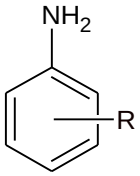
Assessment of regulatory needs

Authority: European Chemicals Agency (ECHA)

Group Name: Aromatic Primary Monoamines

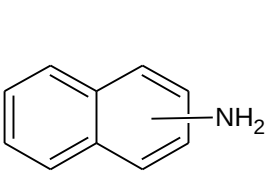
General structures:

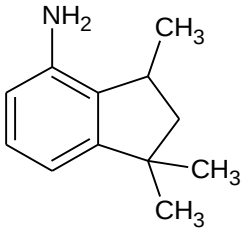


R=H, Me, Et, t-Bu, i-propyl, sec-butyl, 4-methylpentan-2-yl, Ph, C10-13-(branched), C12H25

R=1, 2, 3 substituents

And salts



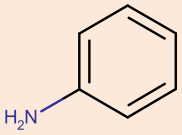
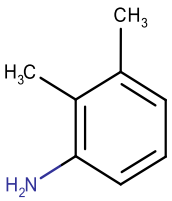
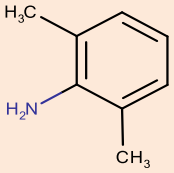
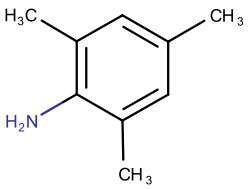
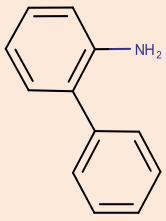


And salts

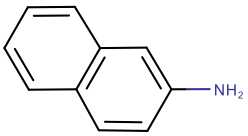
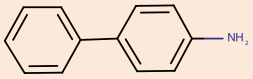
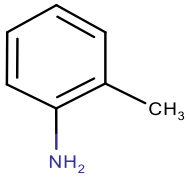
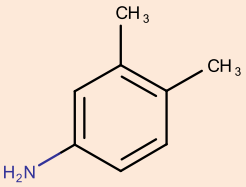
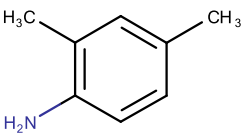
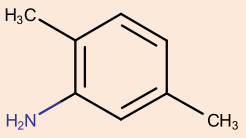
Revision history

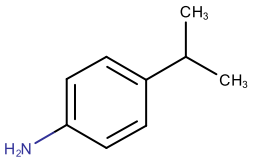
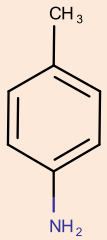
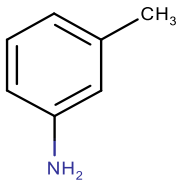
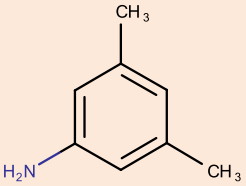
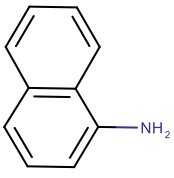
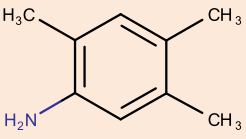
Version	*Date*	*Description*
1.0	16 August 2023	

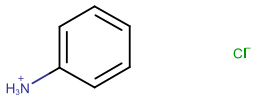
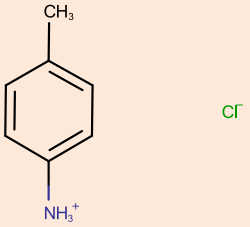
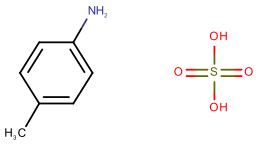
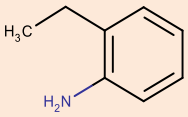
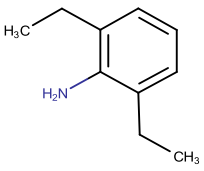
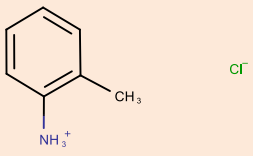
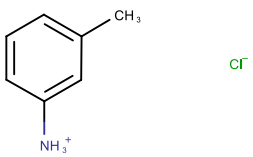
Substances within this group:

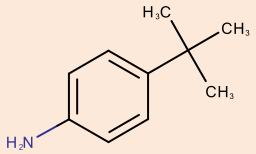
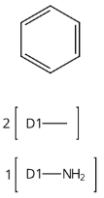
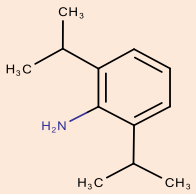
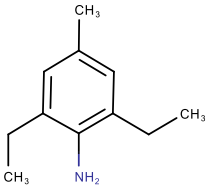
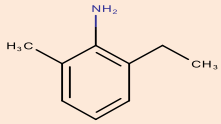
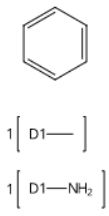
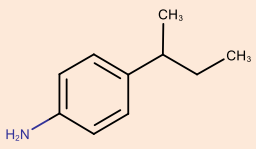
EC/List number	CAS number	Substance name [and/ or Substance name acronyms]	Chemical structures	Registration type (full, OSII or TII, NONS), highest tonnage band among all the registrations (t/y) [1]
200-539-3	62-53-3	aniline		Full, >1000
201-755-0	87-59-2	2,3-xylidine		OSII or TII
201-758-7	87-62-7	2,6-xylidine		Full, not (publicly) available
201-794-3	88-05-1	2,4,6-trimethylaniline		OSII or TII
201-990-9	90-41-5	biphenyl-2-ylamine		Full, not (publicly) available

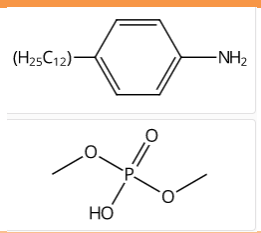
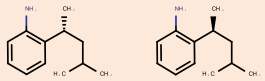
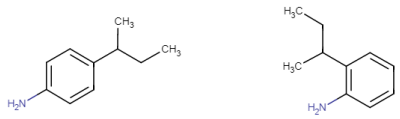
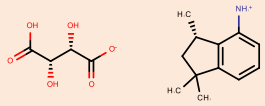
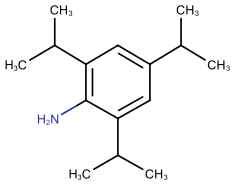
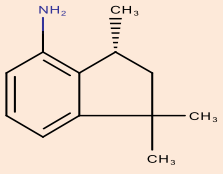
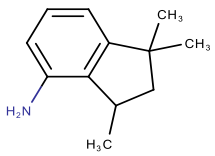
[1] Note that the total aggregated tonnage band may be available on ECHA's webpage at https://echa.europa.eu/information-on-chemicals/registered-substances

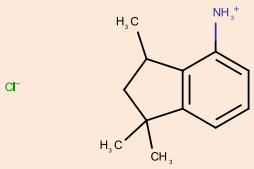
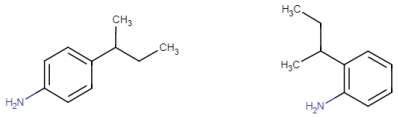
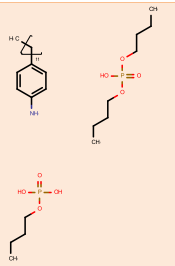
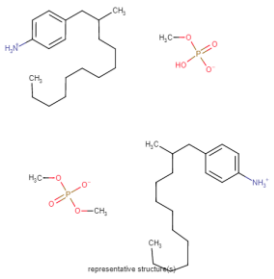
EC/List number	CAS number	Substance name [and/ or Substance name acronyms]	Chemical structures	Registration type (full, OSII or TII, NONS), highest tonnage band among all the registrations (t/y) [1]
202-080-4	91-59-8	2-naphthylamine		C&L notification
202-177-1	92-67-1	biphenyl-4-ylamine		C&L notification
202-429-0	95-53-4	o-toluidine		Full, not (publicly) available
202-437-4	95-64-7	3,4-xylidine		Cease manufacture
202-440-0	95-68-1	2,4-xylidine		OSII or TII
202-451-0	95-78-3	2,5-xylidine		Full, not (publicly) available

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]
202-797-2	99-88-7	4-isopropylaniline		OSII or TII
203-403-1	106-49-0	p-toluidine		Full, not (publicly) available
203-583-1	108-44-1	m-toluidine		Full, not (publicly) available
203-607-0	108-69-0	3,5-xylidine		OSII or TII
205-138-7	134-32-7	1-naphthylamine		OSII or TII
205-282-0	137-17-7	2,4,5-trimethylaniline		C&L notification

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]
205-519-8	142-04-1	anilinium chloride		C&L notification
208-740-8	540-23-8	p-toluidinium chloride		C&L notification
208-741-3	540-25-0	p-toluidine sulphate (1:1)		Not registered
209-424-2	578-54-1	2-ethylaniline		OSII or TII
209-445-7	579-66-8	2,6-diethylaniline		C&L notification
211-252-8	636-21-5	o-toluidinium chloride		C&L notification
211-314-4	638-03-9	m-toluidinium chloride		OSII or TII

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]
212-215-9	769-92-6	p-tert-butylaniline		OSII or TII
215-091-4	1300-73-8	xylidine		OSII or TII
246-305-4	24544-04-5	2,6-diisopropylaniline		OSII or TII
246-307-5	24544-08-9	2,6-diethyl-p-toluidine		OSII or TII
246-309-6	24549-06-2	6-ethyl-2-toluidine		OSII or TII
248-105-2	26915-12-8	toluidine		C&L notification
250-108-9	30273-11-1	4-sec-butylaniline		C&L notification

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]
269-016-5	68170-22-9	dimethyl hydrogen phosphorate, compound with 4-tetrapropyleneaniline		C&L notification
700-095-5	203448-76-4	2-(4-methylpentan-2-yl)aniline		OSII or TII
700-229-2*		Reaction mass of 4-sec-butylaniline and 2-sec-butylaniline		OSII or TII
701-382-8		(3R)-1,1,3-trimethylindan-4-aminium (2S,3S)-3-carboxy-2,3-dihydroxypropanoate		OSII or TII
800-008-1	21524-36-7	2,4,6-triisopropylaniline		OSII or TII
836-285-0	125349-37-3	(3R)-1,1,3-trimethylindan-4-amine		OSII or TII
838-724-1	94568-76-0	1,1,3-trimethylindan-4-amine		OSII or TII

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]
863-466-1	1616291-21-4	1,1,3-trimethylindan-4-aminium chloride		OSII or TII
946-786-7*		Reaction mass of 4-sec-butylaniline and 2-sec-butylaniline		OSII or TII
948-072-0		Phosphoric acid, mono- and dibutyl esters, compds. with C10-13-(branched)-alkylaniline		Full, not (publicly) available
948-073-6		Phosphoric acid, mono- and dimethyl esters, compds. with C10-13-(branched)-alkylaniline		Full, not (publicly) available

*) These two substances are the same

This table contains also 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

Foreword 11

Glossary 12

1 Overview of the group 13

2 Justification for the no need for regulatory risk management action at EU level 14

3 Conclusions and actions 19

Annex 1: Overview of classifications 22

Annex 2: Overview of uses based on information available in registration dossiers 27

Annex 3: Overview of completed or ongoing regulatory risk management activities 28

DISCLAIMER

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

Foreword

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

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

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

The assessment of regulatory needs can be applied to any group of substances or single substance, i.e., any type of hazards or uses and regardless of the previous regulatory history or lack of such. It can be done based on 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

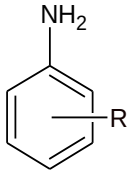
Glossary

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
OEL	Occupational exposure limit
OSII or TII	On-site isolated intermediate or transported isolated intermediate
PBT/vPvB	Persistent, bioaccumulative and toxic/very persistent and very bioaccumulative
RMOA	Regulatory management options analysis
RRM	Regulatory risk management
SEv	Substance evaluation
STOT RE	Specific target organ toxicity, repeated exposure
SVHC	Substance of very high concern

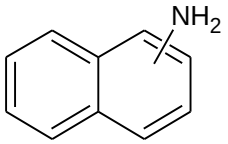
1 Overview of the group

ECHA has grouped together 42 structurally similar substances based on the presence of an aromatic primary mono-amine. Three different core structures were included in this group:

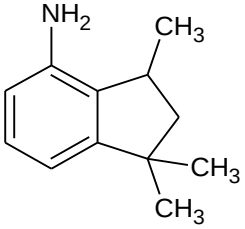
1) Aniline and its mono-, di-, or trisubstituted alkyl derivatives, where alkyl group is: Me, Et, t-Bu, iso-propyl, sec-butyl, 4-methylpentan-2-yl, Ph, C10-13-(branched), $C_{12}H_{25}$. This subgroup includes also some salts.



2) Naphthylamines



3) 1,1,3-trimethylindan-4-amines and their salts



The status of the 42 substances is as such:

- **10** substances with full registrations
- **21** substances with intermediate registrations
- **11** not registered substances

To be noted that the substances identified with List no 700-229-2 and 946-786-7 correspond to the same substance.

An EU Risk Assessment Report is available for the substance EC 200-539-3. Many substances in the group are already subject to regulatory risk management actions. Fifteen of the substances are already in Table 3 of Annex VI to the CLP Regulation. For nearly half the substances in the group (22 of them) their use in cosmetic products is prohibited, and many of these substances are also subject to restriction entry 75 (on tattoo inks). Lastly EU-wide OELS have been established for three of the substances (EC 200-539-3, 202-429-0 and 203-403-1), while a small number of other substances have OELs in some Member States.

Based on information reported in the REACH registration dossiers, the majority of the substances in the group are used only as intermediates, and half (21 out of 42 substances) only have intermediate registrations as OSII/TII, indicating these are used only under strictly controlled conditions. 10 out of 42 substances in the group have an Article 10 (full) registration (although one of these is now inactive). The main use reported for these substances is also as intermediate, although some of the substances indicate further industrial uses from which exposure cannot be excluded. For EC 201-990-9 the only registrant has reported use as dye and optical brightener, while the substance is colourless and is used to manufacture dyes. Potential over-reporting is observed in this case. Similarly, uncertainty on the uses reported for List no 700-095-5 is observed, as one of the two intermediate registrations indicates "plant protection active substance" for which further information cannot be found. The same registration also indicates intermediate use at industrial sites, so it is believed that the substance is used to manufacture a plant protection active substance. Lastly two of the substances (List no 948-072-0 and 948-073-6) have different structures from the rest of the group. As UVCBs with a long branched carbon chain, they exhibit different technical functions, and are used in lubricants and metal working fluids, in industrial, professional and consumer uses (i.e. "widespread" uses where the potential for release/exposure is high).

Note on the scope of ECHA's assessment of regulatory needs

Regarding hazards, the focus of ECHA's assessment is on CMR (carcinogenic, mutagenic and/or toxic to reproduction), sensitiser, ED (endocrine disruptor), PBT/vPvB or equivalent (e.g. substances being persistent, mobile and toxic), aquatic toxicity hazard endpoints and therefore only those are reflected in the table in section 3. This does not mean that the substances do not have other known or potential hazards. In some specific cases, where ECHA identifies a need for regulatory risk management action at EU level for other hazards (e.g. neurotoxicity, STOT RE), such additional hazards may be addressed in the assessment. An overview of classification is presented in Annex 1.

On the exposure side, ECHA is mainly using the information on uses reported in the registration dossiers (IUCLID) as a proxy for assessing the potential for exposure to humans and releases to the environment. The potential for release / exposure is generally considered high for "widespread" uses, i.e. professional and consumer uses and uses in articles. For these uses, normally happening at many places, the expected level of control is *à priori* considered limited. The chemical safety reports are not necessarily consulted and no quantitative exposure assessment is performed at this stage.

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

Based on currently available information, there is no need for (further) EU regulatory risk management for genotoxicity, carcinogenicity, STOT RE and environmental toxicity hazards of the all substances in the group except EC/List no 246-305-4, 246-309-6, 948-072-0 and 948-073-6.

This screening has primarily relied on the information reported in the registration dossiers and on the conclusions of EU RAR for EC 200-539-3[3] and the general IARC monograph discussing common mechanisms of action for aromatic amines[4].

Further analysis of the impact of the type, number and position of the alkyl substituents on the aromatic ring is needed to refine the conclusions of this screening, in particular with regard to carcinogenicity. In this perspective, the QSAR models linking the carcinogenic potency of non-heterocyclic carcinogenic aromatic amines to a series of molecular determinants described by Benigni *et al.* may prove useful[5].

The toxicity of aromatic amines to humans has been largely investigated and is understood to follow a two-step metabolic activation pathway.
The aromatic amine first undergoes cytochrome P450-catalysed N-oxidation to form an arylhydroxylamine. Subsequent O-conjugation by N-acetyltransferases (NATs) leads to the formation of highly unstable acetoxy esters. These esters can decompose into nitrenium intermediate ions that react with and form adducts on cellular macromolecules including DNA. N-acetylation by NATs competes in the liver with the N-oxidation, a step that converts aromatic amines into N-acetate metabolites which are less active than the N-hydroxylated metabolites. The balance of these pathways and their cell-specific expression profiles may contribute to the toxic endpoint in a particular tissue upon aromatic amine exposure.

Structural alterations of aromatic amines which disrupt geometric compatibility with the cytochrome P450, hinder proton abstraction, or strongly destabilize the nitrenium ion, are reported to prevent genotoxicity[6].

Known or potential hazard for genotoxicity, carcinogenicity and STOT RE identified for all substances in the group except EC/ List no 246-305-4, 246-309-6, 948-072-0, and 948-073-6

Based on ECHA's assessment of hazard information currently available in the registration dossiers registration hazard information and considerations of structural similarity and presence of common functional moiety all the substances in the group except EC/ List no 246-305-4, 246-309-6, 948-072-0, and 948-073-6 have (potentially) the following human health/environmental hazards: genotoxicity, carcinogenicity and STOT RE.

Two substances in this group as Carc 1A, 2 substances are classified as Carc 1B, 6 substances as Carc 2 and 3 as Muta 2. The details of the current classification (harmonised or self classification) of the group members for mutagenicity and carcinogenicity is presented in the table in Annex 1.

The group-level conclusion is based on the observation of positive results *in vitro* for either gene mutation or clastogenicity for 12 out of 17 substances for which data are available. Positive results in genotoxicity, in particular in presence of

[3] link to EU RAR for EC 200-539-3.

[4] IARC general discussion of common mechanisms for aromatic amines

[5] Prediction of rodent carcinogenicity of aromatic amines: a quantitative structure–activity relationships model | Carcinogenesis | Oxford Academic (oup.com)

[6] J. Am. Chem. Soc. 2011, 133, 40, 16168–16185:
https://pubs.acs.org/doi/full/10.1021/ja206427u

metabolic activation, is considered as an indication of the potential of the substance undergo the first step in the development of systemic toxicity/carcinogenicity for aromatic amines. This is supported by the observation that all the substances returning positive results in genotoxicity studies also displayed target organ toxicity and/or carcinogenicity consistent with the generic toxicity profile of aromatic amines, where data on target organ toxicity and/or carcinogenicity is available. Therefore the observation of positive results in genotoxicity studies is considered to be indicative of a potential of the substance to cause systemic toxicity/carcinogenicity.

Based on structural similarity the findings from the toxicity studies are extrapolated to the substances where there is limited information for these endpoints.

Potential hazard for skin sensitisation identified for the substances EC/List nr 200-539-3, 203-403-1, 948-072-0, 948-073-6, 836-285-0, and 838-724-1.

Based on ECHA's assessment of currently available hazard information, potential hazards were identified for skin sensitisation for the substances EC/List nr 200-539-3, 203-403-1, 948-072-0, 948-073-6, 836-285-0, and 838-724-1 due to positive findings in experimental studies conducted with these substances. All the substance have harmonised or self-classifications for skin sensitisation 1B. Although there are industrial, professional and consumer uses as lubricants and metal working fluids for List no 948-072-0 and 948-073-6, the substances are self-classified correctly and no further action is warranted.

No likely hazard for genotoxicity, carcinogenicity and STOT RE identified for the substances EC/ List no 246-305-4, 246-309-6, 948-072-0, and 948-073-6

Based on ECHA's assessment of currently available hazard information, no likely potential hazards were identified for repeated dose toxicity and carcinogenicity for the substances EC/ List no 246-305-4, 246-309-6, 948-072-0, and 948-073-6. These conclusions are based on the negative results observed in *in vitro* gene mutation assays.

No repeated dose toxicity study or carcinogenicity study is available on these four substances. In the absence of repeated dose toxicity data, since genotoxicity metabolic activation is considered to be the first step in the development of systemic toxicity/carcinogenicity for aromatic amines, the observation of negative results in genotoxicity studies is considered to be indicative of a low potential of the substance to undergo metabolic activation and to cause systemic toxicity/carcinogenicity.

It is noted that this conclusion carries a particularly high uncertainty as the data sets for these substances only partially address genotoxicity, i.e. information is not available on both gene mutation and clastogenicity for these substances.

No likely hazard for reproductive toxicity and endocrine disruption for all the substances in the group

Based on ECHA's assessment of currently available hazard information, no likely potential hazards were identified for reproductive toxicity and endocrine disruption for all the substances included in this group. These conclusions are based on extrapolation of hazards from the available data to the rest of the group.

This group-level conclusion carries a particular degree of uncertainty due to the very limited data density on the reproductive function and developmental toxicity

across the group. However, this uncertainty is somewhat mitigated by the large data set on repeated dose toxicity available for the substances in this group. No particular effects on endocrine/reproductive organs or tissues are reported in these studies.

No likely skin sensitisation hazard identified for all the substances in the group other than EC/List nr 200-539-3, 203-403-1, 948-072-0, 948-073-6, 836-285-0, and 838-724-1.

Based on ECHA's assessment of currently available hazard information, no or no potential hazards were identified for skin sensitisation for the other substances in this group. These conclusions are based on the available data in the registration dossiers – good data density – and extrapolation of this data to structurally similar substances in the group.

Skin sensitisation properties are associated with the presence of substituents in para-position for this class of compounds. Therefore, unless data are available and demonstrates otherwise, the aromatic amines included in this group without a para-substituent or an aminoindane moiety are considered as unlikely skin sensitisers.

This group level conclusion is based on a high level estimation of a potential structure-activity relationship. As indicated in the beginning of this section, further analysis of the impact of the type, number and position of the alkyl substituents on the aromatic ring is needed to refine the conclusions of this screening.

Environmental hazards

Aquatic toxicity

Based on ECHA's assessment of currently available information, (potential) hazards were identified for aquatic toxicity based on self-classifications, hazard data and/or structural similarity for the whole group. Six substances in the group (EC 200-539-3, 201-758-7, 201-990-9, 202-429-0, 203-403-1, 203-583-1) have harmonized classification as Aquatic Acute 1, Aquatic Chronic 2 or Aquatic Chronic 3.

PBT/vPvB

The substances EC/List no 200-539-3, 201-758-7, 201-990-9, 202-429-0, 202-437-4, 202-440-0, 202-451-0, 203-403-1, 203-583-1, 246-309-6, 201-755-0, 202-797-2, 203-607-0, 211-314-4, 246-307-5, 700-095-5, and 838-724-1 in this group are unlikely to fulfil the PBT/vPvB screening criteria, because they have a low potential for bioaccumulation. In addition, the following substances are likely readily biodgradable based on the currently available data: EC 200-539-3, 202-429-0, 202-440-0, 203-403-1, 203-583-1, 211-314-4. These conclusions are based on ready biodegradability test results and log logKow. It was not possible to conclude on the PBT/vPvB hazards of substances List no 948-072-0, 948-073-6 and 836-285-0 in the group as there is not sufficient information to make a holistic view of available information for the substance(s)/ (sub)group(s).

For the following substances there is no data available to confirm PBT/vPvB hazard: EC/List no 215-091-4, 248-105-2, 250-108-9, 700-095-5, 700-229-2, 838-724-1, 863-466-1, 946-786-7 and extrapolation from substances with data is not possible.

Environmental ED

In general, there are no data available indicating environmental ED properties of

all substances in this group.

PMT/vPvM

For substances that are potentially P/vP (EC 201-758-7, 201-990-9, 202-451-0, 246-309-6, 201-755-0, 202-797-2, 203-607-0, 212-215-9, 246-305-4, 700-095-5, 838-724-1), there is very little data available on properties explaining the mobility of the substances in this group. The few available $logK_{oc}$ values combined with low $logK_{ow}$ would indicate potential "M" concern. However most of the substances in the group do no have any information regarding mobility. Most substances in the group are registered at low tonnages or as intermediates (or no data at all), thus data is not available for a conclusive T assessment.

Use/exposure All the substances registered as intermediates (OSII/TII) are used under strictly controlled conditions, and therefore the exposure is minimised. There is a concern about these substances possibly not being properly classified for carcinogenicity or STOT RE (as 19 of the 21 substances are not classified for those hazards). However with this type of registration it is not possible to request further hazard information to clarify the classification.

For eight of the ten Article 10 registered substances, the main use reported is also as intermediate, although some of the substances indicate further industrial uses from which exposure cannot be excluded. However for these substances (EC 200-539-3, 202-429-0 and 203-403-1) EU wide OELs exist which are sufficient to control worker exposure. For the remaining substances (201-758-7, 201-990-9, 202-437-4, 202-451-0, 203-583-1, 948-072-0 and 948-073-6) an EU wide OEL is not proposed for the industrial (intermediate) uses as none of the substances are classified as CMR category 1. ECs 201-758-7 and 201-990-9 have harmonised classifications which include carcinogenicity cat 2, EC 202-437-4 and 202-245-0 have harmonised classifications which include STOT RE 2 and ECs 203-583-1, 948-072-0 and 948-073-6 are unlikely carcinogens. Therefore it would not be justified to pursue further clarification on classification nor EU-wide OELs. For substance EC 201-90-9 and List no 700-095-5 industry should update their registration dossiers and clarify whether or not the uses reported for this substance are supported. There are two substances ECs 948-072-0 and 948-073-6 where the registrants have reported industrial, professional and consumer uses in lubricants and metral working fluids (i.e. "widespread" uses where the potential for exposure is high), while the main hazard would be skin sensitisation. Although there is potential consumer exposure, for both these substances the registrants have self-classified correctly therefore harmonized classification is not proposed. The remaining substances are registered as intermediates and used under strictly controlled conditions (where exposure is minimised), or have no registered uses.

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

3 Conclusions and actions

Subgroup name, EC/List no	Human Health Hazard	Environmental Hazard	Relevant use(s) & exposure potential	Last foreseen action	Action
Full registrations: 201-758-7, 201-990-9, 202-429-0, 202-437-4, 202-451-0, 200-539-3, 203-403-1 Intermediate only registrations: 201-755-0, 201-794-3, 202-440-0, 203-607-0, 205-138-7, 209-424-2, 211-314-4, 215-091-4, 700-095-5, 700-229-2, 800-008-1, 946-786-7, 202-797-2, 212-215-9, 701-382-8, 836-285-0, 838-724-1, 863-466-1, 212-215-9 Non-registered substances: 202-080-4, 202-177-1, 205-282-0, 208-741-3,	Known or potential hazard for carcinogenicity for STOT RE for mutagenicity for skin sensitisation (ECs: 200-539-3, 203-403-1, 202-797-2, 212-215-9, 701-382-8, 836-285-0, 838-724-1, 863-466-1, 212-215-9, 205-519-8, 208-740-8)	Known or potential hazard for aquatic toxicity Inconclusive hazard for PMT/vPvM (ECs: 201-758-7, 201-990-9, 202-451-0, 201-755-0, 202-797-2, 203-607-0, 212-215-9, 700-095-5, 838-724-1)	Main reported use of the full registrations is as intermediate. Three substance registrations (ECs: 202-429-0, 200-539-3 and 203-403-1) indicate further industrial uses from which exposure cannot be excluded. Intermediate only registrations: substances used under strictly controlled conditions. The remaining substances have no registered uses. Overall, low potential for exposure and release into the	**Currently no need for EU RRM** <u>Justification:</u> Correct classification followed by implementation of necessary RRMs should be sufficient to ensure safe use for the substances with full registrations. EU wide OELs exist for ECs: 202-429-0, 200-539-3 and 203-403-1 which are sufficient to control worker exposure. The remaining substances are either used under strictly controlled conditions (exposure is minimized), or have no registered uses.	No action

Subgroup name, EC/List no	Human Health Hazard	Environmental Hazard	Relevant use(s) & exposure potential	Last foreseen action	Action
209-445-7, 211-252-8, 248-105-2, 250-108-9, 269-016-5, 205-519-8, 208-740-8			environment can be assumed.		
Full registration: 203-583-1	for STOT RE	Known or potential hazard for aquatic toxicity	Only reported use is as intermediate, but includes full (Article 10) registration so exposure cannot be excluded.	**Currently no need for EU RRM** Justification: Harmonised classification followed by implementation of necessary RRMs should be sufficient to ensure safe use.	No action
Intermediate only registrations: **246-305-4,** **246-309-6**	No hazard or unlikely hazard for carcinogenicity for STOT RE for mutagenicity	Inconclusive hazard for PMT/vPvM	Intermediate only registrations, all substances used under strictly controlled conditions, where exposure is minimised.	**Currently no need for EU RRM** Justification: No/unlikely/inconclusive hazards and exposure is minimised.	No action
Full registrations: UVCBs with a long branched carbon chain 948-072-0	Known or potential hazard for skin sensitisation	Known or potential hazard for aquatic toxicity Inconclusive for PBT/vPvB and PMT/vPvM	Industrial, professional and consumer uses as lubricants and metral working fluids (i.e. "widespread" uses	Currently no need for EU RRM Justification: Although there are widespread uses where the potential for	No action

Subgroup name, EC/List no	Human Health Hazard	Environmental Hazard	Relevant use(s) & exposure potential	Last foreseen action	Action
948-073-6			where the potential for exposure is high).	exposure is high, the registrants have self-classified correctly.	

Annex 1: Overview of classifications

Data extracted on 05/01/2023.

EC/ List No	CAS number	Substance name	Harmonised classification	Classification in registrations
200-539-3	62-53-3	aniline	Index number: 612-008-00-7 Acute Tox. 3 Acute Tox. 3 STOT RE 1 Eye Dam. 1 Muta. 2 Hazard Carc. 2 Hazard Acute Tox. 3 Hazard Aquatic Acute 1 Skin Sens. 1	Skin Sens. 1 STOT Rep. Exp. 1, affected organs: blood [Carc. 2 Muta. 2 Acute Tox. 3 Acute Tox. 3 Acute Tox. 3 Eye Damage 1 Skin Sens. 1B STOT Rep. Exp. 1, affected organs: blood and hematopoetic system, specific concentration: >=1 Aquatic Acute 1 Aquatic Chronic 1
201-755-0	87-59-2	2,3-xylidine	Acute Tox. 3 STOT RE 2 Aquatic Chronic 2	STOT Rep. Exp. 2, affected: kidney Acute Tox. 3 Aquatic Chronic 2
201-758-7	87-62-7	2,6-xylidine	Acute Tox. 4 Skin Irrit. 2 STOT SE 3 Carc. 2 Acute Tox. 4 Aquatic Chronic 2	STOT Single Exp. 3, affected organs: high respiratory tract STOT Single Exp. 3, affected organs: Respiratory tract Carc. 2 Flam. Liquid 3 Acute Tox. 3 Acute Tox. 4 Skin Corr. 1A Skin Irrit. 2 Eye Damage 1 Eye Irrit. 2 STOT Single Exp. 3, affected organs: respiratory epithelium Aquatic Chronic 2
201-794-3	88-05-1	2,4,6-trimethylaniline	-	Skin Irrit. 2 Acute Tox. 4 Acute Tox. 2 Eye Irrit. 2 STOT Single Exp. 3, affected organs: respiratory system
201-990-9	90-41-5	biphenyl-2-ylamine	Acute Tox. 4 Carc. 2 Aquatic Chronic 3	Carc. 2 Acute Tox. 4 Aquatic Chronic 3
202-080-4	91-59-8	2-naphthylamine	Acute Tox. 4 Carc. 1A Aquatic Chronic 2	-

EC/ List No	CAS number	Substance name	Harmonised classification	Classification in registrations
202-177-1	92-67-1	biphenyl-4-ylamine	Acute Tox. 4 Carc. 1A	-
202-429-0	95-53-4	o-toluidine	Acute Tox. 3 Eye Irrit. 2 Carc. 1B Acute Tox. 3 Aquatic Acute 1	Carc. 1B Muta. 2 Acute Tox. 3 Acute Tox. 4 Skin Irrit. 2 Eye Irrit. 2 Eye Damage 1 Aquatic Acute 1 Aquatic Chronic 2
202-437-4	95-64-7	3,4-xylidine	Acute Tox. 3 STOT RE 2 Aquatic Chronic 2	Aquatic Chronic 2 Acute Tox. 3 Acute Tox. 4 STOT Rep. Exp. 2 affected organs: respiratory track
202-440-0	95-68-1	2,4-xylidine	Acute Tox. 3 STOT RE 2 Aquatic Chronic 2	Aquatic Chronic 2 Acute Tox. 3 Acute Tox. 2 Eye Irrit. 2 STOT Rep. Exp. 2, affected organs: liver
202-451-0	95-78-3	2,5-xylidine	Acute Tox. 3 STOT RE 2 Aquatic Chronic 2	Acute Tox. 4 STOT Rep. Exp. 2, affected organs: Respiratory organs Aquatic Chronic 3
202-797-2	99-88-7	4-isopropylanilin e	-	Aquatic Chronic 1, Eye Damage 1 Aquatic Acute 1 Acute Tox. 3 Skin Corr. 1B
203-403-1	106-49-0	p-toluidine	Acute Tox. 3 Eye Irrit. 2 Carc. 2 Aquatic Acute 1 Skin Sens. 1	Carc. 2 Acute Tox. 3 Eye Irrit. 2 Skin Sens. 1A Skin Sens. 1 Aquatic Acute 1 Aquatic Chronic 2
203-583-1	108-44-1	m-toluidine	Acute Tox. 3 STOT RE 2 Aquatic Acute	STOT Rep. Exp. 2 Acute Tox. 3 STOT Rep. Exp. 2, affected organs: spleen Aquatic Acute 1 Aquatic Chronic 1
203-607-0	108-69-0	3,5-xylidine	Acute Tox. 3 STOT RE 2 Aquatic Chronic 2	Aquatic Chronic 1 Acute Tox. 3 Eye Irrit. 2 STOT Rep. Exp. 2 affected organs: Liver, Kidney Acute Tox. 3 Aquatic Chronic 2 Acute Tox. 3
205-138-7	134-32-7	1-naphthylamine	Acute Tox. 4 Aquatic Chronic 2	Carc. 1A Acute Tox. 4 Aquatic Chronic 2
205-282-0	137-17-7	2,4,5-trimethylanilin e	Acute Tox. 3 Acute Tox. 3 Carc. 1B Acute Tox. 3 Aquatic Chronic 2	-

EC/ List No	CAS number	Substance name	Harmonised classification	Classification in registrations
205-519-8	142-04-1	anilinium chloride	Acute Tox. 3 STOT RE 1 Eye Dam. 1 Muta. 2 Hazard Carc. 2 Hazard Acute Tox. 3 Hazard Aquatic Acute 1 Skin Sens. 1	-
208-740-8	540-23-8	p-toluidinium chloride	Acute Tox. 3 Acute Tox. 3 Eye Irrit. 2 Carc. 2 Acute Tox. 3 Aquatic Acute 1 Skin Sens. 1	-
208-741-3	540-25-0	p-toluidine sulphate (1:1)	Acute Tox. 3 Eye Irrit. 2 Skin Sens. 1 Acute Tox. 3 Carc. 2 Aquatic Acute 1	-
209-424-2	578-54-1	2-ethylaniline	-	Acute Tox. 3 Acute Tox. 4 Eye Irrit. 2
209-445-7	579-66-8	2,6-diethylaniline	Acute Tox. 4	-
211-252-8	636-21-5	o-toluidinium chloride	-	-
211-314-4	638-03-9	m-toluidinium chloride	-	-
212-215-9	769-92-6	p-tert-butylaniline	-	Eye Irrit. 2 Acute Tox. 4 Aquatic Chronic 1 Aquatic Acute 1 Skin Corr. 1
215-091-4	1300-73-8	xylidine	Acute Tox. 3 STOT RE 2 Aquatic Chronic 2	Aquatic Chronic 2 Carc. 2 Skin Irrit. 2 Acute Tox. 3 STOT Rep. Exp. 2, affected organs: Liver, Kidney Eye Irrit. 2
246-305-4	24544-04-5	2,6-diisopropylaniline	-	Aquatic Chronic 3
246-307-5	24544-08-9	2,6-diethyl-p-toluidine	-	Acute Tox. 4
246-309-6	24549-06-2	6-ethyl-2-toluidine	-	Acute Tox. 4 Aquatic Chronic 3
248-105-2	26915-12-8	toluidine	-	-
250-108-9	30273-11-1	4-sec-butylaniline	-	-

EC/ List No	CAS number	Substance name	Harmonised classification	Classification in registrations
269-016-5	68170-22-9	dimethyl hydrogen phosphorate, compound with 4-tetrapropylene aniline	-	-
700-095-5	203448-76-4	2-(4-methylpentan-2-yl)aniline	-	Aquatic Chronic 2
700-229-2	-	Reaction mass of 4-sec-butylaniline and 2-sec-butylaniline	-	Skin Irrit. 2 Acute Tox. 3 Acute Tox. 3 Acute Tox. 3 Eye Irrit. 2
701-382-8	-	(3R)-1,1,3-trimethylindan-4-aminium (2S,3S)-3-carboxy-2,3-dihydroxypropanoate	-	-
800-008-1	21524-36-7	2,4,6-triisopropylaniline	-	-
836-285-0	125349-37-3	(3R)-1,1,3-trimethylindan-4-amine	-	Skin Sens. 1B Aquatic Chronic 2 Acute Tox. 4
838-724-1	94568-76-0	1,1,3-trimethylindan-4-amine	-	Aquatic Chronic 2 Flam. Liquid 2 Skin Sens. 1B Acute Tox. 4 Repr. 2 Skin Irrit. 2 STOT Rep. Exp. 2 H373, affected organs: nerves, kidneys, liver Eye Irrit. 2 Asp. Tox. 1
863-466-1	1616291-21-4	1,1,3-trimethylindan-4-aminium chloride	-	-
946-786-7	-	Reaction mass of 4-sec-butylaniline and 2-sec-butylaniline	-	Skin Irrit. 2 Eye Irrit. 2
948-072-0	-	Phosphoric acid, mono- and dibutyl esters, compds. with C10-13-(branched)-alkylaniline	-	Skin Sens. 1B Aquatic Acute 2 Aquatic Chronic 2

EC/ List No	CAS number	Substance name	Harmonised classification	Classification in registrations
948-073-6	-	Phosphoric acid, mono- and dimethyl esters, compds. with C10-13-(branched)-alkylaniline	-	Skin Irrit. 2 Skin Sens. 1B Aquatic Acute 1 Aquatic Chronic 1

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

Data extracted on 05/01/2023.

EC /List no	PC 20: Products such as ph-regulators, flocculants, precipitants, neutralisation agents	PC 35: Washing and cleaning products	PC 8: Biocidal products (e.g. disinfectants, pest control)	PC 29: Pharmaceuticals	PC 24: Lubricants, greases, release products	PC 25: Metal working fluids	PC 17: Hydraulic fluids	PC 32: Polymer preparations and compounds	PC 18: Ink and toners	PC 34: Textile dyes, and impregnating products	PC 21: Laboratory chemicals	PC 19: Intermediate
200-539-3	I							I				I
201-758-7												I
201-990-9		I		I						I		I
202-429-0											I, **P**	I
202-437-4 (INACTIVE)												F, I
202-451-0												F, I
203-403-1								I			I, **P**	I
203-583-1												I
948-072-0					F, I, **P, C**	I	F, I, **P, C**				F	
948-073-6					F, I, **P, C**	I	F, I, **P, C**				F	

F: formulation, I: industrial use, P: professional use, C: consumer use; P, and C 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 17/01/2023.

EC/List no	RMOA	Authorisation		Restriction	CLH
		Candidate List	Annex XIV	Annex XVII	Annex VI (CLP)
200-539-3	YES			YES	YES
201-755-0				YES	
201-758-7				YES	YES
201-990-9				YES	YES
202-080-4	YES			YES	YES
202-177-1	YES	YES	PRIO	YES	YES
202-429-0	YES	YES	PRIO	YES	YES
202-437-4				YES	
202-440-0				YES	
202-451-0				YES	
203-403-1				YES	YES
203-583-1				YES	YES
203-607-0				YES	
205-138-7				YES	YES
205-282-0				YES	YES
205-519-8				YES	YES
208-740-8				YES	YES
208-741-3				YES	YES
209-445-7					YES
211-252-8				YES	
211-314-4				YES	
215-091-4				YES	YES
248-105-2				YES	

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

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