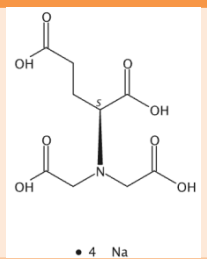
Justification Document for the Selection of a CoRAP Substance

EC/List number	CAS RN	Public Substance name	Chemical structure	Registration type
257-573-7	51981-21-6	Tetrasodium N,N-bis(carboxylatomethyl)-L-glutamate		Full

Authority: France

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Revision history

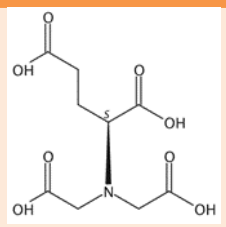
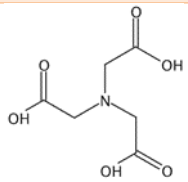
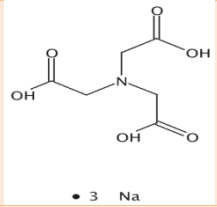
Version	*Date*

Cover Note

This document has been prepared by the evaluating Member State given in the CoRAP update.

1. Background

1.1 Analogue substances

EC/List number	CAS RN	Public Substance name	Chemical structure
261-530-8	58976-65-1	N,N-bis(carboxymethyl)-L-glutamic acid	
205-355-7	139-13-9	nitrilotriacetic acid (NTA)	
225-768-6	5064-31-3	trisodium nitrilotriacetate (Na_3NTA)	

ECHA has grouped together structurally similar substances based on the presence of the monoamino and mono- to polycarboxylic moieties. Based on the hazard and use screening, ECHA has published an Assessment of Regulatory Needs (ARN) on a group of Polycarboxylic acid monoamines, hydroxy derivatives and their salts with monovalent cations in 2022[1]

Tetrasodium N,N-bis(carboxylatomethyl)-L-glutamate (EC 257-573-7), hereafter 'the Substance', is the tetrasodium salt of N,N-bis(carboxymethyl)-L-glutamic acid (EC 261-530-8). Therefore, these two substances are structurally very similar and information on the Substance can be extrapolated to EC 261-530-8.

Additionally, the nitrilotriacetic acid (NTA, EC 205-355-7) and its tetrasodium salt trisodium nitrilotriacetate (Na_3NTA, EC 225-768-6) for which information on their nephrocarcinogenic effects is available can be also considered as analogue substances since substances in the group are all structurally similar and may have similar hazard properties.

[1] https://echa.europa.eu/documents/10162/45dde3f2-73a7-e456-078c-7021a30da8cd

1.2 Overview of ongoing or completed other REACH and CLP processes & other EU legislation

EC/ List number	Evaluation			CLH	Restriction	Authorisation
	CCH	TPE	Previously on CoRAP	Annex VI (CLP)	Annex XVII*	Candidate List/ Annex XIV
257-573-7	X	-	-	-	-	-

**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)*

EC/ List number	Other EU legislation	Previous legislation	Stockholm convention	Other
	PPP/ BPR	NONS/ RAR	POP	(e.g. UNEP)
257-573-7	-	-	-	-

2. Classification

You can find information on classification in the ECHA C&L Inventory database, which includes both harmonised classification (when available) and the notified self-classifications. (http://echa.europa.eu/web/guest/information-on-chemicals/cl-inventory-database]. The CLP Regulation and all published ATPs are available on ECHA website: http://echa.europa.eu/web/guest/regulations/clp/legislation .

EC/ List No	CAS RN	Public Substance name	Harmonised classification	Classification in registrations	Classification in C&L notifications (*)
257-573-7	51981-21-6	Tetrasodium N,N-bis(carboxylatomethyl)-L-glutamate	None	Not classified	Eye Irrit. 2; H319 [78] Met. Corr. 1; H290 [56] STOT SE 3 ; H335 [55] Skin Irrit. 2; H315 [23] Skin Corr. 1A; H314 [3] Eye Dam. 1; H318 [3] Not classified [142]

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

3. Tonnage and uses

3.1 Aggregated Tonnage

EC/ List No	Aggregated tonnage (as per ECHA dissemination website*)[2][3]
257-573-7	≥ 10 000 < 100 000

** The total tonnage band has been calculated by excluding the intermediate uses,- See also the Manual for Dissemination and Confidentiality under REACH (section 2.6.11): https://echa.europa.eu/documents/10162/22308542/manual_dissemination_en.pdf/7e0b87c2-2681-4380-8389-cd655569d9f0*

3.2 Overview of the Uses

The Substance is used as a chelating agent, cleaning agent, complexing agent, processing aid and as a corrosion inhibitor. It is used in various product types including air care products, biocides, perfumes and fragrances, cosmetics and personal care products, textile dyes, washing and cleaning products, ink and toners.

Main types of applications	EC 257-573-7 Key information
Industrial use	The Substance is used in mining and building & construction work. It is used for manufacture or chemicals and mineral products (e.g. plasters, cement).
Professional use	Similar uses as described above for industrial use
Consumer Use	The Substance is used in washing & cleaning products, polishes and waxes, air care products and biocides (e.g. disinfectancts, pest control products)
Article service life	The Substance can be found in products with material based on stone, plaster, cement, glass or ceramic (e.g. dishes, pots/pans, food storage containers, construction and isolation material)
Intermediate use (if TII)	-
Formulation	Formulation of mixtures and formulation in materials.

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

[3] Substance Infocard on ECHA's dissemination website accessed on 22 September 2023. NB. REACH registration data on ECHA's webpage has not been updated since 19 May 2023.

4. Justification for inclusion on the CoRAP

4.1 Legal basis

☒ Article 44(2)[4]

☐ Article 45(5)[5]

4.2 Identification of initial grounds of concern

Hazard-based concerns	
Suspected CMR	☒ Carcinogenic ☐ Mutagenic ☐ Reproductive toxicant
Potential ED	☐ Human Health ☐ Environment
Suspected Sensitiser	☐ Respiratory ☐ Skin
Suspected PBT/ vPvB Suspected PMT/ vPvM	☐ Persistent ☐ Bioaccumulative ☐ Mobile ☐ Toxic (as defined in section 4.3 below) ☐ very Persistent ☐ very Bioaccumulative ☐ very Mobile
Other suspected human health hazard(s) (e.g. STOT RE)	☐ (as defined in section 4.3 below)
Other suspected environmental hazard(s)	☐ (as defined in section 4.3 below)
Exposure/ risk-based concerns	
Wide dispersive use	☒
Consumer use	☒
Exposure of workers	☒
Exposure of sensitive populations	☐
Exposure of environment	☒
Cumulative exposure	☐
High RCR	☐
High (aggregated) tonnages	☒
Others (to be specified)	☐

[4] "The Agency shall use the criteria in paragraph 1 […]. Substances shall be included if there are grounds for considering (either on the basis of a dossier evaluation carried out by the Agency or on the basis of any other appropriate source, including information in the registration dossier) that a given substance constitutes a risk to human health or the environment."

[5] "A Member State may notify the Agency at any time of a substance not on the Community rolling action plan, whenever it is in possession of information which suggests that the substance is a priority for evaluation. […]".

4.3 Justification of the concern(s) – to be clarified under Substance evaluation

Existing data supporting the hazard-based concern and other relevant information to justify the inclusion in CoRAP

The available information indicates potential for carcinogenicity for Polycarboxylic acid monoamines, hydroxy derivatives and their salts with monovalent cations, including the Substance, as described in the ARN report[6]. Kidney is the target organ.

There are no carcinogenicity study(ies) available for the Substance or EC 261-530-8. However, data from repeated dose toxicity studies indicate the same target system/organ as for NTA (EC 205-355-7) and Na_3NTA (EC 225-768-6), i.e. the kidney. Nephrocarcinogenic effects of NTA have been observed in rats and mice. NTA has self-classification as Carc. 2 and Na_3NTA a harmonized classification as Carc. 2. Therefore, carcinogenicity potential for the Substance cannot be excluded based on the available information and the structural similarities.

Additionally, the Substance has a high variety of (wide dispersive) uses including consumer and professional uses, a very high tonnage and therefore high exposure potential. This further supports the need to clarify the concern for carcinogenicity.

A non-genotoxic mode of action has been proposed for Na_3NTA. It seems to be the underlying mechanism also for the potential carcinogenicity of the Substance based on the available negative *in vitro* and *in vivo* mutagenicity studies. Although no hyperplasia or pre-neoplastic findings were reported in the available 90-d repeated dose toxicity study on the Substance, effects in the kidneys were observed. In females at 1000 mg/kg/day, kidney weight and kidney to body weight ratio were increased at the end of the recovery period, but not at the end of the treatment period.

The carcinogenicity conclusion for the Substance would be extrapolated to EC 261-530-8 based on the obvious structural similarity, i.e. the Substance is a tetrasodium salt of EC 261-530-8.

Information to be potentially requested

Further tests may be required to elucidate the concern identified, for instance carcinogenicity study. However, the need and the type of information needed will be assessed further as also other concerns may be identified during the evaluation.

[6] https://echa.europa.eu/documents/10162/45dde3f2-73a7-e456-078c-7021a30da8cd

***Possible follow-up** (demonstrating the improvement of risk management measures)*

EC/ List number	Harmonised C&L	SVHC	Restriction	Authorisation	Other
257-573-7	☒	☐	☒	☐	☐