Assessment of regulatory needs

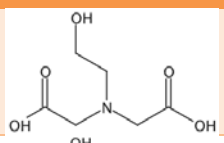
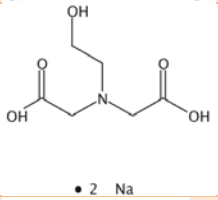
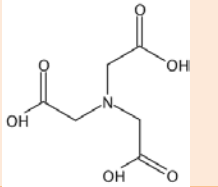
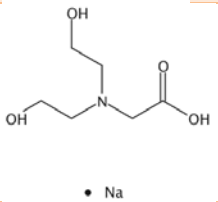
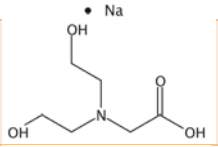
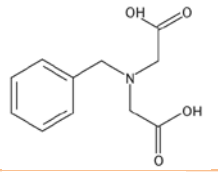
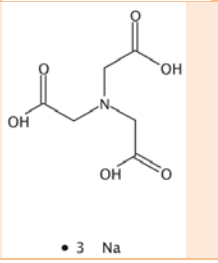
Authority: European Chemicals Agency (ECHA)

Group Name: Polycarboxylic acid monoamines, hydroxy derivatives and their salts with monovalent cations

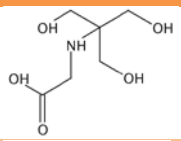
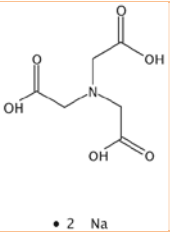
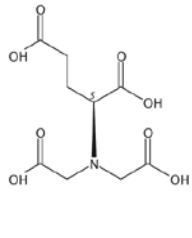
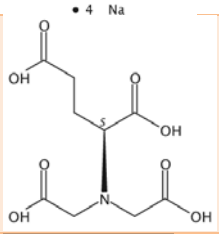
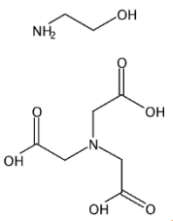
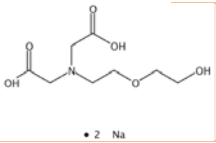
Revision history

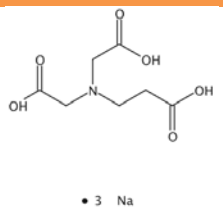
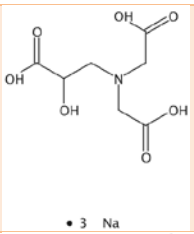
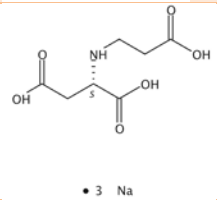
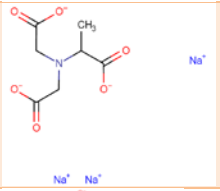
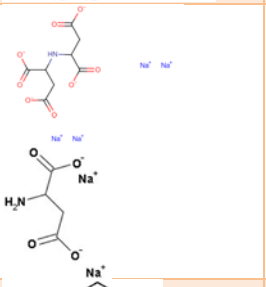
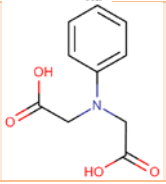
Version	*Date*	*Description*
1.0	15 December 2022	Initial assessment
1.1	16 January 2023	Correction of clerical errors

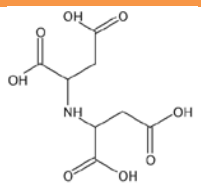
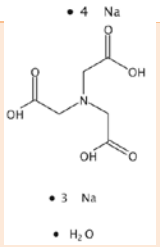
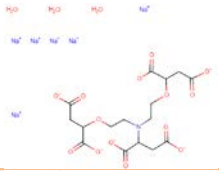
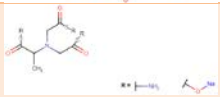
Substances within this group:

EC / List number	CAS number	Substance name and Substance name acronyms	Chemical structures	Registration type (full, OSII or TII, NONS), highest tonnage band among all the registrations (t/y) [1]
202-263-9	93-62-9	2-hydroxyethyliminodi(acetic acid)		Full, Not (publicly) available
205-187-4	135-37-5	Disodium 2-hydroxyethyliminodi(acetate)		Full, 100-1000
205-355-7	139-13-9	2,2',2''-nitrilotriacetic acid (NTA)		Full, 100-1000
205-360-4	139-41-3	sodium [bis(2-hydroxyethyl)amino]acetate		Full, Not (publicly) available
205-755-1	150-25-4	N,N-bis(2-hydroxyethyl)glycine		Full, Not (publicly) available
223-631-5	3987-53-9	N-benzylaminodiacetic acid		OSII or TII
225-768-6	5064-31-3	trisodium 2,2',2''-nitrilotriacetate (Na3NTA)		Full, > 1000

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

EC / List number	CAS number	Substance name and Substance name acronyms	Chemical structures	Registration type (full, OSII or TII, NONS), highest tonnage band among all the registrations (t/y) [1]
227-193-6	5704-04-1	N-[Tris(hydroxymethyl)methyl]glycine		Full, 1-10
239-484-5	15467-20-6	Disodium hydrogen nitrilotriacetate		C&L notification
257-573-7	51981-21-6	tetrasodium (S)-2-[bis(carboxylatomethyl)amino]pentanedioate		Full, > 1000
261-530-8	58976-65-1	2-[bis(carboxymethyl)amino]pentanedioic acid		Full, not (publicly) available
302-766-4	94134-01-7	2,2',2''-nitrilotriacetic acid - 2-aminoethanol (1:3)		Full, not (publicly) available
402-360-8	-	Di-sodium N-carboxymethyl-N-2-(2-hydroxyethoxy)ethylglycinate		NONS
410-710-6	Not (publicly) available	KHMDA	Not (publicly) available	NONS
411-630-4	Not (publicly) available	DIPOTASSIUM MIDA (DIHYDRATE)	Not (publicly) available	NONS

EC / List number	CAS number	Substance name and Substance name acronyms	Chemical structures	Registration type (full, OSII or TII, NONS), highest tonnage band among all the registrations (t/y) [1]
414-070-9	129050-62-0	Trisodium N,N-bis(carboxymethyl)-β-alanine		NONS
414-130-4	119710-96-2	Trisodium N,N-bis(carboxymethyl)-3-amino-2-hydroxypropionate		NONS
422-090-4	172737-80-3	trisodium N-(3-propionato)-.sc.l.sc.-aspartate		Full, not (publicly) available
423-270-5	164462-16-2	Alanine, N,N-bis(carboxymethyl)-, sodium salt (1:3)		Full, > 1000
429-200-1	-	IDS, Na-Salz		Full, not (publicly) available
435-160-4	1137-73-1	Glycine, N-(carboxymethyl)-N-phenyl- (Phenylamino)diacetic acid		NONS

EC / List number	CAS number	Substance name and Substance name acronyms	Chemical structures	Registration type (full, OSII or TII, NONS), highest tonnage band among all the registrations (t/y) [1]
604-420-0	144538-83-0	Aspartic acid, N-(1,2-dicarboxyethyl)-, sodium salt (1:4)		OSII or TII
606-091-9	18662-53-8	Glycine, N,N-bis(carboxymethyl)-, sodium salt, hydrate (1:3:1)		C&L notification
Not (publicly) available	-	Succinic acid derivative, sodium salt	Not publicly available 	Cease manufacture
938-580-0	-	Reaction product of 2-[bis(cyanomethyl)amino]-propanenitrile and sodium hydroxide		OSII or TII

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

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

Foreword

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

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

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

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

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

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

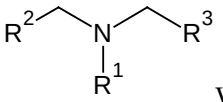
[2] https://echa.europa.eu/understanding-assessment-regulatory-needs

Glossary

ARN	Assessment of Regulatory Needs
CCH	Compliance Check
CLH	Harmonised classification and labelling
CMR	Carcinogenic, mutagenic and/or toxic to reproduction
Dev	Dossier evaluation
ED	Endocrine disruptor
EU RAR	European Union Risk Assessment Report
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 structurally similar substances based on the presence of the monoamino and mono- to polycarboxylic moieties shown in the figure 1 and 2 below. The group contains 25 substances of which 14 have full registrations.



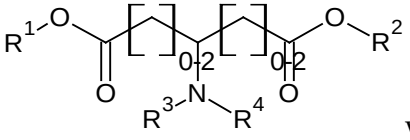
with

R1=

- $-CH_3$
- $-(CH_2)_{1-2}$-COOR with R=H or Na or K
- $-CH_2-CH_2-OH$
- $-CO-NH_2$
- -phenyl
- $-CH_2$-phenyl

R2= -COOR with R=H or Na or K
R3=$-CH_2-CH_2-COOH$

Figure 1



with

R1=H or Na

R2=H or Na

R3=H

R4=

- $-(CH_2)_{1-2}$-COOR with R=H or Na
- $-ROOC-(CH_2)_{1-2}-CH-COOR$ with R=H or Na

Figure 2

Based on information reported in the REACH registration dossiers, a wide variety of uses is reported especially for three substances (EC 257-573-7, 423-270-5 and 225-768-6), as chelating agent in washing and cleaning products, uses in water treatment chemicals, in coatings and paints, thinners, paint removers, in metal and non-metal surface treatment products, in cosmetics and personal care products, uses in biocidal and plant protection products etc. Most substances are registered with high tonnages and used at industrial sites but also by professionals and consumers indicating widespread uses with potential for exposure and releases to the environment. The registrants have indicated that one substance (EC 225-768-

6) has article service life as being used in textiles. For ECs 257-573-7, 423-270-5 and 205-355-7 article service life has been reported in building and construction (stone, plaster, cement, glass, and ceramic articles) by workers (industrial and professional) and other articles used by consumers, respectively.

For some of the substances there are regulatory actions ongoing or concluded. EC 225-768-6 (Na_3NTA) has been assessed in the context of an EU Risk Assessment Report (EU RAR/Annex XV transitional report[3]) contributing to a harmonised classification as Carc. 2, Acute Tox. 4* and Eye Irrit. 2. Furthermore, there are existing harmonised classifications for EC 414-070-9 as Skin Corr. 1B and Aquatic Chronic 3 and for EC 422-090-4 as Eye Dam. 1. An RMOA has been prepared by Ireland (2022) on EC 205-355-7 (NTA) with a proposal for CLH as Carc. 2[4] and an RMOA on EC 225-768-6 (Na_3NTA) prepared by Denmark[5] concluded no further action on top of the already existing harmonised classification as Carc. 2. Under the Detergents Regulation, EC 205-355-7 (NTA) and its salt have a cut-off value of 0,2%, above which there is a need to list the substance in the ingredient datasheet.

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.

[3] EU risk assessment report (europa.eu) / Annex XV transitional report

[4] PACT - Public Activities Coordination Tool - ECHA (europa.eu)

[5] PACT - Public Activities Coordination Tool - ECHA (europa.eu)

2 Justification for the need for regulatory risk management action at EU level

Based on currently available information, there is a need for (further) EU regulatory risk management – restriction for carcinogenicity hazard due to the potential for release/ exposure of all substances in the group.

Based on ECHA's assessment of currently available hazard information, potential hazards were identified for human health.
All group members have the potential to chelate metals although differences in potency are expected.
The available information indicates potential for carcinogenicity, with kidney as the target organ. The nephrocarcinogenic effects of nitrilotriacetic acid (NTA) in rats and mice appear to be related to dose-dependent changes in Zn++ homeostasis seen in animal studies performed with NTA (EC 205-355-7) or Na_3NTA (EC 225-768-6). EC 225-768-6 has been assessed in the context of an EU RAR and it was concluded that the substance is a non-genotoxic carcinogen (target organ kidney/urinary tract)[6], resulting in a harmonised classification as Carc. 2 (concentration limit 5%). In addition, several other group members (EC/List 205-187-4, 205-355-7, 205-360-4, 239-484-5, 302-766-4 and 606-091-9) are self-classified by the registrants and/or notifiers as Carc. 2. For two substances (EC 423-270-5 and 429-200-1), the available data raise some uncertainty as regards carcinogenicity potential. It is assumed that the structural differences comparing to NTA (EC 205-355-7) result in differences in absorption of the substance, the chelation potency and disturbance of metal homeostasis. However, some uncertainty remains on the potential which may need further comparative assessment of the available studies during CLH process. EC 423-270-5 has no harmonised classification and is not self-classified as carcinogen by the registrants and/or notifiers. The substance is widely used in industrial settings, and also many professional and consumer uses are reported by the registrants.

For EC 261-530-8 and its tetrasodium salt EC 257-573-7, there is no available carcinogenicity data to allow conclusion on the carcinogenicity potential. Data from repeated dose toxicity studies indicate the same target system/organ as NTA i.e. kidney. Therefore, carcinogenicity potential cannot be excluded. Substance evaluation is proposed for EC 257-573-7 as the appropriate action to further investigate any carcinogenicity potential of EC 261-530-8 and its tetrasodium salt EC 257-573-7, considering the significant exposure potential for these substances. The carcinogenicity conclusion for EC 257-573-7 would be extrapolated to EC 261-530-8 based on the high structural similarity.

The substance EC 429-200-1[7] did not show clear carcinogenicity potential in a combined chronic and carcinogenicity study (OECD TG 453). However, all group members have common target organ (kidney, urinary tract system) with potential for carcinogenicity based on positive carcinogenicity studies and indications for some substances showing hyperplasia in the same target organ; further comparative assessment of those studies is needed. Due to structural similarity and

[6] Similarly to the conclusions in the EU RAR, the available IARC monograph indicates that "*The nephrocarcinogenic effects of nitrilotriacetic acid in rats and mice appear to be related to dose-dependent changes in Zn++ homeostasis. Although the mechanism of induction of the urothelial effects is not known, they are not related to Zn++ homeostasis but rather correlate with depletion of cellular calcium and possibly the formation of nitrilotriacetic acid-containing microcrystals.*"http://monographs.iarc.fr/ENG/Monographs/vol73/mono73-19.pdf

[7] This substance is not a tertiary amine such as NTA and its salts but consists of main constituents of mono- and secondary amine derivatives.

the common observed effects, the substance is considered as potential Carc. 2 with uncertainty.

In spite of the uncertainties concerning the potential for carcinogenicity for EC 423-270-5, the available information indicates potential for repeated dose toxicity (STOT RE (kidney)) due to findings in a combined chronic and carcinogenicity study (OECD TG 453), showing chronic nephropathy in most males and females with highest gradings in animals treated with top dose, comparing to the positive control substance. In conclusion, the test item showed specific renal toxicity, it was less toxic than the positive substance administered for comparison. Moreover, the test item was not carcinogenic, whereas the positive substance caused tumours in renal pelvis and testes. However, similarity on the target organ (urinary system) for both test and positive control substances, indicates a similar mode of action and potency differences could be taken into account. On that basis, classification potential as Carc. 2 cannot be excluded, with some remaining uncertainty.

Compliance check (CCH) is proposed to be initiated for EC 429-200-1 to fully clarify the potential for mutagenicity and developmental toxicity. The substance is used e.g. in washing and cleaning products, in cosmetics and personal care products also by consumers and professionals. For EC 423-270-5, data generation via CCH is also proposed to fully clarify the developmental toxicity potential as data gaps were identified.

Based on ECHA's assessment of currently available hazard information, no other potential hazards were identified for human health endpoints i.e. for skin sensitisation, mutagenicity, reproductive toxicity and endocrine disruption (ED).

Most substances in the group are unlikely to fulfil the PBT/vPvB screening criteria because they have a low potential for bioaccumulation. These conclusions are based on low log Kow (<1) based on reliable experimental data for most group members present in the dossiers and the fact that the substances are expected to be ionised at environmentally relevant pH 4-9. Based on ECHA's assessment of currently available hazard information for these substances, no potential hazards were identified for aquatic toxicity or ED.

For five substances in the group (EC/List 223-631-5, 414-070-9, 435-160-4, 938-580-0 and succinic acid derivative, sodium salt) potential hazards for the environment were identified. EC 414-070-9 has a harmonised classification as Aquatic Chronic 3. Classification as Aquatic Chronic 3 applies to EC 435-160-4 based on its short-term Daphnia toxicity and lack of ready biodegradability. There are no experimental data available for EC 223-631-5 but since it is structurally very similar to EC 435-160-4, it is likely that EC 223-631-5 also meets the criteria for Aquatic Chronic 3. Classification as Aquatic Chronic 3 applies to succinic acid derivative, sodium salt based on its long-term toxicity to algae and lack of ready biodegradability. EC 938-580-0 is self-classified as Aquatic Chronic 3 although the basis for this is not clear as there is very limited data in the registration dossier.

ECs 223-631-5, 402-360-8, 414-070-9, 435-160-4 and succinic acid derivative, sodium salt are potentially persistent/very persistent and mobile/very mobile. This is based on their lack of ready biodegradability and Log Kow <1. No potential other hazards were identified for the environment.

The first step of the regulatory risk management should the hazard exist, is the confirmation of hazard via **harmonised classification (CLH)** as carcinogenicity (Carc. 2) hazard for all substances within the group. In addition, CLH as STOT RE is proposed for EC 423-270-5 to ensure this hazard is recognised among the registrants and notifiers and necessary risk management measures are undertaken. When preparing the proposals, it may be considered what would be the best way to develop them, for instance whether to make a proposal for the

group of substances, to submit them individually or jointly. CLH will require company level risk management measures (RMM) under the OSH legislation for workers to be in place. In addition, taking into account the reported uses the harmonised classification as Carc. 2 will

- prohibit the substance(s) under the Cosmetic Products Regulation (EC) No 1223/2009 unless an exemption is granted upon assessment of safe use of the substances in cosmetic products by the Scientific Committee on Consumer Safety (SCCS).
- restrict the use of these substances in toys. According to the safety requirements set for chemicals in toys under the Toy Safety Directive (2009/48/EC), substances or mixtures that are classified as CMR category 2 shall not be used in toys, in components of toys or in micro-structurally distinct parts of toys unless they meet the criteria for a derogation. In addition, harmonised classification will facilitate conformity assessment and declaration, particularly when the toy manufacturer bearing obligations is located outside the EU and therefore self-classification in registration dossiers is not applicable to them.
- require that the necessary safety measures are in place for specific sensitive workers, i.e. pregnant women in accordance with Directive 92/85/EEC and young people in accordance with Directive 94/33/EC.

The following consumer and professional uses (e.g. as adhesives, sealants, and paints, thinners, paint removers, washing and cleaning products) are expected to be widespread (at many sites and by many users). Several substances (ECs 205-187-4, 205-355-7, 225-768-6, 257-573-7, 423-270-5) have reported uses with a high potential for exposure for consumers, such as use in cosmetics and personal care products, perfumes and fragrances, adhesives & sealants, lubricants, greases and release products, air care products, washing and cleaning products, polishes and waxes, textile dyes, and impregnating products. For EC 225-768-6 (Na_3NTA), the SCCS has concluded in its opinion[8] in 2010 that its use in cosmetic products is not considered safe, resulting in the inclusion of Na_3NTA in Annex II (entry 1490) of the Cosmetic Products Regulation. Furthermore, in the RMOA by Demark on EC 225-768-6 (Na_3NTA) possible consumer exposure to dust from dishwashing powder containing NTA or use of aerosol spray cans or high-exposure application of aqueous preparations containing NTA may lead to significant inhalations. However, there is some uncertainty remaining on the overall risk for consumers from the use of this substances in the various applications, hence, further investigation on the actual exposure will be needed.

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. Germany has national limit values (OELs) for EC 225-768-6: 2 mg/m^3 (eight hours, inhalable fraction with remark 'Avoid mixed exposures to iron compounds (formation of Fe-NTA)' and 8 mg/m^3 (short term (15 minutes average value), inhalable fraction with remark 'Avoid mixed exposures to iron compounds (formation of Fe-NTA)'. The substance belongs to the group called Nitrilotriacetic acid and its sodium salts as acids[9]. The Annex XV transitional documents prepared under the Existing Substance Regulation (EEC) No 793/93 recommended to establish at community level an occupational exposure limit value for NTA according to Directive

[8] Opinion of the Scientific Committee on Consumer Safety on trisodium nitriloacetate (NTA) (europa.eu)

[9] https://limitvalue.ifa.dguv.de/ Note that this group entry also includes three other substances in this group, namely ECs 205-355-7, 239-484-5 and 606-091-9.

98/24/EEC. It is, however, to be noted that OELs typically do not apply e.g.to self-employed workers.

Consumers may be co-exposed to the substances used by professionals, e.g. house painters.

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

Restriction of consumer uses would ensure that substances are used with concentrations that do not pose a risk. Restriction of professional uses is considered to be efficient and effective to introduce control measures.

Some of the substances do not have currently professional and consumer uses reported in the registration dossiers, and two substances have only C&L notifications, however ECHA considers that they should be considered in the CLH and in the restriction proposal. They have structural similarities with known carcinogenic substances and there is a potential for substitution. EU-wide exposure limit values should be considered as part of the restriction proposal.

Three of the substances (ECs/List 223-631-5, 604-420-0 and 938-580-0) in the group are intermediates with low potential for exposure and/or emissions. Four substances are NONS/have inactive registrations (ECs 402-360-8, 410-710-6, 411-630-4 and 435-160-4, succinic acid derivative, sodium salt/ceased manufacture, ECs 414-070-9 and 414-130-4). Therefore, it is proposed that there is currently no need for EU regulatory risk management with regards to environmental hazards. If the registration status changes for the non-registered substances and the substances subject to NONS registration, data generation and potentially follow-up actions will be re-considered when the assessment will be revisited.

3 Conclusions and actions

The conclusions and actions proposed in the table below are based on the REACH and CLP information available at the time of the assessment by ECHA. The main source of information is the registration dossiers. Relevant public assessments may also be considered. When new information (e.g. on hazards through evaluation processes, or on uses) will become available, the document will be updated, and conclusions and actions revisited

Subgroup name, EC number, substance name	Human Health Hazard	Environmental Hazard	Relevant use(s) & exposure potential	Last foreseen action	Action
202-263-9 **205-187-4** **205-355-7 (NTA)** **205-360-4** **205-755-1** **225-768-6 (Na_3NTA)** **227-193-6** **239-484-5** **257-573-7** **261-530-8** **302-766-4** **606-091-9** **423-270-5** **429-200-1** **223-631-5** **604-420-0** **938-580-0** **402-360-8** **410-710-6** **411-630-4** **435-160-4**	Known or potential hazard for carcinogenicity Known or potential hazard for STOT RE (for EC 423-270-5 and 429-200-1)	No hazard or unlikely hazard Known or potential hazard For aquatic toxicity for ECs/List 223-631-5, 414-070-9, 435-160-4, 938-580-0 and succinic acid derivative, sodium salt. For vPvM for ECs 223-631-5, 402-360-8, 414-070-9, 435-160-4 and succinic acid derivative, sodium salt.	Most of the substances are used by consumers and by professionals as adhesives, sealants, coatings and paints, thinners, paint removes, washing and cleaning products. EC 423-270-5 is widely used in industrial settings, and also many professional and consumer uses are reported by the registrants. EC 429-200-1 is used e.g. in washing and	**Need for EU RRM: Restriction** <u>Justification:</u> The reported consumer and professional uses are widespread (at many sites and many users) with relatively low levels of operational controls and risk management measures but with often frequent exposures with a long duration. Restriction of consumer uses would ensure that substances are used	**First step:** CLH for all substances except EC 257-573-7 and 261-530-8 **In parallel:** CCH for EC 227-193-6, 423-270-5 and 429-200-1 Substance evaluation for EC 257-573-7. Conclusions apply also to EC 261-530-8 **Next steps (if hazard confirmed):** CLH for EC 257-573-7 and 261-530-8

Subgroup name, EC number, substance name	Human Health Hazard	Environmental Hazard	Relevant use(s) & exposure potential	Last foreseen action	Action
414-070-9 **414-130-4** **422-090-4** **Succinic acid derivative, sodium salt**			cleaning products, in cosmetics and personal care products also by consumers and professionals. The substances (EC/List 223-631-5, 604-420-0, 938-580-0, 410-710-6, 411-630-4, 435-160-4, 414-070-9, 414-130-4 and Succinic acid derivative, sodium salt) are either intermediates, NONS or the manufacture has been ceased.	with concentrations that do not pose a risk. Restriction of professional uses is preferred over authorisation as it is considered to be more efficient and effective to introduce controls at the level of placing on the market rather than at the level of uses.	Restriction for all substances

Annex 1: Overview of classifications

Data extracted on 22 April 2022.

EC/ List No	CAS No	Substance name	Harmonised classification	Classification in registrations
202-263-9	93-62-9	2-hydroxyethyliminodi(acetic acid)	-	Acute Tox. 4 H302 Eye Damage 1 H318
205-187-4	135-37-5	disodium 2-hydroxyethyliminodi(acetate)	-	**Carc. 2 H351, specific concentration: >=5** Acute Tox. 4 H302 Eye Irrit. 2 H319
205-355-7	139-13-9	nitrilotriacetic acid	-	**Carc. 2 H351, specific concentration: >=5** Eye Irrit. 2 H319 Acute Tox. 4 H302 **Carc. 2 H351** Eye Irrit. 2A H319
205-360-4	139-41-3	sodium N,N-bis(2-hydroxyethyl)glycinate	-	*Not classified*
205-755-1	150-25-4	N,N-bis(2-hydroxyethyl)glycine	-	*Not classified*
223-631-5	3987-53-9	N-benzylaminodiacetic acid	-	Acute Tox. 4 H302 Acute Tox. 4 H332 Eye Irrit. 2 H319 Skin Irrit. 2 H315 Acute Tox. 4 H312

EC / List No	CAS No	Substance name	Harmonised classification	Classification in registrations
225-768-6	5064-31-3	trisodium nitrilotriacetate	*Acute Tox. 4* H302* *Eye Irrit. 2 H319* ***Carc. 2 H351***	**Carc. 2 H351, specific concentration: >=5** Acute Tox. 4 H302 Eye Irrit. 2 H319
227-193-6	5704-04-1	N-(tri(hydroxymethyl)methyl)glycine	-	*Not classified*
239-484-5	15467-20-6	disodium hydrogen nitrilotriacetate	-	-
257-573-7	51981-21-6	tetrasodium N,N-bis(carboxylatomethyl)-L-glutamate	-	*Not classified*
261-530-8	58976-65-1	N,N-bis(carboxymethyl)-L-glutamic acid	-	Eye Irrit. 2 H319
302-766-4	94134-01-7	N,N-bis(carboxymethyl)glycine, compound with 2-aminoethanol (1:3)	-	**Carc. 2 H351** Acute Tox. 4 H302 Eye Irrit. 2 H319
410-710-6	Not (publicly) available	KHMDA	-	-
411-630-4	Not (publicly) available	DIPOTASSIUM MIDA (DIHYDRATE)	-	Eye Irrit. H319
414-070-9	129050-62-0	trisodium N,N-bis(carboxymethyl)-β-alanine	*Skin Corr. 1B H314* *Aquatic Chronic 3 H412*	-
422-090-4	172737-80-3	trisodium N-(3-propionato)-.sc.l.sc.-aspartate	*Eye Dam. 1H318*	Eye Dam. 1 H318

EC / List No	CAS No	Substance name	Harmonised classification	Classification in registrations
423-270-5	-	Alanine, N,N-bis(carboxymethyl)-, sodium salt (1:3)	-	Not classified
429-200-1	-	IDS, Na-Salz	-	Not classified
604-420-0	144538-83-0	Aspartic acid, N-(1,2-dicarboxyethyl)-, sodium salt (1:4)	-	*Not classified*
606-091-9	18662-53-8	Glycine, N,N-bis(carboxymethyl)-, sodium salt, hydrate (1:3:1)	-	-
Not (publicly) available	-	Succinic acid derivative, sodium salt	-	-
938-580-0	-	Reaction product of 2-[bis(cyanomethyl)amino]-propanenitrile and sodium hydroxide	-	Met. Corr. 1 H290 Skin Corr. 1A H314 Aquatic Chronic 3 H412

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

Data extracted on 22 April 2022.

Main types of applications structured by product or article types	EC 202-263-9	EC 205-187-4	EC 205-355-7	EC 205-360-4	EC 205-755-1	EC 223-631-5	EC 225-768-6	EC 227-193-6	EC 257-573-7	EC 261-530-8	EC 302-766-4	EC 422-090-4	EC 423-270-5	EC 429-200-1	List 604-420-0	Not (publicly) available	List 938-580-0
PC 1: Adhesives, sealants			**C**				**C**		F, I, **P**, **C**				F, I, **P**, **C**				
PC 2: Adsorbents							F, I, **P**		F, I, **P**				F, I, **P**				
PC 3: Air care products			**C**				F, I, **P**, **C**		F, I, **P**, **C**				F, I, **P**				
PC 4: Anti-freeze and de-icing products							F, I, **P**		F, I, **P**				F, I, **P**				
PC 7: Base metals and alloys									F, I, **P**				F, I, **P**				
PC 8: Biocidal products (e.g. disinfectants, pest control)			**C**				**C**		F, I, **P**, **C**				F, I, **P**, **C**				

Main types of applications structured by product or article types	EC 202-263-9	EC 205-187-4	EC 205-355-7	EC 205-360-4	EC 205-755-1	EC 223-631-5	EC 225-768-6	EC 227-193-6	EC 257-573-7	EC 261-530-8	EC 302-766-4	EC 422-090-4	EC 423-270-5	EC 429-200-1	List 604-420-0	Not (publicly) available	List 938-580-0
PC 9a: Coatings and paints, thinners, paint removes			I, **C**				F, I, **P**, **C**		F, I, **P**, **C**				F, I, **P**, **C**				
PC 9b: Fillers, putties, plasters, modelling clay			**C**				**C**		F, I, **P**, **C**				F, I, **P**, **C**				
PC 9c: Finger paint									F, I, **P**, **C**				F, I, **P**, **C**				
PC 11: Explosives									F, I, **P**				F, I, **P**				
PC 12: Fertilisers									F, I, **P**, **C**	F, I, **P**			F, I, **P**, **C**				
PC 13: Fuels									F, I, **P**				F, I, **P**				
PC 14: Metal surface treatment products			**C**				F, I, **P**, **C**		F, I, **P**, **C**	F, I, **P**			F, I, **P**, **C**	F			
PC 15: Non-metal-surface treatment products			**C**				F, I, **P**, **C**		F, I, **P**, **C**	F, I, **P**			F, I, **P**, **C**				
PC 16: Heat transfer fluids									F, I, **P**				F, I, **P**				
PC 17: Hydraulic fluids							F, I, **P**		F, I, **P**		F		F, I, **P**				
PC 18: Ink and toners									F, I, **P**, **C**				F, I, **P**, **C**				

Main types of applications structured by product or article types	EC 202-263-9	EC 205-187-4	EC 205-355-7	EC 205-360-4	EC 205-755-1	EC 223-631-5	EC 225-768-6	EC 227-193-6	EC 257-573-7	EC 261-530-8	EC 302-766-4	EC 422-090-4	EC 423-270-5	EC 429-200-1	List 604-420-0	Not (publicly) available	List 938-580-0
PC 19: Intermediate			I			I	F, I, **P**	I	F, I, **P**	F, I, **P**			F, I, **P**		F		I
PC 20: Products such as ph-regulators, flocculants, precipitants, neutralisation agents			I, **P**		F, I, **P**		F, I, **P**	F, I, **P**	F, I, **P**, **C**	F, I, **P**			F, I, **P**, **C**				
PC 21: Laboratory chemicals	F	F, **P**	F, I, **P**		F		F, I, **P**	F, I, **P**	F, I, **P**	F, I, **P**			F, I, **P**				
PC 23: Leather treatment products									F, I, **P**, **C**	F, I, **P**			F, I, **P**, **C**				
PC 24: Lubricants, greases, release products									F, I, **P**, **C**	F, I, **P**			F, I, **P**, **C**				
PC 25: Metal working fluids							F, I, **P**		F, I, **P**	F, I, **P**			F, I, **P**				
PC 26: Paper and board treatment products							F, I, **P**		F, I, **P**, **C**				F, I, **P**, **C**	F		I	
PC 27: Plant protection products									F, I, **P**				F, I, **P**				

Main types of applications structured by product or article types	EC 202-263-9	EC 205-187-4	EC 205-355-7	EC 205-360-4	EC 205-755-1	EC 223-631-5	EC 225-768-6	EC 227-193-6	EC 257-573-7	EC 261-530-8	EC 302-766-4	EC 422-090-4	EC 423-270-5	EC 429-200-1	List 604-420-0	Not (publicly) available	List 938-580-0
PC 28: Perfumes, fragrances									F, I, **P**, **C**				F, I, **P**, **C**				
PC 29: Pharmaceuticals								F, I, **P**	F, I, **P**, **C**				F, I, **P**, **C**				
PC 30: Photo-chemicals			**C**				F, I, **P**, **C**		F, I, **P**, **C**			I	F, I, **P**, **C**				
PC 31: Polishes and wax blends		F, **P**, **C**	**C**				**C**		F, I, **P**, **C**	F, I, **P**			F, I, **P**, **C**				
PC 32: Polymer preparations and compounds							F, I, **P**	F, I, **P**	F, I, **P**, **C**	F, I, **P**			F, I, **P**, **C**				
PC 33: Semiconductors							F, I, **P**		F, I, **P**	F, I, **P**			F, I, **P**				
PC 34: Textile dyes, and impregnating products			**C**				F, I, **P**, **C**, **A**		F, I, **P**, **C**	F, I, **P**			F, I, **P**, **C**				
PC 35: Washing and cleaning products		F, **P**, **C**	**C**	F			F, I, **P**, **C**		F, I, **P**, **C**	F, I, **P**			F, I, **P**, **C**	F, I, **P**, **C**			
PC 36: Water softeners							F, I, **P**		F, I, **P**, **C**	F, I, **P**			F, I, **P**, **C**	F			
PC 37: Water treatment chemicals							F, I, **P**		F, I, **P**, **C**	F, I, **P**			F, I, **P**, **C**	F, I, **P**			

Main types of applications structured by product or article types	EC 202-263-9	EC 205-187-4	EC 205-355-7	EC 205-360-4	EC 205-755-1	EC 223-631-5	EC 225-768-6	EC 227-193-6	EC 257-573-7	EC 261-530-8	EC 302-766-4	EC 422-090-4	EC 423-270-5	EC 429-200-1	List 604-420-0	Not (publicly) available	List 938-580-0
PC 38: Welding and soldering products, flux products									F, I, **P**	F, I, **P**			F, I, **P**				
PC 39: Cosmetics, personal care products									F, I, **P**, **C**				F, I, **P**, **C**	F, **C**			
PC 40: Extraction agents							F, I, **P**		F, I, **P**	F, I, **P**			F, I, **P**	F, I, **P**			
PC41: Oil and gas exploration or production products							I		I		I						
PC42: Electrolytes for batteries									I								

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

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

Data extracted on 22 April 2022.

EC / List number	RMOA	Authorisation		Restriction*	CLH	Actions not under REACH / CLP
		Candidate list	Annex XIV	Annex XVII	Annex VI (CLP)	
205-355-7	YES					
225-768-6	YES				YES	EU RAR (2005)/Annex XV transitional report (2008)
414-070-9					YES	
422-090-4					YES	
429-200-1					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).
**CLH intention by Germany (DE).

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