Assessment of regulatory needs

Authority: European Chemicals Agency (ECHA)

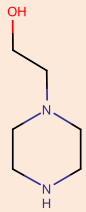
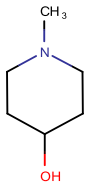
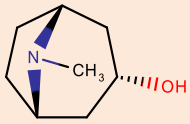
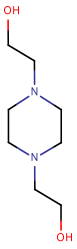
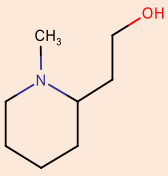
Group Name: Aliphatic hydroxy-functionalised cyclic amines

General structure:

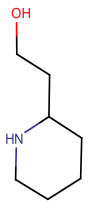
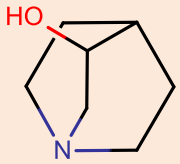
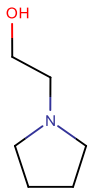
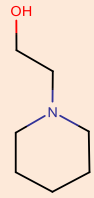
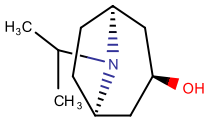
Revision history

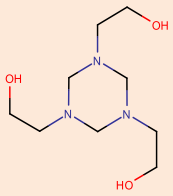
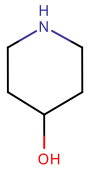
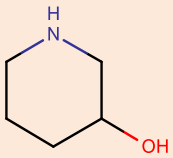
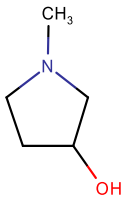
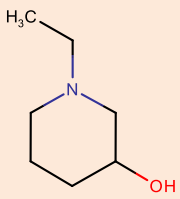
Version	*Date*	*Description*
1.0	3 May 2024	

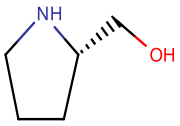
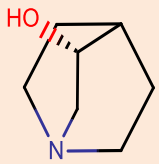
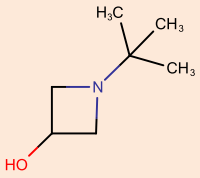
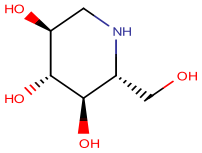
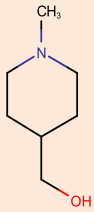
Substances within this group:

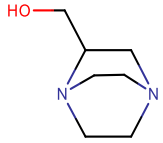
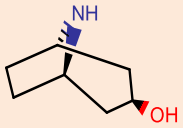
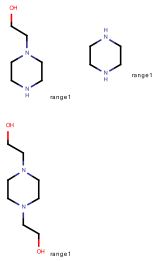
EC/List number	CAS number	Substance name	Chemical structures	Registration type (full, OSII or TII, NONS), highest tonnage band among all the registrations (t/y) [1]
203-142-3	103-76-4	2-piperazin-1-ylethanol		Full, 10-100
203-406-8	106-52-5	1-methylpiperidin-4-ol		Full, not (publicly) available
204-384-2	120-29-6	Tropine		OSII or TII
204-586-0	122-96-3	Piperazine-1,4-diethanol		Full, not (publicly) available
208-554-7	533-15-3	1-methylpiperidine-2-ethanol		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	Chemical structures	Registration type (full, OSII or TII, NONS), highest tonnage band among all the registrations (t/y) [1]
216-059-2	1484-84-0	2-piperidin-2-ylethanol		Full, not (publicly) available
216-578-4	1619-34-7	Quinuclidin-3-ol		OSII or TII
220-976-3	2955-88-6	2-pyrrolidin-1-ylethanol		OSII or TII
221-244-6	3040-44-6	2-piperidinoethanol		Full, not (publicly) available
222-314-9	3423-25-4	Endo-8-isopropyl-8-azabicyclo[3.2.1] octan-3-ol		OSII or TII

EC/List number	CAS number	Substance name	Chemical structures	Registration type (full, OSII or TII, NONS), highest tonnage band among all the registrations (t/y) [1]
225-208-0	4719-04-4	2,2',2''-(hexahydro-1,3,5-triazine-1,3,5-triyl)triethanol		Full, >1000
226-373-1	5382-16-1	Piperidin-4-ol		Full, not (publicly) available
229-957-4	6859-99-0	Piperidin-3-ol		OSII or TII
236-189-3	13220-33-2	1-methylpyrrolidin-3-ol		OSII or TII
236-584-0	13444-24-1	1-ethylpiperidin-3-ol		OSII or TII

EC/List number	CAS number	Substance name	Chemical structures	Registration type (full, OSII or TII, NONS), highest tonnage band among all the registrations (t/y) [1]
245-605-2	23356-96-9	L-(pyrrolidin-1-yl)methanol		OSII or TII
246-857-6	25333-42-0	(R)-quinuclidin-3-ol		Full, not (publicly) available
473-680-3	-	[No public or meaningful name is available]		Not registered
603-494-1	13156-04-2	3-Azetidinol, 1-(1,1-dimethylethyl)-hydrochloride		OSII or TII
606-239-2	19130-96-2	3,4,5-Piperidinetriol, 2-(hydroxymethyl) -, (2R,3R,4R,5S)-		OSII or TII
681-545-7	20691-89-8	1-Methyl-4-piperidinemethanol		OSII or TII

EC/List number	CAS number	Substance name	Chemical structures	Registration type (full, OSII or TII, NONS), highest tonnage band among all the registrations (t/y) [1]
692-731-2	76950-43-1	1,4-Diazabicyclo[2.2.2]octane-2-methanol		Full, not (publicly) available
700-286-3	538-09-0	8-Azabicyclo[3.2.1]octan-3-ol, (3-endo)-		OSII or TII
939-137-4	-	Reaction mass of 2-Piperazin-1-ylethanol and Piperazine-1,4-diethanol and Piperazine		Full, not (publicly) available

This table also contains group members that are only notified under the CLP Regulation, however, the list is not necessarily exhaustive.

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Foreword

The assessment of regulatory needs of a group of substances is an iterative, informal process to help authorities consider the most appropriate way to address an identified concern for a group of substances or a single substance and decide whether further regulatory risk management activities are necessary.

The grouping is mainly based on structural similarity and associations made by the registrants between substances through read-across and category approaches as well as category associations from external sources (e.g. OECD categories)[2]. These methods are different from grouping as defined in Section 1.5 of Annex XI to REACH because the scope and intended use of ECHA's grouping is different. Thus, in this context, grouping does not aim to validate read-across and category approaches according to the Annex XI requirements but rather to support a faster and more consistent approach for regulating chemicals and avoid regrettable substitution.

The focus of the assessment is largely based on information available in the registration dossiers and on properties requiring regulatory risk management action at EU level[3]. The information reported on uses is from the registration dossiers (IUCLID) and is used as a proxy for assessing how widespread uses are and whether potential for exposure to humans and releases to the environment can be expected. The chemical safety reports are not necessarily consulted and no quantitative exposure assessment is performed at this stage.

The outcome of these assessments are proposals for immediate (the first action) and subsequent regulatory action(s), including the foreseen ultimate regulatory action (last foreseen regulatory action) to address the identified concern(s) in case the potential hazards are confirmed. For example, further data generation through compliance check is suggested as a first action, to confirm the identified hazard.

Where hazards are confirmed, regulatory risk management actions could be considered for the whole group, for a subgroup or for individual substances within the group. The robustness of the group depends on the stage of assessment and the level of certainty this stage requires. For example, the needs for grouping under restriction may differ from the needs for grouping for the purpose of harmonised classification. Group membership is reconsidered accordingly throughout the iterative assessment of regulatory needs, for example, after further information is generated and the hazard has been clarified or when new insights on uses and risks are available.

The assessment of regulatory needs in itself does not represent a regulatory action, but rather a preparatory step to consider further possible regulatory actions at the level of individual substances or groups/subgroups of substances.

[2] Working with Groups - ECHA (europa.eu)

[3] Regarding hazard properties the focus is for instance 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 report. This does not mean that the substances do not have other known or potential hazards. In some specific cases, ECHA may consider additional hazards (e.g. neurotoxicity, STOT RE).

Publication of ARNs makes it easier for companies to follow the latest status of their substances of interest, anticipate potential regulatory actions and make strategic choices in their chemicals portfolio.

For more information on assessments of regulatory needs please consult ECHA's website[4].

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

Glossary

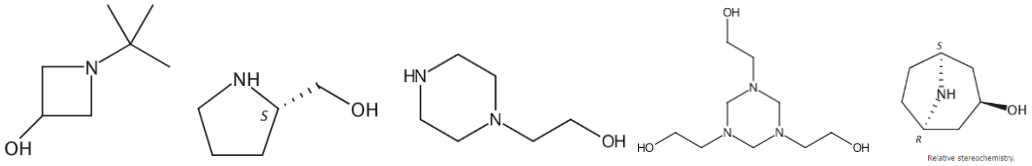
ARN	Assessment of Regulatory Needs
CCH	Compliance Check
CLH	Harmonised classification and labelling
CMR	Carcinogenic, mutagenic and/or toxic to reproduction
DEv	Dossier evaluation
ED	Endocrine disruptor
NONS	Notified new substances
OEL	Occupational exposure limit
OSII or TII	On-site isolated intermediate 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

Explanations on the scope of this assessment are available in the foreword to this document. Please read it carefully before going through the report.

ECHA has grouped together structurally similar substances based on the presence of a cyclic amine functionalized with an aliphatic hydroxy group.

Example of chemical structures of substances in the group:



(A) (B) (C) (D) (E)

The cyclic structures are of four (e.g., A), five (e.g., B), six (e.g., C, D) or seven membered rings (e.g., E). Bridge rings are also allowed (e.g., E). They can have one (e.g., A, B, E), two (e.g., C) or three amine groups (e.g., D). The aliphatic hydroxy group can be either on the amine group (examples A, C, D above - tertiary amines) and/or in the ring (examples A, B, E - secondary amines).

There are 24 substances in the group of which 11 with full registrations, and 12 are registered as intermediates only and one not registered substance.

Based on information reported in the REACH registration dossiers the registered substances of the group are mainly used as intermediates in industrial setting. Few other industrial uses (e.g., laboratory chemicals, pharmaceuticals, polymer preparation) are mentioned in the registration dossiers for a limited number of substances. Two substances report professional uses in laboratory settings, and one substance is used as lubricating agent in professional settings. Overall, the potential for exposure for this group is considered low. Potential environmental exposure is relevant for industrial uses of substance EC 225-208-0 linked to uses in water treatment, fuels and oil and gas production.

2 Conclusions and proposed actions

The conclusions and actions proposed in the table below are based mainly on the REACH and CLP information available at the time of the assessment by ECHA. The conclusions are preliminary suggestions from a screening-level assessment done by ECHA with the aim to propose the next steps for further work (e.g., strengthening of the hazard conclusions, clarification of the uses and/or potential for exposure). 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 may be updated, and conclusions and actions revisited.

Table 1: Conclusions and proposed actions

Subgroup name, EC/List no, substance name	Human Health Hazard	Environmental Hazard	Relevant use(s) & exposure potential	Suggested regulatory actions
225-208-0	Known or potential hazard for reproductive toxicity, STOT RE 1 (resp. system), skin sensitisation (CLH)	No or unlikely hazard for PMT/vPvM and PBT/vPvB	Used in industrial settings in oil, gas, fuel production, water treatment, as pH regulator. Professional uses in laboratory settings with low exposure potential.	**First step:** CCH **Potential next steps (if hazard confirmed after data generation):** CLH Justification: CLH will require company level risk management measures (RMM) under the OSH legislation for workers, to be in place. The harmonised classification as Repr. 1B will require company level risk management measures (RMM) for workers to be in place. Harmonised classification as CMR cat. 1 would render the substances unacceptable co-formulants in biocidal products if present above the concentration limit leading to classification of the mixture as CMR cat 1 according to the Biocidal product regulation

Subgroup name, EC/List no, substance name	Human Health Hazard	Environmental Hazard	Relevant use(s) & exposure potential	Suggested regulatory actions
				(EU) 528/2012. CLH will also trigger regulatory action under the biocidal product regulation.
203-142-2 204-586-0 939-137-4	Known or potential hazard for reproductive toxicity Known or potential hazard for skin sensitisation for List 939-137-4 Inconclusive hazard for skin sensitisation for EC 203-142-2 and 204-586-0 Inconclusive hazard for repeated dose toxicity	Known or potential hazard for PMT/vPvM	Used in industrial settings as intermediates, laboratory chemicals and as extraction agent with low potential for exposure.	**First step:** CCH **Potential next steps (if hazard confirmed after data generation):** No action **Currently no need for EU RRM** Justification: According to the reported uses, low potential for exposure to both human health and environment is expected. Actions may be reconsidered if there is a change in the registration status and/or reported uses, or when the assessment will be revisited. Self-classification (will) require company level risk management measures (RMM) for workers to be in place.
203-406-8 **204-384-2** **208-554-7** 216-059-2 **216-578-4** **220-976-3** **221-244-6**	Inconclusive hazard for skin sensitisation except for EC/List 692-731-2 and 221-244-6 which are sensitisers	Known or potential hazard -for aquatic toxicity for substances EC/List 221-244-6 and 220-976-3	Substances used as intermediate in industrial settings.	**First step:** CCH for EC/List 208-554-7, 216-059-2 and 692-731-2 **Next steps (if hazard confirmed):** No action

Subgroup name, EC/List no, substance name	Human Health Hazard	Environmental Hazard	Relevant use(s) & exposure potential	Suggested regulatory actions
222-314-9 226-373-1 **229-957-4** **236-189-3** **236-584-0** **245-605-2** 246-857-6 **473-680-3** **603-494-1** **606-239-2** **681-545-7** **700-286-3** **692-731-2**	Inconclusive hazard for repeated dose toxicity except for EC/List 692-731-2 and 221-244-6 which are unlikely Inconclusive hazard for reproductive toxicity except for List 692-731-2 which is unlikely	Inconclusive hazard -for PMT/vPvM for substances EC/List 208-554-7, 222-314-9, 246-857-6 and 692-731-2		**Potential next steps (if hazard confirmed after data generation):** No action Justification: According to the reported uses, low potential for exposure to both human health and environment is expected. Actions may be reconsidered if there is a change in the registration status and/or reported uses, or when the assessment will be revisited. Self-classification requires company level risk management measures (RMM) for workers to be in place.

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

Harmonised classification for EC 225-208-0 if reproductive toxicity and STOT RE hazards are confirmed. Based on ECHA's assessment of currently available hazard information it is considered that this substance has (potentially) the following human health hazards: reproductive toxicity, STOT RE 1 (resp. system) and skin sensitisation.

The reproductive toxicity is identified based on the presence of malformations in an OECD 414 study in rabbits, in the absence of an excessive maternal toxicity. The STOT RE effects (histopathology findings in larynx, trachea, and lung) were observed in an OECD 412 study at all doses even ≤ 3mg/m³/6h/day, and a self-classification was applied by the registrant. In addition, the substance has harmonised classification for known skin sensitisation properties. Due to the chemical structural differences to the other substances in the group, it is not possible to extrapolate these effects to the other substances.

From the data available the hazard for ED effects is inconclusive. Based on negative data available, this substance is unlikely mutagenic and unlikely carcinogenic (based on unlikely mutagenicity). It has a harmonized classification as Skin Sens. 1 (H 317) and Acute Tox. 4 (H302).

Based on incomplete data on fast hydrolysis and degradability, the substance is unlikely (with medium uncertainty) to have PBT and PMT properties. Because of its expected fast degradation, bioaccumulation is also considered unlikely. This is also affecting ecotoxicity. As non-persistent substance, the substance is not classified as aquatic toxic while the data available show it has acute aquatic toxicity but not sufficient to classify as Acute 1 and has chronic toxicity for algae only.

The substance is used mainly in industrial settings for fuel and oil production. There is a potential for the release to the environment, however, the degradation of the substance is expected to be fast. Therefore, exposure of workers or humans via the environment is considered likely not significant. Professional use is reported only for use in laboratory settings where relatively high levels of operational controls and risk management measures are expected to be in place. The professional uses in this case are not expected to be widespread (at many sites and by many users).

This substance is currently subject to an evaluation by a competent authority in order to be approved as an active biocidal substance for four product types. In addition, the substance was identified as formaldehyde releaser in the Annex XV restriction report (entry 77). However, no free formaldehyde is being formed during the application of the substance (formulation for use in oilfield and treatment of hydro-carbons, scavenger for sulphide in refinery and/or oilfield application). Additionally, as stated in the restriction, exposure of industrial and professional workers to formaldehyde is already regulated by Council Directive 98/24/EC (9), and Directive 2004/37/EC of the European Parliament and of the Council (10). Therefore, articles exclusively for industrial or professional use are exempted from this restriction unless formaldehyde released from them leads to exposure of the general public under foreseeable conditions of use. Additionally, the formaldehyde and formaldehyde releasers used as a biocide are intended to be exempted from the restriction.

The regulatory risk management action proposed for substance EC 225-208-0 is to confirm the hazard via harmonised classification (CLH) as Repr. 1B and STOT RE

1. CLH will require company level risk management measures (RMM) under the OSH legislation for workers, to be in place. CLH will also support regulatory action under other regulations. For instance, in this specific case, harmonised classification as CMR cat. 1 will trigger regulatory action under the biocidal product regulation (EU) 528/2012, which does not allow the use by the general public of a product containing substances above the concentration limit leading to classification of the mixture as CMR cat. 1.

For industrial and professional uses, harmonised classification for skin sensitisation properties should require adequate risk management measures to be in place according to workplace legislation.

Currently no need to suggest (further) regulatory risk management actions for EC/List 203-142-3, 204-586-0 and 939-137-4 as a result of their limited use and exposure. Potential hazards as CMR cat.2, skin sens. (List 939-137-4), and PMT/vPvM have been identified for substances in this group.

Substance List 939-137-4 contains up to 20 % of piperazine-dihydrochloride (EC 205-551-2). The substance EC 205-551-2 is self-classified as Repr. 2, which triggers concern for reproductive toxicity also for substance List 939-137-4. Furthermore, EC 203-142-3 and 204-586-0 are also part of List 939-137-4 and both substances may potentially hydrolyse in the stomach to give piperazine. Therefore, the potential concern for reproductive toxicity was extrapolated with high confidence also to EC 203-142-3 and 204-586-0. CCHs for all three substances are proposed to clarify the concern for a potential reproductive toxicity hazard for these substances.

Based on the available data there is no indication for an ED effect.

No data are available for repeated dose toxicity for EC 203-142-3 and 204-586-0. For List 939-137-4 the dossier contains a reference to an FDA report on piperazine dihydrochloride where a NOAEL of 627 mg/kg bw/day is reported suggesting no concern for this endpoint. However, as there are no data on the actual substances in the group no conclusion can be made for this endpoint.

For EC 203-142-3 negative results are available for skin sensitisation hazard. However, in the dossier of List 939-137-4, a positive OECD 406 with EC 203-142-3 is also available. On this basis, List 939-137-4 was self-classified as Skin Sens 1B. The conflicting hazard results for these substances should also be clarified during the CCH. No data are available for EC 204-586-0 but for this substance the data are appropriately waived based on corrosion.

Based on negative data available for EC 203-142-3 and 204-586-0, unlikely mutagenicity was extrapolated also to List 939-137-4. Based on unlikely mutagenicity all the substances are considered unlikely carcinogenic by extrapolation with low confidence due to the scarcity of data.

All three substances in this group are potentially persistent, mobile and toxic (PMT). The following substances are potentially P, as they are not readily biodegradable (i.e., <60/70% degradation in OECD 301/302 or 306) and no simulation test is available to allow a conclusion on this property. They are also expected to be mobile in the environment despite the fact that they are ionised at environmental pHs, they are anionic substances which show less adsorption potential to soil. This is also confirmed where available by the Log Koc data showing very low values for EC/List 203-142-2, 204-586-0, 939-137-4. There is potential toxicity stemming from human health but based on the low data density it is not established.

For their bioaccumulation potential, although ionised substances cannot be considered as screening non bioaccumulative based on their Kow (Kow not valid for substances under ionised stage), they are present under anionic phase which is showing less binding behaviour for cells and membranes. Therefore, they are considered as unlikely PBT/vPvB with medium uncertainty.

Finally, none of the substances of this group show classifiable aquatic toxicity based on the available data. Nevertheless, this conclusion is made with medium uncertainty accounting for the data quality and type of testing performed.

The uses of these substances are limited to industrial settings where controlled conditions and appropriate RMM are expected to be in place. Substances EC/List 203-142-3 and 939-137-4 are used as intermediates under strictly controlled conditions and laboratory chemicals and substance EC 204-586-0 is used as an extraction agent to remove SO_2 from gas. Reported uses do not indicate incorporation of the substances into/onto articles. In addition, limited uses (EC/List 203-142-3 and 939-137-4) are low tonnage (EC 204-586-0) indicate limited potential for exposure to workers and the environment. Therefore, no EU regulatory risk management action is currently proposed for any of the aforementioned substances due to low exposure potential. Furthermore, for industrial and professional uses, it is expected that following data generation registrants would adequately self-classify the substances. The self-classification will require company level risk management (RMM) to be in place. In addition, a harmonised classification as CMR cat.2 and skin sens. (List 939-137-4) would not impact any known legislations based on the uses of the substances. Therefore, it is proposed that there is currently no need for EU-wide regulatory risk management. 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.

Since the information on hazard is not sufficient to conclude on reproductive toxicity, repeated dose toxicity, skin sensitisation (only for List 939-137-4), PMT, and aquatic toxicity hazards, compliance check is proposed for all three substances.

Currently no need to suggest (further) regulatory risk management actions for all remaining substances from the group where hazard was not confirmed as a result of their registration status (i.e. TII/OSII or not registered), low tonnage band (Annex VII) and/or limited exposure.

EC/List 221-244-6 and 692-731-2 are self-classified as Skin Sens 1B based on positive data available. For these substances, no further RRM is proposed as sufficient and consistent self-classification by registrants should require adequate risk management measures according to workplace legislation. EC 203-406-8 and TII/OSII substances EC/List 245-605-2, 606-239-2 and 700-286-3 have negative data available for sensitisation. Due to both positive and negative results within this group of substances no extrapolation can be made and for the rest of substances the hazard for sensitisation remains inconclusive.

All the substances in this group are considered unlikely mutagenic on the basis of a constant pattern of negative results for several substances in the group and extrapolated with medium confidence. Based on unlikely mutagenicity all the substances are considered unlikely carcinogenic by extrapolation with low confidence.

No data are available for reproductive toxicity and repeated dose toxicity for any of the TII/OSII or not registered and for the low tonnage band substances. Only

for EC 221-244-6 an OECD 422 was available. The NOAEL was the highest dose of 250 mg/kg bw/d for male and the mid-dose of 75 mg/kg bw/d for female based on a reduction in water and food consumption and a decrease in body weight change at 250 mg. For List 692-731-2 (high tonnage band but limited exposure) an OECD 422 showed no reproductive toxicity effects up to 1000 mg/kg bw/d and an OECD 408 showed no repeated dose toxicity up to 1000 mg/kg bw/d. The available data gave no indication for an ED effect. Due to the very limited data available, at the moment, these hazards for all the other substances with this status remain inconclusive.

EC/List 222-314-9, 246-857 and 692-731-62 are potentially P, as they are not readily biodegradable (i.e., <60/70% degradation in OECD 301 B/C/F) and no simulation test is available to allow a conclusion on this property. They are also expected to be mobile (M) in the environment although ionised at environmental pHs, all of them are under anionic forms, which are not adsorptive to soil, in addition where available they have a very low logKoc. However due to the low tonnage band and in absence of reliable data for human health it is not possible to establish any concern for toxicity at this stage. Hence, all the substances of this group are considered as inconclusive for PMT/vPvM.

For their bioaccumulation potential, although ionised substances cannot be considered as screening non bioaccumulative based on their Kow (Kow not valid for substances under ionised stage), they are present under anionic phase which is showing less binding behaviour for cells and membranes. Therefore, they are considered as unlikely PBT/vPvB with medium uncertainty.

The other substances in this group for which there are ready biodegradation data available EC/List 216-059-2, 221-244-6, 606-239-2 and 220-976-3 are unlikely to fulfil the PMT/vPvM or PBT/vPvB screening criteria, because they are very likely readily biodegradable for most of them or by extrapolation between structures (above 60/70% degradation in OECD 301 B/C and QSAR estimation) hence even if potentially mobile (M) they would not meet the P criterion. They also have a low potential for bioaccumulation and are unlikely to fulfil the T criterion. However, these conclusions are based on ready biodegradability test results, low logKow, using the few experimental data present in the dossiers.

Only two substances would show some aquatic toxicity hazard, with high uncertainty due to the low data density available. As such only EC 221-244-6 and 220-976-3 could be considered as Aquatic chronic 2. For all the other substances it is either unlikely or inconclusive in absence of reliable data for aquatic toxicity.

Majority of the substances in this subgroup are only used as intermediates in industrial settings under strictly controlled conditions. 12 substances from this group are registered as TII/OSII, 1 substance is not registered, 5 substances are registered at low tonnage band (Annex VII) and only 2 substances are registered at higher tonnage. Additionally, substances EC 208-554-7, 226-373-1 and 246-857-6 are also used as intermediates in pharmaceuticals and substances EC/List 216-059-2 and 692-731-2 are used in polymer preparation as a catalyst and monomer. Professional uses are reported only for one substance in this subgroup, EC 221-244-6. This substance is used as lubricating agent in lubricants and hydraulic fluids with potential for exposure to workers, and as intermediate and in laboratory chemicals. Substances EC/List 221-244-6 and 692-731-2 are both self-classified as skin sens. 1B, therefore no further RRM is proposed.

CCH is proposed for substances EC/List 208-554-7, 216-059-2 and 692-731-2 to clarify human health, PMT, and aquatic toxicity hazard properties.

Annex 1: Overview of classifications

Data extracted on 28/03/23

EC/ List No	CAS No	Substance name	Harmonised classification	Classification in registrations
203-406-8	106-52-5	1-methylpiperidin-4-ol	-	Eye Irrit. 2 H319 Skin Irrit. 2 H315 [intermediate (active)] STOT Single Exp. 3 H335, affected organs: Respiratory tracts [intermediate (active)]
208-554-7	533-15-3	1-methylpiperidine-2-ethanol	-	Acute Tox. 4 H302 Skin Corr. 1 H314 Eye Damage 1 H318 Aquatic Chronic 3 H412
216-059-2	1484-84-0	2-piperidin-2-ylethanol	-	Acute Tox. 4 H302 Skin Corr. 1B H314
226-373-1	5382-16-1	piperidin-4-ol	-	Skin Irrit. 2 H315 Eye Damage 1 H318
229-957-4	6859-99-0	piperidin-3-ol	-	Eye Irrit. 2 H319 [intermediate (active)] STOT Single Exp. 3 H335, affected organs: Respiratory tracts [intermediate (active)] Skin Irrit. 2 H315 [intermediate (active)]

EC/ List No	CAS No	Substance name	Harmonised classification	Classification in registrations
236-189-3	13220-33-2	1-methylpyrrolidin-3-ol	-	Skin Irrit. 2 H315 [intermediate (active)] Eye Irrit. 2 H319 [intermediate (active)] STOT Single Exp. 3 H335, affected organs: lungs [intermediate (active)] Acute Tox. 4 H302 [intermediate (active)]
236-584-0	13444-24-1	1-ethylpiperidin-3-ol	-	Eye Irrit. 2 H319 [intermediate (active)] Flam. Liquid 3 H226 [intermediate (active)] Skin Irrit. 2 H315 [intermediate (active)]
245-605-2	23356-96-9	L-(pyrrolidin-1-yl)methanol	-	Eye Damage 1 H318 [intermediate (active)] Acute Tox. 4 H302 [intermediate (active)] STOT Single Exp. 3 H335, affected organs: lungs [intermediate (active)]
603-494-1	13156-04-2	603-494-1	-	-
606-239-2	19130-96-2	606-239-2	-	-
204-384-2	120-29-6	tropine	-	Acute Tox. 4 H302 [intermediate (active)]
216-578-4	1619-34-7	quinuclidin-3-ol	-	STOT Single Exp. 3 H335, affected organs: Respiratory tracts [intermediate (active)] Eye Irrit. 2 H319 [intermediate (active)] Skin Irrit. 2 H315 [intermediate (active)]
222-314-9	3423-25-4	endo-8-isopropyl-8-azabicyclo[3.2.1]octan-3-ol	-	Acute Tox. 4 H302 [intermediate (active)]
246-857-6	25333-42-0	(R)-quinuclidin-3-ol	-	Skin Corr. 1B H314 [intermediate (active)] Flam. Solid 1 H228 Acute Tox. 4 H302 Skin Corr. 1 H314 Eye Damage 1 H318

EC/ List No	CAS No	Substance name	Harmonised classification	Classification in registrations
700-286-3	538-09-0	8-azabicyclo[3.2.1]octan-3-ol	-	Acute Tox. 4 H302 [intermediate (active)] Acute Tox. 5 H303 [intermediate (active)]
203-142-3	103-76-4	2-piperazin-1-ylethanol	-	Skin Irrit. 2 H315 Eye Damage 1 H318
204-586-0	122-96-3	piperazine-1,4-diethanol	-	Eye Damage 1 H318
221-244-6	3040-44-6	2-piperidinoethanol	-	Acute Tox. 4 H302 Acute Tox. 4 H312 Skin Corr. 1B H314 Eye Damage 1 H318 Skin Sens. 1B H317 Aquatic Chronic 3 H412
225-208-0	4719-04-4	2,2',2''-(hexahydro-1,3,5-triazine-1,3,5-triyl)triethanol	Category: Skin Sens. 1 Class: Skin sensitizers Statement: H317: C>=0.1% Index number: 613-114-00-6 Acute Tox. 4 Hazard Statement: H302 (Minimum classification) Skin Sens. 1 Statement: H317	Acute Tox. 4 H302 Acute Tox. 2 H330 Skin Corr. 1 H314 Eye Irrit. 2 H319 Skin Sens. 1 H317, specific concentration: >=.1 Skin Sens. 1 H317 STOT Rep. Exp. 1 H372, affected organs: respiratory system STOT Rep. Exp. 1 H372, affected organs: Respiratory tract STOT Single Exp. 3 H335, affected organs: Respiratory tract

EC/ List No	CAS No	Substance name	Harmonised classification	Classification in registrations
692-731-2	76950-43-1	1,4-diazabicyclo[2.2.2]oct-2-ylmethanol	-	Flam. Solid 1 H228 Skin Sens. 1B H317
939-137-4	-	Reaction mass of 2-piperazin-1-ylethanol and piperazine and piperazine-1,4-diethanol	-	Repr. 2 H361 Skin Corr. 1B H314 Eye Damage 1 H318 Resp. Sens. 1 H334 Skin Sens. 1 H317
220-976-3	2955-88-6	2-pyrrolidin-1-ylethanol	-	Flam. Liquid 3 H226 [intermediate (active)] Acute Tox. 4 H302 [intermediate (active)]
681-545-7	20691-89-8	(1-methylpiperidin-4-yl)methanol	-	-

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

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

Data extracted on 28/03/2023

Main types of applications structured by product or article types	PC 20: Products such as ph-regulators, flocculants, precipitants, neutralisation agents	PC 37: Water treatment chemicals	PC 29: Pharmaceuticals	PC 24: Lubricants, greases, release products	PC 17: Hydraulic fluids	PC 13: Fuels	PC 32: Polymer preparations and compounds	PC 21: Laboratory chemicals	PC 19: Intermediate	PC 40: Extraction agents	PC41: Oil and gas exploration or production products
203-142-3								I	I		
203-406-8									I		
204-384-2									I		
204-586-0										I	
208-554-7			I						I		
216-059-2							I		I		
216-578-4									I		

221-244-6				I, **P**	**P**			I, **P**	I		
225-208-0	F, I	I				I		**P**			I
226-373-1								I	I		
236-189-3									I		
236-584-0									I		
246-857-6			I						I		
603-494-1									I		
606-239-2									I		
681-545-7									I		
692-731-2							I				
700-286-3									I		
939-137-4								I	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 12/04/2023

EC/List number	RMOA	Authorisation		Restriction*	CLH	Actions not under REACH/ CLP
		Candidate list	Annex XIV	Annex XVII	Annex VI (CLP)	
225-208-0				YES	YES	BPR, PPP

*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.