Assessment of regulatory needs

Authority: European Chemicals Agency (ECHA)

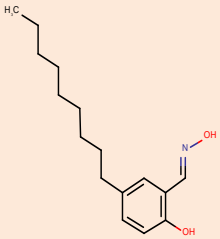
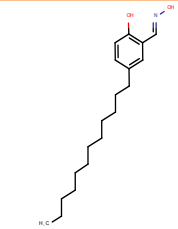
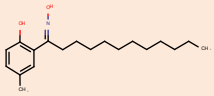
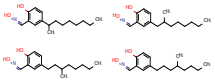
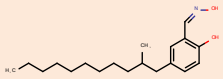
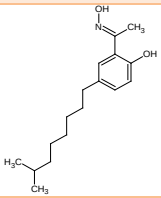
Group Name: Hydroxybenzenecarbonyl oxime derivatives

General structure: -

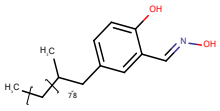
Revision history

Version	*Date*	*Description*
1.0	3 May 2022	

Substances within this group:

EC / List number	CAS number	Substance name [and / or Substance name acronyms]	Chemical structures	Registration type (full, OSII or TII, NONS), highest tonnage band among all the registrations (t/y) [1]
256-798-8	50849-47-3	5-nonyl-salicylaldehyde oxime		Not registered
278-736-9	77635-32-6	5-dodecyl-2-hydroxybenzaldehyde oxime		Not registered
433-200-5	50652-76-1	1-(2-hydroxy-5-methylphenyl)dodecan-1-one oxime (LPO)		NONS, not updated
605-717-8	174333-80-3	Benzaldehyde, 2-hydroxy-5-nonyl-, oxime, branched (C9 aldoxime)		Full, >1000
627-071-6	1233873-37-4	Benzaldehyde, 5-dodecyl-2-hydroxy-, oxime, branched (C12 aldoxime)		Inactive registration
627-083-1	244235-47-0	1-(2-hydroxy-5-nonyl(branched)-phenyl)ethanone oxime (C9 ketoxime)		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	Substance name [and / or Substance name acronyms]	Chemical structures	Registration type (full, OSII or TII, NONS), highest tonnage band among all the registrations (t / y) [1]
-	-	No public or meaningful name is available	-	Full, not publicly available
944-572-8	2156592-48-0	Benzaldehyde, 2-hydroxy-, oxime, 5-C11-12-branched alkyl derivs. (C11-C12 aldoxime)	C11-C12 aldoxime 	Full, not (publicly) available

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

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

Foreword

The purpose of the assessment of regulatory needs of a group of substances is to help authorities conclude on the most appropriate way to address the identified concerns for a group of substances or a single substance, i.e. the combination of the regulatory risk management instruments to be used and any intermediate steps, such as data generation, needed to initiate and introduce these regulatory measures.

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

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

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

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

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

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

Glossary

ARN	Assessment of Regulatory Needs
CCH	Compliance Check
CLH	Harmonised classification and labelling
CMR	Carcinogenic, mutagenic and/or toxic to reproduction
DEv	Dossier evaluation
ED	Endocrine disruptor
NONS	Notified new substances
4-NP	4- nonyl phenol
MOCS	More than one constituent 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
PDDP	Phenol, alkylation products (mainly in para position) with C12-rich branched alkyl chains from oligomerisation, covering any individual isomers and/ or combinations thereof
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
UVCB	Substances of Unknown or Variable composition, Complex reaction products or Biological materials

1 Overview of the group

ECHA has grouped together structurally similar substances based on the presence of the hydroxybenzenecarbonyl oxime moiety.

One feature of the group members is the linear or branched alkyl chain that is attached to the phenol ring in the para position forming 4-nonyl phenol or 4-dodecyl phenol moieties (also other alkyl chains are present in some substances). The other feature of the group members is the oxime or ketoxime functionality in the ortho position of the phenol ring.

The group consists of eight substances from which five are registered. Five substances (List No. 605-717-8, 627-083-1, 627-071-6, 944-572-8, substance X) in this group are substances of unknown or variable composition, complex reaction products or biological materials (UVCBs). Three group members (EC 256-798-8, EC 278-736-0 and EC 433-200-5) are well-defined, mono-constituent substances.

One substance (EC 433-200-5) is a ketoxime where the alkyl chain is directly attached to the oxime functional group and a methyl group is located in the para position of the phenol ring. Despite the fact that this substance significantly differs from the other members in this group, it was agreed to keep the substance (NONS that has not been updated) in the group due to potential similar uses in metal extraction.

The main derivative that potentially drives the hazard is the '4-alkyl phenol, branched' being a constituent stemming from the unreacted starting material as such or from the final manufactured substances which themselves contain '4-alkyl phenol, branched' moieties in their chemical structures.

These constituents can be found in five substances (i.e. all except EC 256-798-8, EC 278-736-9 and EC 433-200-5) at concentrations well above 0.1 %:

- 4-NP (4-nonylphenol branched, EC 284-325-5) is a constituent of List Nos. 605-717-8 and 627-083-1;
- PDDP (4-dodecylphenol branched, EC 310-154-3) is a constituent of List Nos. 627-071-6 and 944-572-8;
- 2-methyl-4-nonylphenol (EC 238-392-2) is a constituent of substance X.

There are hazards for endocrine disruption (ED) for 4-NP and PDDP confirmed by authorities: 4-NP has been identified as SVHC[3] and included in the Candidate list based on its endocrine disrupting properties for the environment; PDDP has been identified as SVHC[4] and included in the Candidate list based on its endocrine disrupting properties for the environment and human health as well as reproductive toxicity. ED activity could be suspected for 2-methyl-4-nonylphenol since it is a 4-NP derivative, but there is no data to conclude since it is not registered.

Based on information reported in the REACH registration dossiers, all registered substances are used as chelating agents in extraction processes at mining operation (in some case it is specified for copper extraction). One substance (List No. 605-717-8) is also used as rust / corrosion inhibitor for metal surface treatments. Although only uses under industrial setting have been reported, there seems to be

[3] https://echa.europa.eu/fi/registry-of-svhc-intentions/-/dislist/details/0b0236e180e4ba35
[4] https://echa.europa.eu/registry-of-svhc-intentions/-/dislist/details/0b0236e1854508be

potential for exposure for workers and environment due to open systems and potential for releases into environment via wastewater discharges.

There is PBT/vPvB concern for 4-NP, which is being clarified under substance evaluation (SEv)[5]. C9 ketoxime (List No. 627-083-1) was assessed under SEv to clarify concerns about PBT/vPvB and high tonnage. The evaluation was concluded in 2016 without asking further information, but the PBT concern remains unverified since it is related to the PBT/vPvB concern of one of the constituents (i.e. 4-NP) that is still under clarification under the ongoing SEv process.

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.

[5] https://echa.europa.eu/fi/information-on-chemicals/evaluation/community-rolling-action-plan/corap-table/-/dislist/details/0b0236e1806b811b

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 –authorisation for reproductive toxicity, ED, skin sensitiser, PBT/vPvB, due to the potential for release/ exposure of the substances List Nos. 605-717-8, 627-083-1, 627-071-6, 944-572-8 and substance X in the group.

All substances have potential endocrine disruption (ED) properties linked both to the substances themselves but also to specific constituents or impurities that have been reported in their composition. Although none of the substances have been identified as SVHCs themselves, some of their impurities/constituents have already been identified as SVHC for ED properties for environment and/or human health and as such included in the Candidate List (4-nonylphenol, EC 284-325-5; dodecylphenol, EC 310-154-3). Due to the ED properties of the substances themselves we also see the benefit of confirming the ED hazard for human health and environment via SVHC identification for all relevant group members. Since ED and other hazard properties have been already identified in the reported (eco)tox studies, there is no need to further clarify such properties via data generation during compliance check (CCH) or SEv.

The registered substances are also correctly self-classified as Repro 1B, skin sensitiser 1, aquatic toxic chronic 1 and three of them also as STOT RE, target organ kidney. In addition, several substances have likely PBT/vPvB properties due to the presence of 4-NP as a constituent that is pending for PBT/vPvB clarification under SEv.

The first step of the regulatory risk management action proposed, is the confirmation of hazard via SVHC identification and inclusion on the Candidate List as ED.

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

Authorisation has been preferred over restriction as the most appropriate regulatory management option due to the very targeted industrial uses and no widespread uses of the substances reported in the registrations. The substances are used as chelating agent or rust inhibitor in industrial setting in open systems with likelihood of emissions via wastewater. Since the ED properties relate to both human health and environment, the authorisation will target both via minimisation of worker exposure and release to environment.

Although a conclusion on PBT/vPvB properties cannot be made until data generation has concluded, it is suspected that the proposed authorisation for ED environment properties would likely also address risks related to PBT/vPvB. However, the strategy will be updated as needed following clarification of the PBT/vPvB concern. It was considered whether harmonised classification would be needed, particularly in respect to Repro 1B. However, there was a concern that CLH would delay the authorisation process and would not be of added value for an effective risk management of the substances because: a) authorisation will anyway address the risk by worker exposure due to the confirmed ED properties for human

health and b) the correct self-classification constitutes a first safety net by triggering company-level risk management measures while waiting for the authorisation entering into force.

It is important to note that ECHA has grouped structurally related hydrocarbylphenols (i.e. phenols with any kind of saturated or unsaturated hydrocarbon substituent(s) on the phenol ring). Some hydrocarbylphenols have already been scrutinised by Member State Competent Authorities. For some others, regulatory activities are ongoing. The use of hydrocarbylphenols as such, as a constituent/impurity, in mixtures or articles with (potential) endocrine properties (ED), toxicity to reproduction and/or PBT/vPvB properties and potential exposure to human health and the environment is of concern. ECHA is currently assessing the regulatory needs of several groups of hydrocarbylphenols. ECHA already concluded that for substances containing 4-tert-butylphenol (4-TBP) restriction is the most appropriate EU-wide regulatory risk management to mitigate the risks associated with 4-TBP and stated the following: "*Restriction of 4-TBP as a substance, constituent or impurity in other substances, mixtures and articles up to a certain threshold is proposed to ensure that environmental emissions of 4-TBP are minimised".* A similar approach could be taken to address the presence of other hydrocarbylphenols such as 4-NP or dodecylphenol.

Therefore, substances in this group will most likely be impacted by potential regulatory actions for other hydrocarbylphenols. However, in the event that producers are able to remove or adequately minimise the hydrocarbylphenol minor constituents/impurities of concern (e.g. 4-nonylphenol, dodecylphenol) from the manufactured substances, there would still be a concern due to the ED properties of the hydrocarbylphenol main/major constituents present in most substances in this group. Therefore, authorisation may still be needed to address the concern related to the substances as such.

Based on currently available information, there is no need for (further) EU regulatory risk management for the substances EC 256-798-8, EC 278-736-9 and EC 433-200-5 in the group.

For the substances EC 256-798-8, EC 278-736-9 and EC 433-200-5 the ED hazard is considered unlikely due to their structures, where structural elements identified as associated with reprotoxicity and ED properties are not present and QSAR screening showed no strong evidence suggesting potential ED properties.

One substance (EC 433-200-5) screens as potential PBT/vPvB (not readily biodegradable and LogKow = 7). However, it is a non-updated NONS which is also a structural outlier and consequently, it is not possible to clarify the potential hazards of the substance. Therefore, it is proposed that there is currently no need for EU RRM action on the substances. If the registration status changes, data generation and potentially follow up actions will be re-considered when the assessment will be revisited.

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.

EC/ List number	Human Health Hazard	Environmental Hazard	Relevant use(s) & exposure potential	Last foreseen action	Action
605-717-8 **627-083-1** **substance X**	Known or potential hazard for reproductive toxicity, ED, skin sensitisation, STOT RE	Known or potential hazard for ED, PBT/vPvB	Industrial use as chelating agent in mining extraction process – potential for exposure for workers and release to the environment; 605-717-8 also used as corrosion inhibitor in metal surface treatment	**Need for EU RRM: Authorisation** <u>Justification:</u> Authorisation is preferred as the most appropriate Regulatory Management Option due to the very targeted industrial uses.	**First step:** SVHC identification **Next steps (if hazard confirmed):** Authorisation
627-071-6 **944-572-8**	Known or potential hazard for reproductive toxicity, ED, skin sensitisation	Known or potential hazard for ED	Industrial use as chelating agent in mining extraction process – potential for exposure for workers and release to the environment for 944-572-8; inactive registration for 627-071-6		

EC/ List number	Human Health Hazard	Environmental Hazard	Relevant use(s) & exposure potential	Last foreseen action	Action
EC 256-798-8 **EC 278-736-9**	No hazard or unlikely hazard	No hazard or unlikely hazard	Not registered	**Currently no need for EU RRM** <u>Justification:</u> Due to NONS/ not registered no data generation is possible to clarify the hazards currently. Actions (including data generation) will be re-considered when the assessment will be revisited if the registration status and/or uses change.	No action
EC 433-200-5		Known or potential hazard for PBT/vPvB	NONS registration		

Annex 1: Overview of classifications

Data extracted on 19 April 2021.

EC/ List No	Harmonised classification	Classification in registrations	Classification in C&L notifications (*)
256-798-8		/	*Aquatic Chronic 2 H411* *Acute Tox. 4 H302* *Eye Irrit. 2 H319* *Aquatic Chronic 1 H410* *Skin Irrit. 2 H315* *Skin Sens. 1 H317* *Repr. 2 H361, specific effect: FD* *Aquatic Acute 1 H400*
278-736-9		/	*Skin Irrit. 2 H315* *Skin Sens. 1 H317* *Eye Irrit. 2 H319* *Aquatic Chronic 1 H410* *Acute Tox. 4 H302*
433-200-5		/	*Aquatic Chronic 4 H413*
605-717-8		*Repr. 1B H360, specific effect: FD* *Skin Irrit. 2 H315* *Eye Damage 1 H318* *Skin Sens. 1 H317* *STOT Rep. Exp. 2 H373, affected organs: general toxicity, kidney* *Aquatic Chronic 1 H410, M-factor: 10*	*Acute Tox. 4 H302* *Aquatic Acute 1 H400* *Repr. 1B H360, specific effect: F* *Aquatic Chronic 1 H410* *Eye Irrit. 2 H319*
627-071-6		/	*Skin Sens. 1 H317* *Skin Irrit. 2 H315* *Eye Irrit. 2 H319* *Repr. 1B H360, specific effect: F* *Aquatic Chronic 1 H410, M-factor: 10* *Acute Tox. 4 H302*
627-083-1		*Repr. 1B H360, specific effect: FD* *Skin Irrit. 2 H315* *Eye Irrit. 2 H319* *Skin Sens. 1 H317* *STOT Rep. Exp. 2 H373, affected organs: general toxicity, kidney* *Aquatic Acute 1 H400* *Aquatic Chronic 1 H410, M-factor: 10*	*Repr. 1B H360, specific effect: F*
substance X		*Repr. 1B H360, specific effect: FD* *Skin Irrit. 2 H315* *Skin Sens. 1 H317* *STOT Rep. Exp. 2 H373, affected organs: kidney* *Aquatic Chronic 1 H410, M-factor: 10*	*n.a.*

EC/ List No	Harmonised classification	Classification in registrations	Classification in C&L notifications (*)
944-572-8		*Repr. 1B H360, specific effect: FD* *Acute Tox. 4 H302* *Skin Irrit. 2 H315* *Eye Irrit. 2 H319* *Skin Sens. 1 H317* *Aquatic Chronic 1 H410, M-factor: 10*	/
256-798-8		/	*Aquatic Chronic 2 H411* *Acute Tox. 4 H302* *Eye Irrit. 2 H319* *Aquatic Chronic 1 H410* *Skin Irrit. 2 H315* *Skin Sens. 1 H317* *Repr. 2 H361, specific effect: FD* *Aquatic Acute 1 H400*

(*) 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 19 April 2021.

Main types of applications structured by product or article types	627-083-1	substance X	605-717-8	944-572-8
Use in extraction process at mining operations (PC40)	F, I	F, I	F, I	F
Use in metal surface treatments (PC14)	-	-	I	

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

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

Data extracted on 6 May 2021.

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