5] have a harmonised classification for reproductive toxicity 1B. Two of the alpha-amino acetophenones EC 400-600-6 and 404-360-3 have been identified as substances of very high concern (SVHC) based on the

[4] RAC Opinion adopted on 2.06.2022

[5] RAC Opinion adopted on 16.09.2021

reproductive toxic category 1B H360FD and H360D classifications, respectively, in accordance with Article 57 (c) of REACH and recommended for the inclusion in Annex XIV to REACH[6], for EC 438-340-0 an intention has been recently included in the Registry of SVHC intentions[7]. The phosphine oxide EC 278-355-8 has been recently identified as SVHC[8]. The alpha-hydroxy acetophenone EC 444-860-9 has a harmonised classification for STOT RE 2 (kidney, thymus), and several phosphine oxides (ECs 278-355-8, 412-010-6, 423-340-5) and one phenoxyglyoxylate (EC 442-300-8) have an agreed or proposed harmonised classification for skin sensitisation.

According to the EC 400-600-6 and EC 404-360-3 RMOA conclusion document[9] the harmonised classification as Repr. 1B (H360FD and H360D, respectively) for the two substances has already led to a move towards alternative substances, especially in printing inks, as for example demonstrated by the recommendations in the European Printing Ink Association (EuPIA) exclusion list. However, exemptions from this EuPIA voluntary restriction initiative may be applied for. Alternatives have to be determined use by use, in view of the specific properties needed (wavelength, moisture sensitivity, O_2-inhibition, yellowing, etc.) and may come from the wide family of alpha amino acetophenone photoinitiators.

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.

[6] 11th Recommendation for inclusion in Annex XIV, ECHA, 12.04.2023

[7] SVHC intention-AT CA, 5.06.2023

[8] ECHA decision. Entry into force 14.06.2023.

[9] RMOA Conclusion document, AT CA, June 2019

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

Based on ECHA's assessment of hazard information available in the registration dossiers the following conclusions can be drawn for all substances in the group. No potential for mutagenicity is observed based on the available in vitro and in vivo data. No potential for carcinogenicity based on both systemic toxicity data and absence of mutagenic potential based on available experimental data.

It is not possible to conclude on ED hazards (human health and environment) for all group members due to lack of specific data to allow robust conclusion for endocrine properties; some group members are reproductive toxicants and the information available does not allow to conclude on potential ED mediated pathways. As indicated in the RMOA conclusion document[9] for the two alpha-amino acetophenones ECs 400-600-6 and 404-360-3, it is acknowledged that further information would be necessary to further clarify presence or absence of endocrine disruption potential. However, due to the clear human health hazard already identified (Repr. 1B) for some group members and the high substitution potential for the two substances, it is suggested not to do anything for the time being to clarify ED properties and to rather await the impact of the proposed regulatory measures which could potentially result in a withdrawal of these substances from the market. Further assessment for the remaining group members under CCH will examine reproductive toxicity potential and ED.

For environmental hazards, the substances in the group are toxic to aquatic organisms. Group members are very reactive (including under light) and due to this it can be concluded that there is no potential for them to be persistent. There is remaining uncertainty regarding potential for bioaccumulation of degradation products.

Based on currently available information, there is a need for (further) EU regulatory risk management – restriction (possibly combined with Authorisation) for reproductive toxicity hazard due to the potential for release/ exposure of substances in the subgroups alpha-amino acetophenones (ECs 400-600-6, 404-360-3, 438-340-0), alpha-hydroxy acetophenones (ECs/Lists 402-990-3, 444-860-9, 445-510-8, 472-110-0, 696-038-6, 700-676-3) and phosphine oxides (EC 278-355-8).
Based on ECHA's assessment of hazard information currently available in the registration dossiers some substances in the subgroups of alpha-amino acetophenones, alpha-hydroxy acetophenones, and phosphine oxides have known or potentially reproductive toxicity hazard as summarised below.

The **alpha-amino acetophenones** ECs 400-600-6, 404-360-3, 438-340-0[4] have a harmonised classification for Repr. 1B.

For the **alpha-hydroxy acetophenones** the available information indicates potential for reproductive toxicity for the substances ECs 402-990-3 and 444-860-9. For EC 402-990-3 effects on female gonadal function and oestrus cycles influencing the reproductive function have been observed whereas for EC 444-860-9 reproductive performance findings are observed but in presence of parental toxicity. For the substances ECs/Lists 445-510-8, 472-110-0, 696-038-6, and 700-676-3 extrapolation of the reproductive toxicity potential from EC 402-990-3 is

assumed based on structural similarity due to the presence of two functional photoinitiating moieties with remaining uncertainty due to differences in alkyl substitution.

For the **phosphine oxides,** EC 278-355-8 has a harmonised classification for reproductive toxicity 1B[5] (due to effects in male reproductive system in a screening reproductive toxicity study and skeletal malformation) and EC 282-810-6 is self classified as Repr. 2 due to effects observed in a developmental toxicity study. No effects in male reproductive systems like the ones observed with EC 278-355-8 have been observed in a 90 day repeated-dose toxicity study. The substance has structural difference from EC 278-355-8 as it contains two instead of three aromatic rings that can alter the toxicological profile, therefore the findings from EC 278-355-8 are not extrapolated.

Based on the information available on composition provided in (some) registration dossiers, the phopshine oxide EC 282-810-6 contains as impurity the substance EC 278-355-8 with harmonised classification as Repr. 1B at concentration (concentration range 0-1%) potentially above generic concentration limits under the CLP Regulation (0.3%), justifying the classification of the substance. Such classification is however not yet applied by those registrants where the substance is present in the composition. Therefore, registrants are invited to update their registration dossiers and revise the classification of the substance based on impurities, as appropriate, or if technically feasible to ensure that the concentration of the impurity is below the relevant concentration limit for reproductive toxicity (Repr.1B). The Safety Data Sheet needs to be updated accordingly.

In addition, the phospine oxide EC 278-355-8 is a known skin sensitiser (CLH Skin Sens. 1B). Potential for systemic toxicity in relation to STOT RE has been identified for some members with thymus as common target organ. This applies to alpha-hydroxy acetophenones ECs 402-990-3 and 472-110-0, and EC 444-860-9 that has a harmonised classification for STOT RE 2 (kidney, thymus). The potential for other group members to have such hazard can be examined under CCH where relevant.

Based on the information summarised above, the hazard triggering risk management regulatory actions for the indicated photoinitiators is the reproductive toxicity. For the substances of the alpha-hydroxy acetophenones subgroup, 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. 1B. When preparing the proposals, it may be considered what would be the best way to develop them, for instance whether to make a proposal for the group of substances, to submit them individually or jointly.

CLH as Repr. 1B i) will require company level risk management measures (RMM) for workers to be in place; ii) is needed or highly recommended in support of further regulatory processes under REACH; and iii) would lead to generic restriction of the substance(s) in consumer mixtures by means of restriction entry 30.

For substances used in clothing, other textiles and footwear articles CLH is also a prerequisite to restrict the presence of the substances in clothing, other textiles, and footwear articles, by means of the restriction entry 72 of REACH Annex XVII (this would require addition of the relevant substances to Appendix 12 by the Commission through Article 68(2)).

CLH will also support regulatory action under other legislations. For instance, in this specific case harmonised classification as Repr. 1B will trigger regulatory action under the Cosmetic products regulation (EC) No 1223/2009 since CMR Cat. 1 are restricted by this regulation.

The substances of the group have all industrial and professional uses, among others, in coatings, paints, thinners, paint removers, inks and toners, expected to be widespread (at many sites and by many users). Professional use is often widespread with relatively low levels of operational controls and risk management measures but with often frequent exposures with a long duration. In addition, professional users may be self-employed and therefore not covered by occupational safety and health (OSH) legislation. Consumer use in coatings and paints is also reported for the substance EC 278-355-8. Consumers may be co-exposed to the substances used by professionals (e.g. house painters).

Therefore, a restriction of the substance as such or in mixtures (concentration limit in mixtures) used by professionals is suggested after CLH.

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.

In addition, the use of the most harmful substances by professional workers has been recognised as an area of concern under the European Commission's Chemicals Strategy for Sustainability which aims to extend to professional users under REACH the level of protection granted to consumers.

The two alpha-amino acetophenones EC 400-600-6 and 404-360-3 have already been identified as SVHC (reproductive toxicity) and recommended by ECHA for inclusion into Annex XIV[6], for EC 438-340-0 an intention has been recently included in the Registry of SVHC intentions[7]. The phosphine oxide EC 278-355-8 has been recently identified as SVHC (Repr. 1B)[8]. For the reasons indicated above, restriction would be the preferred regulatory measure to address these substances together with the other substances of the group with confirmed reproductive toxicity hazard. However, the need for authorisation might be considered for specific industrial uses excluded from the scope of the restriction as it may not be proportionate to restrict all uses.

Restriction would target professional uses and the presence in articles reported for several substance due to use in e.g. coatings and paints, inks and toners, and paper and board treatment products. Potential exposure from articles can be expected also for other substances of the group due to their use in the same applications. However, since available data on the concentration of unreacted photoinitiators in articles or products seems to be very limited it is suggested that potential exposure from articles is further investigated. Consequently, the need for restricting substances in articles used by professionals or consumers should be considered in the context of the restriction of professional uses.

With regards to skin sensitisation for the indicated phosphine oxides, for industrial and professional uses, CLH requires company level risk management measures (RMM) to be in place for workers.

The concern related to skin sensitisers (potentially) present in consumer mixtures will be addressed anyway via the generic restriction of the substance(s) in consumer mixtures by means of restriction entry 30.

To be noted that the substance EC 278-355-8 (CLH Skin Sens. 1B) for which article service life is reported in textiles due to use in textile dyes and impregnating products, may fall under the scope of the ongoing restriction proposal from FR/SE on skin sensitisers (and skin irritants and corrosive substances) used in textiles, leather, fur and hide articles.

Therefore, it is proposed that there is currently no further need for EU-wide regulatory risk management to address the skin sensitisation.

Based on currently available information, there is no need for (further) EU regulatory risk management for the remaining substances of the subgroups alpha-amino acetophenones, alpha-hydroxy acetophenones, phosphine oxides and all substances in the subgroups alpha-acetal ketones and alpha-sulfo acetophenones.

The **alpha-amino acetophenone** List 819-558-9 has no potential hazards except for potential aquatic toxicity, as explained above. No similar reproductive effects compared to the other alpha-amino acetophenones of the group have been observed; this might be due to strutural differences in substitution of the aromatic ring although they all have the same functional moiety. Based on the available screening reproductive toxicity test there is no potential for reproductive toxicity for this substance; however, further assessment of the information under CCH is required to clarify this hazard.

The **alpha-hydroxy acetophenones** EC 204-331-3 (209-441-5), 213-426-9, 231-272-0, 274-071-3, 402-670-3 and List 600-033-6 have no potential hazards, as explained above, with exception of potential aquatic toxicity.

For EC 213-426-9 and EC 231-272-0 the available information indicates no potential for reproductive toxicity hazard. The reproductive toxicity studies with EC 213-426-9 do not indicate developmental or fertility effects that would meet classification criteria for reproductive toxicity whereas the developmental toxicity study with EC 231-272-0 does not indicate any effects.

The unlikely reproductive toxicity conclusion is extrapolated on the basis of structural similarity from EC 231-426-9 to EC 204-331-3, 402-670-3, 600-033-6 based on presence of one functional photoinitiating moiety, but remaining uncertainty regarding some structural differences (e.g. presence of additional unsaturated ring that could alter the toxicokinetics of the substance, alkyl substitution on the aromatic ring). For EC 274-071-3, the unlikely reproductive toxicity conclusion is extrapolated from EC 231-272-0 based on the presence of one functional photonitiating moiety with remaining uncertainty due to additional alkyl substitution of the aromatic ring.

The **phospine oxide** EC 423-340-5 has no potential hazards, as explained above, with the exception for potential aquatic toxicity. No specific effects in PNDT and RDT studies available for the substance EC 423-340-5 indicate no potential for reproductive toxicity hazard for this substance. In addition, known or potential skin sensitisation is identified for the 3 substances EC 282-810-6 (self classified Skin Sens.1), EC 412-010-6 (CLH Skin Sens.1) and EC 423-340-5 (CLH Skin Sens. 1A).

For the **phenylglyoxylates** the available data on reproductive toxicity (negative pre-natal developmental toxicity and repeated dose toxicity studies) with EC 239-263-3 and EC 442-300-8 indicate no potential for reproductive toxicity hazard for these substances. EC 216-504-0 and List 689-353-5 for which no data is available on reproductive toxicity are structurally similar to EC 239-263-3, thus the no potential for reproductive toxicity hazard can be extrapolated.

The available data indicated skin sensitising properties for 3 of the substances of this subgroup. EC 239-263-3 is self-classified for Skin Sens 1 and substance EC 442-300-8 has a harmonised classification Skin Sens 1A. For List 689-353-5, a substance that is not registered, Skin Sens 1B is notified.

For **alpha-acetal ketone** EC 246-386-6, there is no experimental data available on reproductive toxicity; for the purpose of the screening assessment extrapolation from EC 239-263-3 is made based on the presence of similar functional moiety (alpha hydroxy acetephenone) but with remaining uncertainty that needs to be further assessed under CCH.

For **alpha-sulfo acetophenones**, EC 429-040-0, has no potential hazard, with exception for potential aquatic toxicity. The unlikely reproductive toxicity is based on some available information from repeated dose toxicity study but some uncertainty remains.

Overall, no or unlikely hazard that would lead to concern for the reported uses.

With regards to skin sensitisation for the indicated phenylglyoxylates, for industrial and professional uses, sufficient and consistent self-classification by registrants should require company level risk management measures (RMM) to be in place for workers.

With regards to potential aquatic toxicity identified for these substances, it is expected that following data generation for aquatic toxicity registrants would adequately self-classify the substances. The self-classification will require company level risk management measures (RMM) for environment to be in place.

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

For the following remaining substances of phosphine oxides and apha-sulfo acetophenones subgroups currently available information is not sufficient to conclude on hazard.

For **phosphine oxides**, for EC 806-801-9, no conclusion can be made on reproductive toxicity due to absence of information and no extrapolation from other subgroup members is made due to additional moiety (aromatic ring) that might affect the toxicological profile. For EC 412-010-6, no extrapolation is also possible due to the presence of methoxy groups on aromatic rings and additional alkyl chains.

For **alpha-sulfo acetophenones**, for EC 415-410-9 no extrapolation is possible as it contains two functional photoinitiating moieties compared to EC 429-040-0, that might have impact in toxicological profile.

Despite the uncertainties on hazard for these substances, due to the current registration status for EC 412-010-6 and EC 415-410-9 no data generation is possible to clarify the hazards. Actions (including data generation) will be re-considered when the assessment will be revisited if the registration status and/or uses change. For List 806-801-9 only few industrial uses are reported with limited exposure potential. For these reasons it is proposed that there is currently no need for EU-wide regulatory risk management.

Compliance check is proposed for clarifying hazard of the following group members with active REACH registration: ECs/Lists 400-600-6, 404-360-3, 819-558-9 (alpha-amino acetophenones); ECs/Lists 204-331-3, 231-272-0, 402-670-3, 402-990-3, 444-860-9, 472-110-0,600-033-6, 696-038-6, and 700-676-3 (alpha-hydroxy acetophenones); ECs/List 278-355-8, 282-810-6, 423-340-5, 806-801-9 (phospine oxides); EC/List 442-300-8 and 689-353-5 (phenylglyoxylates); EC 246-386-6 (alpha-acetal ketone); and EC 429-040-0 (alpha-sulfo acetophenone).

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/List number	Human Health Hazard	Environmental Hazard	Relevant use(s) & exposure potential	Last foreseen action	Action
Alpha-amino acetophenones 400-600-6 404-360-3 438-340-0 **Phosphine oxides** 278-355-8	Known or potential hazard for reproductive toxicity for skin sensitisation for ECs/Lists 204-331-3, 282-810-6, 423-340-5, 472-110-0, 600-033-6, 700-676-3, 819-558-9 for STOT RE ECs 402-990-3, 444-860-9, 472-110-0	Known or potential hazard for aquatic toxicity No hazard or unlikely hazard for PBT/vPvB	Industrial, widespread professional use in inks and toners, coatings and paints, thinners and paint removers. For EC 278-355-8 consumer use is reported and for ECs 438-340-0, 472-110-8, 278-355-8, 423-340-5 article service life is reported, but could be expected for all substances. Potential for exposure of workers and consumers and release into the environment can be assumed for most	**Need for EU RRM: Restriction** possibly combined with Authorisation for specific industrial uses <u>Justification:</u> The reported professional uses are widespread (at many sites and many users) with relatively low levels of operational controls and risk management measures but with often frequent exposures with a long duration. Restriction of professional uses is	**First step:** Restriction and in parallel CCH for ECs 400-600-6, 404-360-3 and 278-355-8
Alpha-hydroxy acetophenones 402-990-3 444-860-9 445-510-8 472-110-0 696-038-6 700-676-3					**First step:** CLH for all and in parallel CCH for ECs/Lists 402-990-3, 444-860-9, 472-110-0, 696-038-6, 700-676-3

Subgroup name, EC/List number	Human Health Hazard	Environmental Hazard	Relevant use(s) & exposure potential	Last foreseen action	Action
			substances in the group.	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. Potential exposure from articles needs further investigation, restriction for use in articles to be considered together with the restriction of professional uses. However, the need for authorisation might be considered for specific industrial uses excluded from the scope of the restriction as it may not be proportionate to restrict all uses.	**Next steps (if hazard confirmed):** Restriction

Subgroup name, EC/List number	Human Health Hazard	Environmental Hazard	Relevant use(s) & exposure potential	Last foreseen action	Action
Alpha-amino acetophenones 819-558-9 **Alpha-hydroxy acetophenones** 204-331-3 (209-441-5) 213-426-9 231-272-0 274-071-3 402-670-3 600-033-6 **Phosphine oxides** 282-810-6 412-010-6 423-340-5 806-801-9 **Phenylglyoxylates** 239-263-3 442-300-8 216-504-0 689-353-5	No hazard or unlikely hazard for reproductive toxicity for all except for Inconclusive hazard for reproductive toxicity for ECs 412-010-6, 415-410-9, List 806-801-9 Known or potential hazard for skin sensitisation for EC 239-263-3, EC 442-300-8, List 689-353-5			**Currently no need for EU RRM** <u>Justification:</u> Harmonised/self classification for skin sensitisation requires company level risk management measures (RMM) for workers to be in place. The concern related to the presence of skin sensitisers in consumer mixtures is under investigation. Harmonised/self-classification will require company level risk management measures (RMM) for environment to be in place	CCH for ECs/Lists 819-558-9, 204-331-3, 231-272-0, 402-670-3, 600-033-6, 282-810-6, 423-340-5, 806-801-9, 442-300-8, 689-353-5, 246-386-6, 429-040-0

Subgroup name, EC/List number	Human Health Hazard	Environmental Hazard	Relevant use(s) & exposure potential	Last foreseen action	Action
Alpha-acetal ketones 246-386-6 **Alpha-sulfo acetophenones** 415-410-9 429-040-0					

Annex 1: Overview of classifications

Data extracted on 14.06.2023

EC/ List No	Substance name	Harmonised classification	Classification in registrations
400-600-6		Acute Tox 4 H302 Repr. 1B H360FD Aquatic Chronic 2 H411	Repr. 1B H360, specific effect:May damage fertility. May damage the unborn child. Repr. 1B H360 Repr. 1B H360, specific effect:adverse effects on fertility and developmental toxicity Acute Tox. 4 H302 Aquatic Chronic 2 H411
404-360-3		Repr. 1B H360D Aquatic Acute 1 H400 Aquatic Chronic 1 H410	Repr. 2 H361 Repr. 2 H361, specific effect:H361d: suspected of damaging the unborn child Repr. 1B H360 Aquatic Acute 1 H400 Aquatic Chronic 1 H410 Aquatic Chronic 1
438-340-0		RAC Opinion : Repr. 1B H360Df Aquatic Acute 1 H400 Aquatic Chronic 1 H410 M=1;	Repr. 2 H361, specific effect:developmental toxicity Aquatic Chronic 1 H410
819-558-9		-	
204-331-3 (209-441-5)		-	
213-426-9		-	-
231-272-0		-	Acute Tox. 4 H302 Aquatic Chronic 3 H412
274-071-3		-	Not registered
402-670-3		-	-
402-990-3		-	Repr. 2 H361 STOT RE 1 H372, affected organs: Ovaries Aquatic Chronic 4 H413
444-860-9		STOT RE 2 H373, affected organs: kidney, thymus Aquatic Acute 1 H400 Aquatic Chronic 1 H410	STOT RE 2 H373, affected organs: Kidneys, Thymus Aquatic Acute 1 H400 Aquatic Chronic 1 H410
445-510-8		-	Aquatic Chronic 4 H413
472-110-0		-	Aquatic Chronic 2 H411

EC/ List No	Substance name	Harmonised classification	Classification in registrations
600-033-6		-	Aquatic Chronic 1 H410
696-038-6		-	-
700-676-3		-	-
278-355-8		Repr 2 H361f Proposal agreed in RAC-58 Sep 2021: Repr 1B H360Fd Skin Sens 1B H317	Repr. 2 H361, specific effect:testes atrophy (fertility), bent limb bones (unborn child) Repr. 1B H360, specific effect: testes atrophy (fertility), bent limb bones (unborn child) Skin Sens. 1B H317 Aquatic Chronic 2 H411
282-810-6	-		Skin Sens. 1 H317 Aquatic Chronic 2 H411
412-010-6 inactive		Skin Sens. 1 H317 Aquatic Acute 1 H400 Aquatic Chronic 1 H410	Skin Sens. 1 H317 Aquatic Acute 1 H400 Aquatic Chronic 1 H410
423-340-5		Skin Sens. 1A H317 Aquatic Chronic 4 H413	Skin Sens.1 H317 Skin Sens. 1A H317 Skin Sens. 1B H317 Aquatic Chronic 4 H413
806-801-9	-		Aquatic Chronic 1 H410
216-504-0	-	-	
239-263-3	-		Skin Sens. 1 H317
442-300-8		Skin Sens. 1A H317	Skin Sens. 1A H317
689-353-5	-	-	
246-386-6	-		Acute Tox. 4 H302 STOT Rep. Exp. 2 H373, affected organs: liver, kidney Aquatic Chronic 3 H412
415-410-9 NONS		-	-
429-040-0		Eye Damage 1 H318 Aquatic Chronic 4 H413	Eye Damage 1 H318 Aquatic Chronic 4 H413

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

Data extracted on 14.06.2023

Main types of applications structured by product or article types	PC 35: Washing and cleaning products	PC 39: Cosmetics, personal care products	PC 32: Polymer preparations and compounds	PC 1: Adhesives, sealants	PC 9c: Finger paint	PC 9b: Fillers, putties, plasters, modelling clay	PC 9a: Coatings and paints, thinners, paint removes	PC 18: Ink and toners	PC 26: Paper and board treatment products	PC 34: Textile dyes, and impregnating products	PC 14: Metal surface treatment products	PC 38: Welding and soldering products, flux products	PC 21: Laboratory chemicals	PC 19: Intermediate	PC 30: Photo-chemicals	Other
Alpha-amino acetophenones																
400-600-6			I	I, **P**		I	F, I, **P**	F, I, **P**					F, I, **P**			
404-360-3	F, I		F, I, **P**	F, I, **P**	F, I	F, I, **P**	F, I, **P**	F, I, **P**					F, I, **P**		I	PC 7: Base metals and alloys (F,I,**P**)
438-340-0			**A**		F, I	F, I	F, I, **P**	F, I, **P**, **A**	**A**				F, I, **P**		I	
819-558-9								F, I, **P**, **A**					F, I, **P**			
Alpha-hydroxy acetophenones																
204-331-3							I, **P**	F, I, **P**					F, I, **P**	I	F, I	PC11: explosives (**P**)

Main types of applications structured by product or article types	PC 35: Washing and cleaning products	PC 39: Cosmetics, personal care products	PC 32: Polymer preparations and compounds	PC 1: Adhesives, sealants	PC 9c: Finger paint	PC 9b: Fillers, putties, plasters, modelling clay	PC 9a: Coatings and paints, thinners, paint removes	PC 18: Ink and toners	PC 26: Paper and board treatment products	PC 34: Textile dyes, and impregnating products	PC 14: Metal surface treatment products	PC 38: Welding and soldering products, flux products	PC 21: Laboratory chemicals	PC 19: Intermediate	PC 30: Photo-chemicals	Other
213-426-9	I	F, **P**	F, I, **P**	F, I, **P**	F, **P**	F, I, **P**	F, I, **P**, **A**	F, I, **P**, **A**	F, I, **P**		F, I		F, I, **P**		F, I, **P**	
231-272-0	F	F, I, **P**	F, I, **P**	F, I, **P**, **A**			F, I, **P**, **A**	F, I, **P**, **A**	F, I, **P**				F, I, **P**		F, I, **P**	
402-670-3	F, I		F, I, **P**	F, I, **P**	F, I, **P**	F, I, **P**	F, I, **P**	F, I, **P**	F, I, **P**			**P**	F, I, **P**		F, I, **P**	PC 33: Semiconductors (**P**)
402-990-3		F, I, **P**	F, I, **P**	F, I, **P**			F, I, **P**	F, I, **P**					F, I, **P**	I	F, I, **P**	
444-860-9				F, I, **P**			F, I, **P**	F, I, **P**					F, I, **P**			
445-510-8	I, **P**	F, I, **P**	F, I, **P**	F, I, **P**		F, I, **P**	F, I, **P**	F, I, **P**	F, I, **P**		F, I, **P**		F, I, **P**			
472-110-0	I, **P**		F, I, **P**	F, I, **P**, **A**	F, I, **P**	F, I, **P**	F, I, **P**, **A**	F, I, **P**, **A**	F, I, **P**		F, I		F, I, **P**			
600-033-6							F, I						F, I			
696-038-6	F, I		F, I, **P**	F, I, **P**			F, I, **P**	F, I, **P**					F, I, **P**			

Main types of applications structured by product or article types	PC 35: Washing and cleaning products	PC 39: Cosmetics, personal care products	PC 32: Polymer preparations and compounds	PC 1: Adhesives, sealants	PC 9c: Finger paint	PC 9b: Fillers, putties, plasters, modelling clay	PC 9a: Coatings and paints, thinners, paint removes	PC 18: Ink and toners	PC 26: Paper and board treatment products	PC 34: Textile dyes, and impregnating products	PC 14: Metal surface treatment products	PC 38: Welding and soldering products, flux products	PC 21: Laboratory chemicals	PC 19: Intermediate	PC 30: Photo-chemicals	Other
700-676-3	F, I		F, I, **P**	F, I, **P**			F, I, **P**	F, I, **P**					F, I, **P**			
Phosphine oxides																
278-355-8	F, I, **P**		F, I, **P**	F, I, **P**		F, I, **P**	F, I, **P**, **A**	F, I, **P**, **C**, **A**	F, I, **P**, **A**	**A**			F, I, **P**		F, I, **P**	PC 15: Non-metal-surface treatment products (F, I, **P**)
282-810-6			F, I, **P**	F, I, **P**			F, I, **P**	F, I, **P**					F, I, **P**		F, I, **P**	
423-340-5	F, I	F, I, **P**	F, I, **P**	F, I, **P**	F, I, **P**	F, I, **P**	F, I, **P**, **A**	F, I, **P**, **A**	F, I, **P**			**P**	F, I, **P**	F	F, I	PC 2 - Adsorbent (I)
Phenylglyoxylates																
806-801-9							F, I	F, I					F, I		F, I	
216-504-0													I	I		

Main types of applications structured by product or article types	PC 35: Washing and cleaning products	PC 39: Cosmetics, personal care products	PC 32: Polymer preparations and compounds	PC 1: Adhesives, sealants	PC 9c: Finger paint	PC 9b: Fillers, putties, plasters, modelling clay	PC 9a: Coatings and paints, thinners, paint removes	PC 18: Ink and toners	PC 26: Paper and board treatment products	PC 34: Textile dyes, and impregnating products	PC 14: Metal surface treatment products	PC 38: Welding and soldering products, flux products	PC 21: Laboratory chemicals	PC 19: Intermediate	PC 30: Photo-chemicals	Other
239-263-3			F, I, **P**	F, I, **P**		F, I	F, I, **P**	F, I, **P**	**P**				F, I, **P**	I	F, I	PC 29: pharmaceuticals (I)
442-300-8				I, **P**			I, **P**	I, **P**					F, I, **P**			
Alpha-acetal ketones																
246-386-6	F, **P**		F, I	I, **P**		F, I	F, I, **P**	F, I, **P**					F, I, **P**	I	F, I	
Alpha-sulfo acetophenones																
415-410-9													I, **P**			
429-040-0							F, I, **P**	F, I, **P**					F, I, **P**			

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

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

Data extracted on 14 June 2023

EC / List number	RMOA	Authorisation		Restriction*	CLH	Actions not under REACH / CLP
		Candidate list	Annex XIV	Annex XVII	Annex VI (CLP)	
278-355-8		YES			Update for existing entry pending (RAC opinion Sep 2021): add Skin sens 1B, H317, modify Repr. 1B, H360FD	Use in cosmetics not permitted/ subject to the restrictions laid down (Reg. EC No 1223/2009, Annex III)
400-600-6	YES	YES				Use prohibited in cosmetics (Regulation EC No 1223/2009, Annex II)
404-360-3	YES	YES				Use prohibited in cosmetics (Reg. EC No 1223/2009, Annex II)
438-340-0	YES				Update of existing entry pending (RAC Opinion Jun 2022): Repr. 1B H360Df, Aquatic Acute 1 H400, Aquatic Chronic 1 H410 M-factor=1	

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

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