Assessment of regulatory needs

Authority: European Chemicals Agency (ECHA)

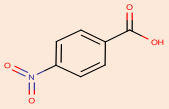
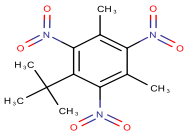
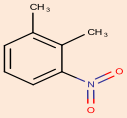
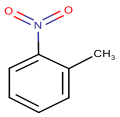
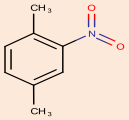
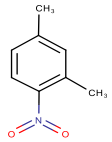
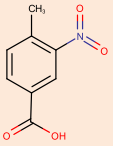
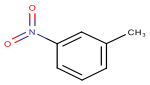
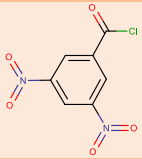
Group Name: Carboxylated/methylated nitrobenzenes and their derivatives

General structure: -

Revision history

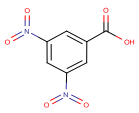
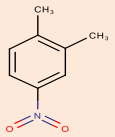
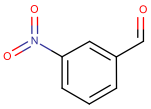
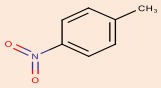
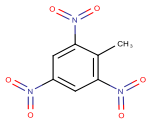
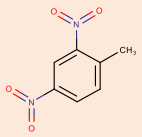
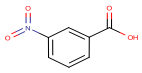
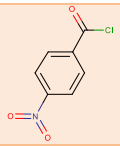
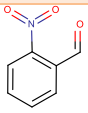
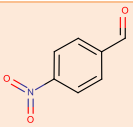
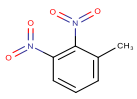
Version	*Date*	*Description*
1.0	5 September 2023	

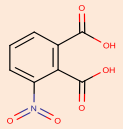
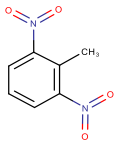
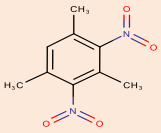
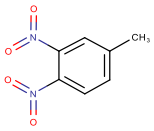
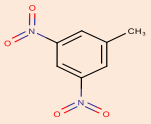
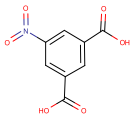
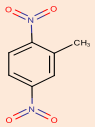
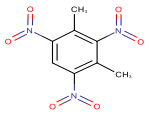
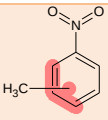
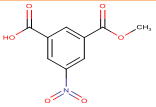
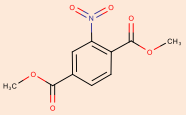
Table 1, substances within this group:

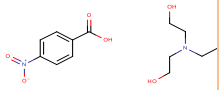
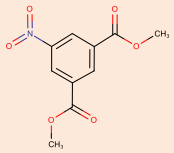
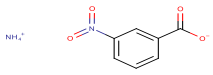
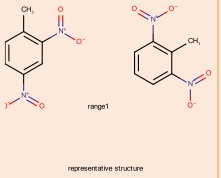
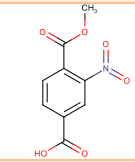
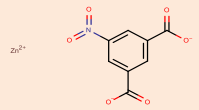
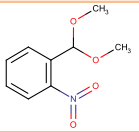
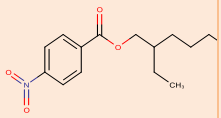
EC/List number	CAS number	Substance name	Chemical structures	Registration type (full, OSII or TII, NONS), highest tonnage band among all the registrations (t/y) [1]	SG[2]
200-526-2	62-23-7	4-nitrobenzoic acid		Full, not (publicly) available	1a
201-329-4	81-15-2	5-tert-butyl-2,4,6-trinitro-m-xylene		C&L notification	3c
201-474-3	83-41-0	3-nitro-o-xylene		OSII or TII	1b
201-853-3	88-72-2	2-nitrotoluene		Full, not (publicly) available	1a
201-920-7	89-58-7	2-nitro-p-xylene		Cease manufacture	1b
201-947-4	89-87-2	4-nitro-m-xylene		Cease manufacture	1b
202-549-3	96-98-0	3-nitro-p-toluic acid		OSII or TII	2
202-728-6	99-08-1	3-nitrotoluene		OSII or TII	1a
202-750-6	99-33-2	3,5-dinitrobenzoyl chloride		OSII or TII	2

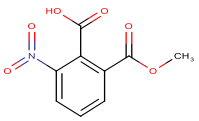
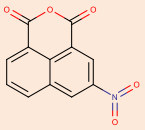
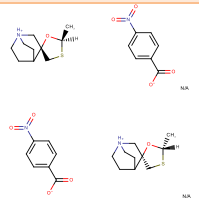
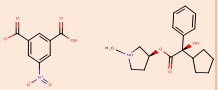
[1] Note that the total aggregated tonnage band may be available on ECHA's webpage at https://echa.europa.eu/information-on-chemicals/registered-substances

[2] Subgroup added to support the proposed regulatory action.

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]	SG[2]
202-751-1	99-34-3	3,5-dinitrobenzoic acid		Full, not (publicly) available	2
202-761-6	99-51-4	4-nitro-o-xylene		Cease manufacture	1b
202-772-6	99-61-6	3-nitrobenzaldehyde		OSII or TII	1a
202-808-0	99-99-0	4-nitrotoluene		Full, not (publicly) available	1a
204-289-6	118-96-7	2,4,6-trinitrotoluene		Full, >1000	3a
204-450-0	121-14-2	2,4-dinitrotoluene		C&L notification	2
204-508-5	121-92-6	3-nitrobenzoic acid		Full, 10-100	2
204-517-4	122-04-3	4-nitrobenzoyl chloride		OSII or TII	1a
209-025-3	552-89-6	2-nitrobenzaldehyde		OSII or TII	1a
209-084-5	555-16-8	4-nitrobenzaldehyde		OSII or TII	1a
210-013-5	602-01-7	2,3-dinitrotoluene		C&L notification	2

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]	SG[2]
210-030-8	603-11-2	3-nitrophthalic acid		OSII or TII	1b
210-106-0	606-20-2	2,6-dinitrotoluene		C&L notification	2
210-164-7	608-50-4	2,4-dinitromesitylene		OSII or TII	2
210-222-1	610-39-9	3,4-dinitrotoluene		C&L notification	2
210-566-2	618-85-9	3,5-dinitrotoluene		C&L notification	2
210-568-3	618-88-2	5-nitroisophthalic acid		Full, not (publicly) available	1b
210-581-4	619-15-8	2,5-dinitrotoluene		C&L notification	2
211-187-5	632-92-8	2,4,6-trinitro-m-xylene		Not registered	3b
215-311-9	1321-12-6	Nitrotoluene		OSII or TII	1
217-793-6	1955-46-0	Methyl 5-nitrohydrogen.isophthalate		OSII or TII	1b
226-134-1	5292-45-5	Dimethyl 2-nitroterephthalate		OSII or TII	1b

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]	SG[2]
230-989-6	7394-38-9	p-nitrobenzoic acid, compound with 2,2',2''-nitrilotriethanol (1:1)		Full, not (publicly) available	1a
236-307-3	13290-96-5	Dimethyl 5-nitroisophthalate		OSII or TII	1b
242-965-2	19328-56-4	Ammonium 3-nitrobenzoate		Full, not (publicly) available	1a
246-836-1	25321-14-6	Dinitrotoluene		Full, not (publicly) available	2
252-360-5	35092-89-8	Methyl hydrogen 2-nitroterephthalate		OSII or TII	1b
262-309-9	60580-61-2	Zinc 5-nitroisophthalate		Full, not (publicly) available	1b
423-830-9	20627-73-0	1-dimethoxymethyl-2-nitro-benzene		NONS	1a
605-350-3	16397-70-9	Benzoic acid, 4-nitro-, 2-ethylhexyl ester		OSII or TII	1a

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]	SG[2]
606-804-3	21606-04-2	1,2-Benzenedicarboxylic acid, 3-nitro-, 1-methyl ester		OSII or TII	1b
629-274-5	3027-38-1	1H,3H-Naphtho[1,8-cd]pyran-1,3-dione, 5-nitro-		OSII or TII	1c
696-667-6	1292815-90-7	Benzoic acid, 4-nitro-, compd. with rel-(2'R,3R)-2'-methylspiro[1-azabicyclo[2.2.2]octane-3,5'-[1,3]oxathiolane] (1:1)		OSII or TII	1a
825-756-6	1955516-58-1	rel-(3R)-3-{[(2S)-2-cyclopentyl-2-hydroxy-2-phenylacetyl]oxy}-1-methylpyrrolidinium 3-carboxy-5-nitrobenzoate		OSII or TII	1b

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

Contents

DISCLAIMER

The author does not accept any liability with regard to the use that may be made of the information contained in this document. Usage of the information remains under the sole responsibility of the user. Statements made or information contained in the document are without prejudice to any further regulatory work that ECHA, the Member States or other regulatory agencies may initiate at a later stage. Assessments 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 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)[3]. 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[4]. 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.

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

[4] 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[5].

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

Glossary

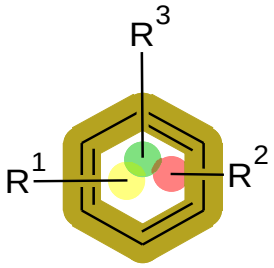
ARN	Assessment of Regulatory Needs
CCH	Compliance Check
CLH	Harmonised classification and labelling
CMR	Carcinogenic, mutagenic and/or toxic to reproduction
DEv	Dossier evaluation
ED	Endocrine disruptor
NONS	Notified new substances
OEL	Occupational exposure limit
OSII or TII	On-site isolated intermediate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

1 Overview of the group

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

ECHA has grouped together structurally similar aromatic substances based on the presence of at least one nitro and one carboxylate functionality on the aromatic ring where the presence of hydrocarbyl substituents is permitted. In addition the respective aldehydes, esters, acid halides and salts are also permitted.

R^1: NO_2 group; The number of R^1 groups can vary from 1 to 3.
R^2: hydrocarbyl (e.g. methyl, tert-butyl). The number of R^2 groups can vary from 1 to 3.
R^3: carboxylic acid, aldehydes, acid halides and esters. The number of R^3 can vary from 1 to 2.



Combinations of different R-groups can be present in the same substance, but the combinations do differ per substance and the R-groups need not all be present in each substance. The salts included in the group have different counter ions varying from metals (zinc) to complex organic structures.

The group consists of 43 mainly well-defined substances (i.e. 42). The majority of these substances are identified by the registrant as mono constituent. EC 246-836-1 and List 696-667-6 are identified as multi-constituent. EC 215-311-9 is reported as UVCB. Of the 43 substances in the group, eleven have a full registration, twenty are only registered as OSII/TII, one is a NONS, three have ceased manufacture and one is not registered. Seven are only notified under CLP.

Based on information reported in the REACH registration dossiers, most substances in the group are used as intermediate. Those registered only as OSII/TII are used under strictly controlled conditions only, and therefore exposure to humans and the environment is considered not relevant. The 12 that have full (Art. 10) registrations (in addition to being registered as OSII/TII) vary considerably in their uses. Several of these are used in industrial or professional settings for which exposure cannot be excluded. Two of these are used either as explosive (i.e. EC 204-289-6, TNT)[6] or as intermediate in the formulation of explosives (i.e. EC 246-836-1). Two others, ECs 204-508-5 and 242-965-2, are used in industrial and professional settings in washing and cleaning, including metal- and non-metal treatment processes as oxidizing/cleaning agent (EC 204-508-5) or as stripping agent (EC 242-965-2) with the possibility for exposure of both workers and the environment. A fifth, EC 262-309-9, is used by industrial and professional workers as corrosion inhibitor in coatings, adhesives and sealants. Article service life is indicated by the registrants and, though expected limited because the corrosion inhibitor is generally embedded in the matrix of the coating/adhesive, exposure during use of (metal) articles

[6] For TNT, exposure of professional workers and during article service life is specified to be negligible as the substance is described to be enclosed in the article and is detonated upon use.

cannot be excluded. A sixth, EC 200-526-2, is used as electrolytic solvent in small batteries, capacitors and/or condensers. Use by industrial workers, professional workers and consumers is indicated for this substance and based on the information available in the registration dossier, exposure of professional users and consumers cannot be excluded. For the remaining six with full registrations, potential for exposure is considered lower. Two are only used as intermediate in industrial settings, and ECs 201-853-3 and 202-808-0 are used as intermediate and laboratory chemical with consequent limited exposure assumed for industrial and professional workers. EC 230-989-6 is only used as pH-regulating agent in industrial settings with possibility of worker and environmental exposure. And finally, EC 204-517-4 is used as precursor in the production of pharmaceuticals. Based on the relatively varied uses, interchangeability or substitution between substances within this group with Art. 10 registrations is expected limited.

For several of the substances in the group, some regulatory measures have been put in place already. Most noteworthy are EC 201-329-4 which is in REACH Annex XIV (Authorisation list) based on vPvB properties, EC 201-853-3 which is harmonised classified as Carc 1B, Muta 1B and Repro 2 (fertility) and ECs 204-450-0, 210-013-5, 210-106-0, 210-222-1, 210-566-2, 210-581-4, 246-836-1, which are already harmonised classified among other hazards as Carc 1B. EC 204-450-0 is furthermore in the process of being restricted for use in articles by consumers via Art. 69(2).

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 number, substance name	Human Health Hazard	Environmental Hazard	Relevant use(s) & exposure potential	Suggested regulatory actions
Subgroup 1a 215-311-9 Para: 202-808-0 209-084-5 200-526-2 204-517-4 230-989-6 605-350-3 Meta: 202-728-6	Known or potential hazards: for carcinogenicity for mutagenicity for reproductive toxicity	Known or potential hazard for aquatic toxicity for 201-853-3 202-728-6 202-772-6 202-808-0 423-830-9 Known or potential hazard for PMT/vPvM for 201-853-3 202-808-0 423-830-9 Inconclusive hazard	Most substances are used as intermediate on industrial sites in the production of other substances. Potential for exposure for workers may be suspected for ECs 200-526-2, 204-508-5, 230-989-6 and 242-965-2. EC 200-526-2 is used as electrolyte in batteries. Based on current registrations, there seems little overlap between the uses of the substances and hence, substitution potential is suspected low. Widespread use might be relevant for EC 204-508-5.	CLH <u>Justification:</u> According to the reported uses, typically low total tonnages and the exposure expected for human health and environment, CLH is considered sufficient to trigger company risk management and generic restrictions as available under REACH. Actions may be re-considered when the assessment will be revisited.

Subgroup name, EC number, substance name	Human Health Hazard	Environmental Hazard	Relevant use(s) & exposure potential	Suggested regulatory actions
202-772-6 204-508-5 242-965-2 Ortho: 201-853-3 210-302-6 209-025-3 423-830-9		for aquatic toxicity for 200-526-2 204-508-5 204-517-4 209-084-5 215-311-9 230-989-6 242-965-2 605-350-3 Inconclusive hazard for PBT/vPvB for 202-772-6 204-517-4 209-025-3 209-084-5 215-311-9 Inconclusive hazard for PMT/vPvM for 202-772-6 204-517-4 209-025-3 209-084-5 215-311-9		

Subgroup name, EC number, substance name	Human Health Hazard	Environmental Hazard	Relevant use(s) & exposure potential	Suggested regulatory actions
Subgroup 1b, 2,5-dimethyl-nitrobenzenes: 201-920-7 202-549-3 252-360-5 226-134-1 2,4-dimethyl-nitrobenzenes: 201-947-4 2,3-dimethyl-nitrobenzenes: 201-474-3 210-030-8 606-804-3 3,5-dimethyl-nitrobenzenes: 210-568-3 262-309-9		Known or potential hazard for aquatic toxicity for 201-474-3 201-920-7 Known or potential hazard for PBT/vPvB for 201-474-3 201-920-7 202-549-3 202-761-6 Known or potential hazard for PMT/vPvM for 201-474-3 201-920-7 202-549-3 202-761-6 210-030-8 252-360-5 262-309-9 Inconclusive hazard	Two substances are registered with an Art. 10 full registration (i.e. 262-309-9 and 210-568-3). The substances are used in (non)-metal treatment, soldering and welding, as intermediate or as laboratory agent with expected limited potential for exposure. EC 262-309-9 is also used in adhesives and coatings and paints with potential for exposure of professional and industrial workers. Widespread use might be relevant for this substance	

Subgroup name, EC number, substance name	Human Health Hazard	Environmental Hazard	Relevant use(s) & exposure potential	Suggested regulatory actions
217-793-6 236-307-3 3,4-dimethyl-nitrobenzenes: 202-761-6		for aquatic toxicity for 201-947-4 202-549-3 202-761-6 210-030-8 210-568-3 217-793-6 226-134-1 236-307-3 252-360-5 262-309-9 606-804-3 Inconclusive hazard for PBT/vPvB for 226-134-1 236-307-3 Inconclusive hazard for PMT/vPvM for 217-793-6 226-134-1 236-307-3 606-804-3		

Subgroup name, EC number, substance name	Human Health Hazard	Environmental Hazard	Relevant use(s) & exposure potential	Suggested regulatory actions
Subgroup 1c, mono-nitro napthalene EC 629-274-5		Inconclusive hazard for aquatic toxicity for PBT/vPvB and for PMT/vPvM	Used as OSII/TII	
Subgroup 2, dinitro-toluenes/xylenes 246-836-1 210-581-4 210-566-2 202-751-1 202-750-6 210-106-0 204-450-0 210-164-7 210-222-1 210-013-5		Known or potential hazard for aquatic toxicity for 202-751-1 204-450-0 210-013-5 210-106-0 210-222-1 210-566-2 246-836-1 Known or potential hazard for PBT/vPvB for 210-013-5 210-164-7 210-222-1 Known or potential hazard for PMT/vPvM for 202-751-1	Four substances are registered, of which 2 with an Art. 10 full registration (i.e. EC 202-751-1 and 246-836-1), and 2 as OSII/TII (i.e. 202-750-6 and 210-164-7). For both EC 202-751-1 and 246-836-1, the exposure potential is expected limited but cannot be excluded.	

Subgroup name, EC number, substance name	Human Health Hazard	Environmental Hazard	Relevant use(s) & exposure potential	Suggested regulatory actions
		210-013-5 210-106-0 210-164-7 210-222-1 Inconclusive hazard for aquatic toxicity for 202-750-6 210-164-7 210-581-4 Inconclusive hazard for PBT/vPvB for 202-750-6 210-566-2 210-581-4 Inconclusive hazard for PMT/vPvM for 202-750-6 204-450-0 210-566-2 210-581-4		
Subgroup 3a 204-289-6 (TNT)	Known or potential hazards: for carcinogenicity for mutagenicity	Known or potential hazard for aquatic toxicity	Use as explosive by industrial and professional workers under controlled conditions	

Subgroup name, EC number, substance name	Human Health Hazard	Environmental Hazard	Relevant use(s) & exposure potential	Suggested regulatory actions
	for reproductive toxicity for STOT RE			
Subgroup 3b 211-187-5	Known or potential hazards: for carcinogenicity for mutagenicity for reproductive toxicity	Inconclusive hazard for aquatic toxicity for PBT/vPvB and for PMT/vPvM	No relevant uses (not registered)	
Subgroup 3c 201-329-4 (Musk xylene)	Known or potential hazards: for carcinogenicity	Known or potential hazard for aquatic toxicity and for PBT/vPvB	No relevant uses (C&L notified, already on Annex XIV for PBT/vPvB)	

3 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 – CLH for carcinogenicity, mutagenicity, and/or reproductive toxicity hazards for all substances in the group.

Based on ECHA's assessment of hazard information currently available in the registration dossiers and considerations of structural similarity and presence of common functional moiety, all the substances in the group have (potentially) the following human health hazards: Carc. 1B, Muta 1B and Repr. 1B (CMR1B). However, differences in availability of data on metabolic conversions, and slight differences observed in the metabolic conversions, make some extrapolations more robust than others, which is the basis for subgrouping (SG). SG1 contains all mono-nitroaromatic compounds, subgrouped further in SG1a, containing mono-nitroaromatic compounds with one other substituent, SG1b containing mono-nitroaromatic compounds with two other substituents, and SG1c containing other mononitroaromatic compounds. SG2 contains the di-nitro-aromatic compounds, and SG3 contains the tri-nitroaromatic compounds, subdivided in SG3a, 3b and 3c each containing a single substance with each a different other substituent.

These hazards are identified based on effects observed with (ordered according to the level of information available):

- SG2: a high number of substances *in vivo* in humans and animals, and a high number of substances with *in vitro* (genotoxicity) data;
- SG1a: a limited number of substances *in vivo* in humans and animals, and a high number of substances with *in vitro* (genotoxicity) data;
- SG3a (EC 204-298-6 - TNT): human and animal *in vivo* data, *in vitro* (genotoxicity) data and a preliminary web-search indicating that data beyond the registration dossiers is available;
- SG1b: a high number of substances with *in vitro* (genotoxicity) data; no human or animal data available;
- SG1c: *in vitro* (genotoxicity) data; no human or animal data available;
- SG3b (EC 211-187-5): substance is not registered;
- SG3c (EC 201-329-4 - Musk xylene): substance is already identified as PBT/vPvB and included in REACH Annex XIV. A preliminary web-search indicates that data beyond the registration dossiers is available (inactive dossier, cease of manufacture).

The experimental outcomes are supported by computational toxicology methods. Based on structural similarity, similarities in toxicokinetics and toxicodynamics for SG1a and toxicodynamics in SG2, the findings from the toxicity studies are extrapolated to all other substances in the other subgroups where there is limited information for these endpoints.

Within SG1a, EC 201-853-3 has a harmonised classification as Carc 1B, Muta 1B and Repr. 2, and EC 215-311-9 is self-classified for these endpoints by the registrants. In SG2, seven substances have harmonised classifications as Carc 1B, Muta 2 and Repro 2 (i.e. EC 204-450-0, 210-013-5, 210-106-0, 210-222-1, 210-

566-2, 210-581-4 and 246-836-1), and in SG3, TNT (EC 204-298-6) is self-classified as Carc 1B, Muta 2, Repr. 2.

For the substances of SGs1a and 2, there is evidence that they are metabolised into each other through oxidative (and reductive) processes in the liver (and microflora). Further reductive and oxidative (redox-active) mechanisms are responsible for the activation of the nitro-functional group to hydroxyl-amine (Casarett & Doull 2013)[7], which shows high DNA-reactivity (IARC 2018)[8]. The experimental evidence from humans and rodents (1921-2005) for substances in SGs1a and 2 indicates that the same biochemistry applies within subgroups, and strong similarities exist between the subgroups (Sherwin & Hynes 1921[9]; Rickert 1987[10]; NTP 1994[11]; NTP 2002a[12]; NTP 2002b[13]; Jones et al., 2005[14]).

These similarities in toxicokinetics and toxicodynamics are the foundation to conclude possible CMR1B properties for all substances in the group and to tentatively extrapolated these also to SGs1c, 3a, b, and c, to which the same principles may apply.

A further analysis of the available hazard and metabolism data for the SGs is out of the scope of this exercise. Should the hazard exist, the confirmation of hazard via harmonised classification (CLH) as CMR1B is proposed as first and final regulatory risk management action for all substances in the group. When preparing the proposals, it may be considered what would be the best way to develop them, for instance whether to make a proposal for the group of substances, per subgroup, to submit them individually or jointly. The subgrouping may support these considerations.

CLH for CMR 1B i) will require company level risk management measures (RMM) for workers to be in place; ii) is needed or highly recommended in support of further regulatory processes under REACH; and iii) would lead to generic restriction of the substance(s) in consumer mixtures by means of the restriction entries 28, 29, 30.

For those substances only registered as OSII/TII, exposure of workers, consumers and the environment are considered unlikely. Exposure is also considered unlikely for EC 201-920-7, 201-947-4 and 202-761-6 that have ceased manufacture. CLH is being proposed for these for transparency reasons to consistently communicate CMR1B properties. Should substitution be possible between substances currently only used as intermediate and those with also non-intermediate uses, CLH may also prevent regrettable substitution. Because exposure is considered unlikely, no EU regulatory risk management action (beyond CLH) is currently proposed for any of these substances. 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.

Exposure cannot be excluded for those substances registered according to Art. 10.

---

[7] Casarett & Doull 2013 https://accesspharmacy.mhmedical.com/content.aspx?bookid=958&sectionid=53483726
[8] IARC 2018 https://monographs.iarc.who.int/wp-content/uploads/2018/06/mono99-6.pdf
[9] Sherwin & Hynes 1921 https://www.sciencedirect.com/science/article/pii/S002192581886077X
[10] Rickert 1987 https://www.tandfonline.com/doi/abs/10.3109/03602538708998299
[11] NTP 1994 https://ntp.niehs.nih.gov/ntp/htdocs/lt_rpts/tr442.pdf
[12] NTP 2002a https://ntp.niehs.nih.gov/ntp/htdocs/lt_rpts/tr504.pdf?utm_source=direct&utm_medium=prod&utm_campaign=ntpgolinks&utm_term=tr504
[13] NTP 2022b https://ntp.niehs.nih.gov/ntp/htdocs/lt_rpts/tr498.pdf?utm_source=direct&utm_medium=prod&utm_campaign=ntpgolinks&utm_term=tr498
[14] Jones et al., 2005 https://www.tandfonline.com/doi/abs/10.1080/13547500500079670

Based on the assessment of the information in the registration dossiers on total registered tonnages, uses and exposure scenario's though, ECHA concludes that for most of these the uses may not be widespread (due to the total tonnage band) and/or the potential for exposure for workers and/or consumers may be considered low. EC 201-853-3, 202-751-1, 202-808-0, and 210-568-3 are all registered at low total tonnage bands of 0–10 t/y, suggesting unlikely widespread use. Moreover, these four are exclusively registered for use as intermediate and/or laboratory chemical with consequent low exposure expected for industrial and professional workers. Consequently, like for the substances registered as OSII/TII, CLH is suggested sufficient for these substances to trigger company level risk management for workers to be in place.

For three others, EC 200-526-2, 242-965-2 and 246-836-1, the low total tonnage registered (0–10 t/y) also render widespread use unlikely. EC 262-309-9 and 204-508-5 are registered at somewhat higher total tonnages of 10-100 t/y, and consequent somewhat higher potential for widespread use. EC 230-989-6 and 204-289-6 are registered at high total tonnages of 100-1.000 t/y and 1.000-10.000 t/y, respectively, suggesting that for these latter two, EU wide use is likely.

Based on the information available in the registration dossiers, high exposure potential is expected for industrial and professional workers for EC 204-508-5, used in washing and cleaning operations, and for ECs 204-508-5, 242-965-2 and 262-309-9, used in (non)-metal treatment and/or soldering and welding. EC 204-508-5 and 242-965-2 are also used in products such as ph-regulators, flocculants, precipitants and neutralisation agents by industrial and professional workers. EC 262-309-9 is also used in coatings and paints by industrial and professional workers and article service life is indicated by the registrant(s).

EC 230-989-6 is used as pH regulator, flocculant, precipitant and neutralisation agent with potential for exposure but is only used in industrial settings.

ECs 204-289-6 and 246-836-1 are used as or in the formulation of explosives under highly controlled conditions and detonate (as part of the intended article) upon use by professionals. Consequently, exposure for industrial and professional workers, and potentially also for consumers upon use of the article, is considered low.

For EC 200-526-2, which is registered for use as electrolyte by industrial and professional workers and consumers and for which article service life is indicated, is suggested that exposure to consumers from intact batteries is most likely negligible unless consumers would handle the electrolyte. In that case Annex XVII entry 28 – 30 would most likely be sufficient to address CMR 1B in mixtures.

Combining the information on total tonnage and exposure potential suggests that for none of the substances regulatory action beyond CLH seems warranted, either because they are most likely not being used widespread in Europe (i.e. EC 200-526-2, 242-965-2 and 246-836-1), because they are likely used under controlled conditions (i.e. ECs 200-526-2, 204-289-6 and 246-836-1), or because they are only used in industrial setting (i.e. 230-989-6). EC 204-508-5 and 262-309-9 are the only two where EU RRM for industrial and professional uses might be considered. EU RRM may moreover be considered because of the somewhat larger number of product categories for which they are registered, which may further point to a possible widespread use. The professional uses as ph-regulator, flocculant, precipitant and neutralisation agent, washing and cleaning agent, adhesives, coatings and paints, and (non-) metal surface treatment are normally expected to be widespread (at many sites and by many users). Professional use is often widespread with relatively low levels of operational controls and risk management measures but with often frequent exposures with a long duration. In addition, professional users may be self-employed and therefore not covered by occupational safety and health (OSH) legislation. Moreover, consumers may be co-exposed to the substances used by professionals, e.g. in case of house painters.

Therefore, a restriction of the substance as such or in mixtures (concentration limit in mixtures) used by professionals could be suggested after CLH. However, given the relatively low total tonnage of ECs 204-508-5 and 262-309-9, and the fact that for industrial and professional uses, the CLH requires company level risk management measures (RMM) for workers to be in place, it is proposed that there is currently no need for further EU-wide regulatory risk management and to await the further developments under the European Commission's Chemicals Strategy for Sustainability[15] which aims to extend to professional users under REACH the level of protection granted to consumers.

In addition, national occupational exposure limit values (OELs) have been established in several Member States for at least nine substances in the group (i.e. EC 201-329-4, 201-853-3, 202-808-0, 204-289-6, 204-517-4, 210-106-0, 210-222-1, 215-311-9 and 246-836-1) to manage occupational exposure. However, not all Member States implemented the same values, and many Member States have no limit values implemented for these substances. Harmonising the limit values available and setting an OEL for all Member States might therefore be of added value to further support occupational health and safety. The presence of national OELs for several of the substances may hint at some national priority to have OELs in place to support safe work. However, as the current uses of the substances are mostly not considered widespread, the regulatory impact of deriving EU OELs may be limited, and the perceived national interest might rather be a leftover from times when these substances were more widely used. The fact that ECs 201-329-4, 210-106-0 and 210-222-1 have no active registrations but only C&L notifications may support this interpretation. EC 204-289-6 (TNT) may be the only exception, but due to its use as explosive, stringent risk management measures are already described in the CSR to prevent exposure. Deriving EU OELs in addition to harmonising the classification is therefore currently also not proposed for any of the substances.

To conclude, based on ECHA's assessment, according to the reported uses and total registered tonnages, it is expected that, should hazards be confirmed through harmonised classification, based on this harmonised classification sufficient regulatory action will be triggered to ensure safe use for industrial and professional workers at the workplace. For EC 200-526-2, it is furthermore expected that the regulatory action triggered through Annex XVII entry 28 – 30 will be sufficient to ensure safe use. Therefore, it is proposed that there is currently no further need for EU-wide regulatory risk management beyond CLH.

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.

No further action is proposed for now based on environmental hazards for all substances in the group. The environmental hazard conclusions are derived from a screening that incorporates in-house QSAR predictions. This is because for the environment, there is limited experimental data available for most substances in the group. By relying solely on experimental data on the registered substances, the hazard screening outcome for most group members would be inconclusive for all or some environmental hazards.

Musk xylene, EC 201-329-4, is already on the Authorisation List (Annex XIV, entry 1) of REACH for vPvB, but is considered an 'outlier' with regard to potential PBT/vPvB properties, being also the only fully substituted xylene structure. 20 Substances in the group screen as unlikely PBT/vPvB, based on a combination of screening tests (for biodegradation), QSAR, and available toxicokinetic data from

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

mammalian studies (for bioaccumulation), or were assessed previously as unlikely PBT/vPvB under the Existing Substances Regulation (2-nitrotoluene/EC 201-853-3 and 2,4-dinitrotoluene/EC 204-450-0)[16]. Furthermore, 11 substances screen as unlikely PMT/vPvM based on a combination of screening tests (for biodegradation), as well as QSAR (mobility). Almost all of the remaining substances screen as inconclusive or potentially PBT/vPvB or PMT/vPvM, due to the absence of experimental data (e.g. for biodegradation) and being ionisable at environmentally relevant pH (for mobility and bioaccumulation). 16 Substances of the group have known or potential aquatic toxicity hazards, mostly based on existing harmonised and/or self-classifications. Most have either a harmonised classification for these endpoints (11 substances) or are self-classified (4 substances). The remaining substances screen as inconclusive for aquatic toxicity, due to the absence of experimental data (either for all or for some of the trophic levels) and the information available doesn't allow extrapolation to the above 16 substances with known or potential aquatic toxic hazard. Possibilities for requesting further data to clarify environmental hazards through CCH and/or SEv to clarify aquatic toxicity, persistence, bioaccumulation and mobility are limited for all substances in the group due to the registration status and the exposure potential and will therefore not be pursued for now. Should their registration status change, regulatory needs should be reconsidered.

[16] 2-nitrotoluene: see European Union Risk Assessment Report on 2-nitrotoluene (2008); and 2,4-dinitrotoluene: see Fact Sheet: TC NES Subgroup on Identification of PBT and vPvB Substances – Results of the Evaluation of the PBT/vPvB Properties of 2,4-dinitrotoluene (2008). Neither of the two substances are identified as PBT/vPvB.

Annex 1: Overview of classifications

Data extracted on 12.10.2022

EC/ List No	Substance name	Harmonised classification	Classification in registrations
200-526-2	4-nitrobenzoic acid	-	Carc. 2 H351 Muta. 2 H341 Repr. 2 H361, specific effect:reproductive organs and fertility Acute Tox. 4 H302 Skin Irrit. 2 H315 Eye Irrit. 2 H319
201-329-4	5-tert-butyl-2,4,6-trinitro-m-xylene	Index number: 609-068-00-1 Carc. 2 Hazard Statement: H351 Notes: T Hazard Category: Expl. 1.1 Hazard Statement: H201 Notes: T Aquatic Acute 1 Statement: H400 Additional Info: T Aquatic Chronic 1 Statement: H410 Additional Info: T	-
201-474-3	3-nitro-o-xylene	-	Aquatic Chronic 2 H411 [intermediate (active)]
201-853-3	2-nitrotoluene	Index number: 609-065-00-5 Acute Tox. 4 Hazard Statement: H302 (Minimum classification) Hazard Category: Repr. 2 Hazard Statement: H361f (Hazard statements H360 and H361 indicate a general concern for effects on both fertility and development: May damage/Suspected of damaging fertility or the unborn child; According to the criteria, the general hazard statement can be replaced by the hazard statement indicating the specific effect of concern in accordance with section 1.1.2.1.2; When the other differentiation is not mentioned, this is due to evidence proving no such effect, inconclusive data or no data and the obligations in Article 4(3) shall apply for that differentiation) Muta. 1B Hazard Statement: H340	Carc. 1B H350 Muta. 1B H340 Repr. 2 H361, specific effect:f***: Suspected of damaging fertility. Acute Tox. 4 H302 Aquatic Chronic 2 H411 Repr. 2 H361 [intermediate (active)]

EC/ List No	Substance name	Harmonised classification	Classification in registrations
		Carc. 1B Hazard Statement: H350 Aquatic Chronic 2 Statement: H411	
201-920-7	2-nitro-p-xylene	-	Acute Tox. 4 H312 [intermediate (inactive)] Acute Tox. 4 H302 [intermediate (inactive)] Acute Tox. 4 H332 [intermediate (inactive)] Aquatic Chronic 2 H411 [intermediate (inactive)]
201-947-4	4-nitro-m-xylene	-	Acute Tox. 4 H302 [intermediate (inactive)]
202-549-3	3-nitro-p-toluic acid	-	-
202-728-6	3-nitrotoluene	-	Acute Tox. 3 H331 [intermediate (active)] Acute Tox. 3 H301 [intermediate (active)] Aquatic Chronic 2 H411 [intermediate (active)] Acute Tox. 3 H311 [intermediate (active)]
202-750-6	3,5-dinitrobenzoylchloride	-	Skin Corr. 1B H314 [intermediate (active)]
202-751-1	3,5-dinitrobenzoic acid	-	Acute Tox. 4 H302 Skin Irrit. 2 H315 Eye Irrit. 2 H319 STOT Single Exp. 3 H335, affected organs: Respiratory track Aquatic Chronic 4 H413
202-761-6	4-nitro-o-xylene	-	-

EC/ List No	Substance name	Harmonised classification	Classification in registrations
202-772-6	3-nitrobenzaldehyde	-	Aquatic Chronic 2 H411 [intermediate (inactive);intermediate (active)] Skin Irrit. 2 H315 [intermediate (inactive);intermediate (active)] STOT Single Exp. 3 H335, affected organs: respiratory system [intermediate (inactive)] Acute Tox. 4 H302 [intermediate (active);intermediate (inactive)] Eye Irrit. 2 H319 [intermediate (active);intermediate (inactive)] STOT Single Exp. 3 H335, affected organs: High respiratory tract [intermediate (active)]
202-808-0	4-nitrotoluene	Index number: 609-006-00-3 Acute Tox. 3 Hazard Statement: H301 (Minimum classification) Acute Tox. 3 Hazard Statement: H311 (Minimum classification) STOT RE 2 Hazard Statement: H373 (Minimum classification; No information to prove exclusion of certain routes of exposure) Acute Tox. 3 Hazard Statement: H331 (Minimum classification) Aquatic Chronic 2 Statement: H411	Acute Tox. 3 H301 Acute Tox. 3 H311 Acute Tox. 3 H331 STOT Rep. Exp. 2 H373, affected organs: testis, spleen, lever Aquatic Chronic 2 H411 STOT Rep. Exp. 2 H373 [intermediate (inactive)]
204-289-6	2,4,6-trinitrotoluene	Index number: 609-008-00-4 Acute Tox. 3 Hazard Statement: H301 (Minimum classification) Acute Tox. 3 Hazard Statement: H311 (Minimum classification) STOT RE 2 Hazard Statement: H373 (Minimum classification; No information to prove exclusion of certain routes of exposure) Acute Tox. 3 Hazard Statement: H331 (Minimum classification)	Carc. 1B H350 Muta. 2 H341 Repr. 2 H361, specific effect:H361d: Suspected of damaging the unborn child Expl. Div. 1.1 H201 Acute Tox. 3 H301 Acute Tox. 3 H311 Acute Tox. 3 H331 STOT Rep. Exp. 2 H373, affected organs: liver, eyes,

EC/ List No	Substance name	Harmonised classification	Classification in registrations
		Hazard Category: Expl. 1.1 Hazard Statement: H201 Aquatic Chronic 2 Statement: H411	nervous system, circulatory system Aquatic Chronic 2 H411
204-450-0	2,4-dinitrotoluene	Index number: 609-007-00-9 Acute Tox. 3 Hazard Statement: H301 (Minimum classification) Acute Tox. 3 Hazard Statement: H311 (Minimum classification) Hazard Category: Repr. 2 Hazard Statement: H361f (Hazard statements H360 and H361 indicate a general concern for effects on both fertility and development: May damage/Suspected of damaging fertility or the unborn child; According to the criteria, the general hazard statement can be replaced by the hazard statement indicating the specific effect of concern in accordance with section 1.1.2.1.2; When the other differentiation is not mentioned, this is due to evidence proving no such effect, inconclusive data or no data and the obligations in Article 4(3) shall apply for that differentiation) STOT RE 2 Hazard Statement: H373 (Minimum classification; No information to prove exclusion of certain routes of exposure) Muta. 2 Hazard Statement: H341 Carc. 1B Hazard Statement: H350 Acute Tox. 3 Hazard Statement: H331 (Minimum classification) Aquatic Acute 1 Statement: H400 Aquatic Chronic 1 Statement: H410	-
204-508-5	3-nitrobenzoic acid	-	Eye Irrit. 2 H319
204-517-4	4-nitrobenzoyl	-	Skin Corr. 1C H314 [intermediate (active)]

EC/ List No	Substance name	Harmonised classification	Classification in registrations
	chloride		
209-025-3	2-nitrobenzaldehyde	-	Skin Irrit. 2 H315 [intermediate (active)] STOT Single Exp. 3 H335, affected organs: respiratory tract [intermediate (active)] STOT Single Exp. 3 H335, affected organs: High respiratory tract [intermediate (active)] Acute Tox. 4 H302 [intermediate (active)] Aquatic Chronic 3 H412 [intermediate (active)] Eye Irrit. 2 H319 [intermediate (active)]
209-084-5	4-nitrobenzaldehyde	-	Skin Irrit. 2 H315 [intermediate (active)] Aquatic Chronic 3 H412 [intermediate (active)] Eye Irrit. 2 H319 [intermediate (active)] STOT Single Exp. 3 H335, affected organs: respiratory system [intermediate (active)] Skin Sens. 1 H317 [intermediate (active)]
210-013-5	2,3-dinitrotoluene	Index number: 609-050-00-3 Acute Tox. 3 Hazard Statement: H301 (Minimum classification) Acute Tox. 3 Hazard Statement: H311 (Minimum classification) Hazard Category: Repr. 2 Hazard Statement: H361f (Hazard statements H360 and H361 indicate a general concern for effects on both fertility and development: May damage/Suspected of damaging fertility or the unborn child; According to the criteria, the general hazard statement can be replaced by the hazard statement indicating the specific effect of concern in accordance with section 1.1.2.1.2;	-

EC/ List No	Substance name	Harmonised classification	Classification in registrations
		When the other differentiation is not mentioned, this is due to evidence proving no such effect, inconclusive data or no data and the obligations in Article 4(3) shall apply for that differentiation) STOT RE 2 Hazard Statement: H373 (Minimum classification; No information to prove exclusion of certain routes of exposure) Muta. 2 Hazard Statement: H341 Carc. 1B Hazard Statement: H350 Acute Tox. 3 Hazard Statement: H331 (Minimum classification) Aquatic Acute 1 Statement: H400 Aquatic Chronic 1 Statement: H410	
210-030-8	3-nitrophthalic acid	-	Eye Damage 1 H318 [intermediate (active)] Skin Irrit. 2 H315 [intermediate (active)] STOT Single Exp. 3 H335, affected organs: Respiratory system [intermediate (active)]
210-106-0	2,6-dinitrotoluene	Index number: 609-049-00-8 Acute Tox. 3 Hazard Statement: H301 (Minimum classification) Acute Tox. 3 Hazard Statement: H311 (Minimum classification) Hazard Category: Repr. 2 Hazard Statement: H361f (Hazard statements H360 and H361 indicate a general concern for effects on both fertility and development: May damage/Suspected of damaging fertility or the unborn child; According to the criteria, the general hazard statement can be replaced by the hazard statement indicating the specific effect of concern in accordance with section 1.1.2.1.2; When the other differentiation is not mentioned, this is due to evidence proving no such effect, inconclusive data or no data and the obligations in Article 4(3) shall apply for that differentiation)	-

EC/ List No	Substance name	Harmonised classification	Classification in registrations
		STOT RE 2 Hazard Statement: H373 (Minimum classification; No information to prove exclusion of certain routes of exposure) Muta. 2 Hazard Statement: H341 Carc. 1B Hazard Statement: H350 Acute Tox. 3 Hazard Statement: H331 (Minimum classification) Aquatic Chronic 3 Statement: H412	
210-164-7	2,4-dinitromesitylene		Eye Irrit. 2 H319 [intermediate (active)] Skin Irrit. 2 H315 [intermediate (active)] STOT Single Exp. 3 H335, affected organs: respiratory system, lung [intermediate (active)]
210-222-1	3,4-dinitrotoluene	Index number: 609-051-00-9 Acute Tox. 3 Hazard Statement: H301 (Minimum classification) Acute Tox. 3 Hazard Statement: H311 (Minimum classification) Hazard Category: Repr. 2 Hazard Statement: H361f (Hazard statements H360 and H361 indicate a general concern for effects on both fertility and development: May damage/Suspected of damaging fertility or the unborn child; According to the criteria, the general hazard statement can be replaced by the hazard statement indicating the specific effect of concern in accordance with section 1.1.2.1.2; When the other differentiation is not mentioned, this is due to evidence proving no such effect, inconclusive data or no data and the obligations in Article 4(3) shall apply for that differentiation) STOT RE 2 Hazard Statement: H373 (Minimum classification; No information to prove exclusion of certain routes of exposure) Muta. 2 Hazard Statement: H341 Carc. 1B Hazard Statement: H350	-

EC/ List No	Substance name	Harmonised classification	Classification in registrations
		Acute Tox. 3 Hazard Statement: H331 (Minimum classification) Aquatic Chronic 2 Statement: H411	
210-566-2	3,5-dinitrotoluene	Index number: 609-052-00-4 Acute Tox. 3 Hazard Statement: H301 (Minimum classification) Acute Tox. 3 Hazard Statement: H311 (Minimum classification) Hazard Category: Repr. 2 Hazard Statement: H361f (Hazard statements H360 and H361 indicate a general concern for effects on both fertility and development: May damage/Suspected of damaging fertility or the unborn child; According to the criteria, the general hazard statement can be replaced by the hazard statement indicating the specific effect of concern in accordance with section 1.1.2.1.2; When the other differentiation is not mentioned, this is due to evidence proving no such effect, inconclusive data or no data and the obligations in Article 4(3) shall apply for that differentiation) STOT RE 2 Hazard Statement: H373 (Minimum classification; No information to prove exclusion of certain routes of exposure) Muta. 2 Hazard Statement: H341 Carc. 1B Hazard Statement: H350 Acute Tox. 3 Hazard Statement: H331 (Minimum classification) Aquatic Chronic 3 Statement: H412	-
210-568-3	5-nitroisophthalic acid	-	Eye Irrit. 2 H319 STOT Single Exp. 3 H335, affected organs: respiratory system [intermediate (active)]
210-581-4	2,5-dinitrotoluene	Index number: 609-055-00-0 Acute Tox. 3 Hazard Statement: H301 (Minimum classification) Acute Tox. 3 Hazard Statement: H311	-

EC/ List No	Substance name	Harmonised classification	Classification in registrations
		(Minimum classification) Hazard Category: Repr. 2 Hazard Statement: H361f (Hazard statements H360 and H361 indicate a general concern for effects on both fertility and development: May damage/Suspected of damaging fertility or the unborn child; According to the criteria, the general hazard statement can be replaced by the hazard statement indicating the specific effect of concern in accordance with section 1.1.2.1.2; When the other differentiation is not mentioned, this is due to evidence proving no such effect, inconclusive data or no data and the obligations in Article 4(3) shall apply for that differentiation) STOT RE 2 Hazard Statement: H373 (Minimum classification; No information to prove exclusion of certain routes of exposure) Muta. 2 Hazard Statement: H341 Carc. 1B Hazard Statement: H350 Acute Tox. 3 Hazard Statement: H331 (Minimum classification) Aquatic Chronic 2 Statement: H411	
215-311-9	nitrotoluene	-	Repr. 2 H361, specific effect:fertility [intermediate (active)] Acute Tox. 2 H330 [intermediate (active)] Carc. 1B H350 [intermediate (active)] Acute Tox. 3 H301 [intermediate (active)] Aquatic Chronic 2 H411 [intermediate (active)] Acute Tox. 3 H311 [intermediate (active)] Acute Tox. 3 H331 [intermediate (active)] STOT Rep. Exp. 2 H373, affected organs: testes, spleen, liver [intermediate (active)]

EC/ List No	Substance name	Harmonised classification	Classification in registrations
			Muta. 1B H340 [intermediate (active)]
217-793-6	methyl 5-nitrohydrogen.isophthalate	-	-
226-134-1	dimethyl 2-nitroterephthalate	-	Aquatic Chronic 2 H411 [intermediate (active)] Aquatic Acute 2 H401 [intermediate (active)]
230-989-6	p-nitrobenzoic acid, compound with 2,2',2''-nitrilotriethanol (1:1)	-	-
236-307-3	dimethyl 5-nitroisophthalate	-	-
242-965-2	ammonium 3-nitrobenzoate	-	Acute Tox. 4 H302 Skin Irrit. 2 H315 Eye Irrit. 2 H319
246-836-1	dinitrotoluene	Index number: 609-007-00-9 Acute Tox. 3 Hazard Statement: H301 (Minimum classification) Acute Tox. 3 Hazard Statement: H311 (Minimum classification) Hazard Category: Repr. 2 Hazard Statement: H361f (Hazard statements H360 and H361 indicate a general concern for effects on both fertility	STOT Rep. Exp. 2 H373 [intermediate (inactive)] Carc. 1B H350 Muta. 2 H341 Repr. 2 H361, specific effect:Suspected of damaging fertility Acute Tox. 3 H301 Acute Tox. 3 H311

EC/ List No	Substance name	Harmonised classification	Classification in registrations
		and development: May damage/Suspected of damaging fertility or the unborn child; According to the criteria, the general hazard statement can be replaced by the hazard statement indicating the specific effect of concern in accordance with section 1.1.2.1.2; When the other differentiation is not mentioned, this is due to evidence proving no such effect, inconclusive data or no data and the obligations in Article 4(3) shall apply for that differentiation) STOT RE 2 Hazard Statement: H373 (Minimum classification; No information to prove exclusion of certain routes of exposure) Muta. 2 Hazard Statement: H341 Carc. 1B Hazard Statement: H350 Acute Tox. 3 Hazard Statement: H331 (Minimum classification) Aquatic Acute 1 Statement: H400 Aquatic Chronic 1 Statement: H410	Acute Tox. 3 H331 STOT Rep. Exp. 2 H373, affected organs: liver Aquatic Acute 1 H400 Aquatic Chronic 1 H410
252-360-5	methyl hydrogen 2-nitroterephthalate	-	Aquatic Chronic 3 H412 [intermediate (active)] Aquatic Acute 3 H402 [intermediate (active)] Eye Irrit. 2 H319 [intermediate (active)]
262-309-9	zinc 5-nitroisophthalate	-	Aquatic Acute 1 H400 Aquatic Chronic 2 H411
423-830-9	1-dimethoxymethyl-2-nitro-benzene	Index number: 601-071-00-6 Aquatic Chronic 2 Statement: H411 Skin Sens. 1 Statement: H317	-

EC/ List No	Substance name	Harmonised classification	Classification in registrations
605-350-3	605-350-3	-	Muta. 2 H341 [intermediate (active)]
606-804-3	606-804-3	-	Eye Irrit. 2 H319 [intermediate (active)] Aquatic Chronic 3 H412 [intermediate (active)]
629-274-5	5-nitro-1H,3H-naphtho[1,8-cd]pyran-1,3-dione	-	STOT Single Exp. 3 H335, affected organs: Respiratory tract [intermediate (active)] Eye Irrit. 2 H319 [intermediate (active)] Skin Irrit. 2 H315 [intermediate (active)]
696-667-6	Reaction mass of (2R,2'R)-2'-methyl spiro[4-azoniabicyclo[2.2.2]octane-2,5'-[1,3]oxathiolane] 4-nitrobenzoate and (2S,2'S)-2'-methyl spiro[4-azoniabicyclo[2.2.2]octane-2,5'-[1,3]oxathiolane] 4-	-	Acute Tox. 4 H302 [intermediate (active)] Carc. 2 H351 [intermediate (active)] Repr. 2 H361 [intermediate (active)] Acute Tox. 4 H332 [intermediate (active)]

EC/ List No	Substance name	Harmonised classification	Classification in registrations
	nitrobenzoate		

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

Data extracted on 16/11/2022

Main types of applications	204-508-5	242-965-2	230-989-6	262-309-9	200-526-2	204-289-6	246-836-1	202-808-0	204-517-4	201-853-3
PC 20: Products such as ph-regulators, flocculants, precipitants, neutralisation agents	f, i, p	f, p	i							
PC 11: Explosives						f, i, p, a	f			
PC 35: Washing and cleaning products	f, i, p									
PC 29: Pharmaceuticals									i	
PC 15: Non-metal-surface treatment products	f, i	f, i								
PC 32: Polymer preparations and compounds					i					
PC 1: Adhesives, sealants				f, i, p						
PC 9a: Coatings and paints, thinners, paint removes				f, i, p, a						
PC 14: Metal surface treatment products	f, i	f, i, p		f, i, p, a						
PC 38: Welding and soldering products, flux products		f, i								
PC 7: Base metals and alloys		i								
PC 21: Laboratory chemicals	f, i, p, a							i, p	i	i, p
PC 19: Intermediate	i				i,		i	i	f, i	i
PC 42: Electrolytes for batteries					f, i, p, c,					

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

All other substances for which uses have been reported are used as intermediate only at industrial sites, often indicated to be handled under strictly controlled conditions. 26 of 35 substances with registered uses are registered as TII/OSII. 6 of 35 have also other uses.

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

Data extracted on 16/11/2022

EC/List number	RMOA	Authorisation		Restriction*	CLH	Actions not under REACH/ CLP
		Candidate list	Annex XIV	Annex XVII	Annex VI (CLP)	
201-329-4		X	X	X	X	Cosmetics[1)]; PIC; National occupational limit values (0.1-0.5 mg/m3 TGG 8h)
201-853-3				X	X	Cosmetics[2)]; National occupational limit values (0.1-12 mg/m3 TGG 8h)
202-808-0					X	National occupational limit values (6-12 mg/m3 TGG 8h)
204-289-6					X	National occupational limit values (0.1-0.5 mg/m3 TGG 8h)
204-450-0	X	X	X	X	X	Cosmetics[2)]
204-517-4						National occupational limit values (1 mg/m3 TGG 8h)
204-517-4						National occupational limit values (1 mg/m3 TGG 8h)
209-025-3				X (entry 9)		
210-013-5				X	X	Cosmetics[2)]
210-106-0				X	X	Cosmetics[2)]; National occupational limit values (0.05 mg/m3 TGG 8h)
210-222-1				X	X	Cosmetics[2)]; National occupational limit values (6 mg/m3 TGG 8h)
210-566-2				X	X	Cosmetics[2)]
210-581-4				X	X	Cosmetics[2)]
215-311-9					X	National occupational limit values (5.5-12 mg/m3 TGG 8h)

EC/List number	RMOA	Authorisation		Restriction*	CLH	Actions not under REACH/ CLP
		Candidate list	Annex XIV	Annex XVII	Annex VI (CLP)	
215-311-9					X	National occupational limit values (5.5-12 mg/m3 TGG 8h)
246-836-1				X	X	Cosmetics[2)]; National occupational limit values (0.15-0.2 mg/m3 TGG 8h)

*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).

All substances restricted are at least restricted under Annex XVII entry 75, *Substances in tattoo inks and permanent make up*. EC 209-025-3 is restricted as part of a group under Annex XVII, entry 9.

1) Cosmetics Regulation Annex III: List of substances which cosmetic products must not contain except subject to the restrictions laid down

Cosmetics Regulation Annex II of prohibited substances in cosmetic products