Justification for the selection of a substance for CoRAP inclusion

Substance Name (Public Name):	3-aminopropyldimethylamine
Chemical Group:	aliphatic diamines
EC Number:	203-680-9
CAS Number:	109-55-7
Submitted by:	Umweltbundesamt GmbH on behalf of the Austrian Competent Authority (Austrian Federal Ministry of Agriculture, Forestry, Environment and Water Management)
Published:	26/03/2014

Note

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

Contents

1 IDENTITY OF THE SUBSTANCE

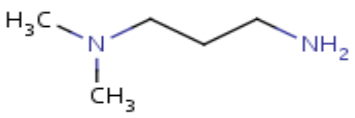
1.1 Other identifiers of the substance

Table 1: Substance identity

EC name:	3-aminopropyldimethylamine
IUPAC name:	N,N-dimethylpropane-1,3-diamine
Index number in Annex VI of the CLP Regulation	612-061-00-6
Molecular formula:	C5H14N2
Molecular weight or molecular weight range:	102,18
Synonyms/Trade names:	*1,3-Propanediamine;* *N,N-dimethyl-1-(Dimethylamino)-3-aminopropane;* *1-Amino-3-dimethylaminopropane;* *3-(Dimethylamino)-1-propanamine;* *3-(Dimethylamino)-1-propylamine;* *3-(Dimethylamino)propylamine;* *3-Amino-1-(dimethylamino)propane;* *N,N-Dimethyl-1,3-diaminopropane;* *N,N-Dimethyl-1,3-propanediamine;* *N,N-Dimethyl-1,3-propylenediamine;* *N,N-Dimethyl-N-(3-aminopropyl)amine;* *N,N-Dimethylpropylenediamine;* *N,N-Dimethyltrimethylenediamine;* *N-Dimethyltrimethylenediamine;* *Propylamine, 3-(N,N-dimethylamino)-gamma-(Dimethylamino)propylamine*

Type of substance ☒ Mono-constituent ☐ Multi-constituent ☐ UVCB

Structural formula:



1.2 Similar substances/grouping possibilities

--

2 CLASSIFICATION AND LABELLING

2.1 Harmonised Classification in Annex VI of the CLP

Table 3: Harmonised classification of 3-aminopropyldimethylamine according to the entry in table 3.1 in Annex VI of CLP

Index No	Inter-national Chemical Identifica-.ion	Classification		Labelling			Spec. Conc. Limits, M-factors	Notes
		Hazard Class and Category Code(s)	Hazard statement code(s)	Pictogram, Signal Word Code(s)	Hazard statement code(s)	Suppl. Hazard statement code(s)		
612-061-00-6	3-aminopropyl-dimethylamine N,N-dimethyl-1,3-diaminopropane	Flam. Liq. 3 Acute Tox. 4 * Skin Corr. 1B Skin Sens. 1	H226 H302 H314 H317	GHS07 GHS02 GHS05 Dgr	H226 H302 H314 H317			

2.2 Self classification

- In the registration

The registrant classifies the substance according to CLP/GSH system as skin sensitisation 1B and additionally with:
Eye Dam. 1;H318 and Acute Tox. 4; H312.

The other classifications are in accordance with the harmonized classification (Annex VI of Regulation (EC) No 1272/2008 (CLP Regulation).

- The following hazard classes are in addition notified among the aggregated self classifications in the C&L Inventory:

Table 4 depicts additional notified classifications summarized in the C&L inventory including information on the classification and labeling and the specific concentration limits.

Table 4: Additional notified classification and labelling according to CLP criteria (beside of harmonized classification and the ones of registrants)

Classification		Labelling			Spec. Conc. Limits, M-factors	Notes
Hazard Class and Category Code(s)	Hazard statement code(s)	Pictogram, Signal Word Code(s)	Hazard statement code(s)	Suppl. Hazard statement code(s)		
Acute Tox. 3 Acute Tox. 3 Met. Corr. 1	H311 H331 H290	GHS06 GHS01 GHS08	H311 H331 H290	--	--	--

2.3 Proposal for Harmonised Classification in Annex VI of the CLP

None

3 INFORMATION ON AGGREGATED TONNAGE AND USES

From ECHA dissemination site		
☐ 1 – 10 tpa	☐ 10 – 100 tpa	☐ 100 – 1000 tpa
☐ 1000 – 10,000 tpa	☐ 10,000 – 100,000 tpa	☐ 100,000 – 1,000,000 tpa
☐ 1,000,000 – 10,000,000 tpa	☐ 10,000,000 – 100,000,000 tpa	☐ > 100,000,000 tpa
☒ 10,000 + tpa (e.g. 10+ ; 100+ ; 10,000+ tpa)		☒ Confidential
Some member(s) in the joint submission has claimed the tonnage confidential.		

☒ Industrial use	☒ Professional use	☐ Consumer use	☐ Closed System

3-aminopropyldimethylamine has a wide dispersive use and is manufactured at high tonnages. Workers, as well professionals are expected to be exposed regarding the identified uses.
Uses like use as additive for coatings and cement/concrete imply potential relevant exposure of professionals and general public. Exposure of consumers was excluded by the registrants.

4 JUSTIFICATION FOR THE SELECTION OF THE CANDIDATE CoRAP SUBSTANCE

4.1 Legal basis for the proposal

☒ Article 44(2) (refined prioritisation criteria for substance evaluation)

☐ Article 45(5) (Member State priority)

4.2 Selection criteria met (why the substance qualifies for being in CoRAP)

☐ Fulfils criteria as CMR/ Suspected CMR

☒ Fulfils criteria as Sensitiser/ Suspected sensitiser

☐ Fulfils criteria as potential endocrine disrupter

☐ Fulfils criteria as PBT/vPvB / Suspected PBT/vPvB

☒ Fulfils criteria high (aggregated) tonnage (*tpa > 1000*)

☒ Fulfils exposure criteria

☐ Fulfils MS's (national) priorities

4.3 Initial grounds for concern to be clarified under Substance Evaluation

Hazard based concerns		
CMR ☐C ☐M ☐R	Suspected CMR[1] ☐C ☐M ☐R	☐ Potential endocrine disruptor
☒ Sensitiser	☐ Suspected Sensitiser[1]	
☐ PBT/vPvB	☐ Suspected PBT/vPvB[1]	☐ Other (please specify below)
Exposure / risk based concerns		
☒ Wide dispersive use	☐ Consumer use	☐ Exposure of sensitive populations
☐ Exposure of environment	☒ Exposure of workers	☐ Cumulative exposure
☐ High RCR	☒ High (aggregated) tonnage	☐ Other (please specify below)

Hazard based concerns:

Sensitising properties:

3-aminopropyldimethylamine is harmonised classified according to the entry in table 3.1 in Annex VI of CLP- regulation for skin sensitisation category 1.

Study outcomes for the skin sensitising endpoint (e.g., local lymphnode assay, guinea pig maximization test) give evidence that the substance might be sub-categorised into skin sensitisation category 1B. The registrant classifies 3-aminopropyldimethylamine as skin sensitisation category 1B. Further evaluation is needed to clarify this issue.

The registrant declares that no information regarding the respiratory sensitisation properties is available.

Within the SEV process it should be further evaluated wether the substance might have sensitising properties to the respiratory tract (human data, animal data, QSAR, in vitro test methods, read across). Likewise, the physchemical properties (e.g., vapor pressure) should be considered in the evaluation regarding its sensitisation potential.

For sensitizing substances a qualitative risk management should be applied. Additionally, if applicable it is proposed to set a DNEL to judge the remaining/residual likelihood of risks after risk management measures and operational conditions are implemented.

In the current version of the CSR no additional quantitative assessment has been applied for the dermal exposure route (details see: exposure based concern, dermal route).

Furthermore, there are evidences from human studies that 3-aminopropyldimethylamine impurities in liquid soaps, shampoos and other cleansing products lead to skin sensitisation (e.g., Knopp E. et al., 2008; Hervella et al., 2006; Moreau and Sasseville, 2004).

[1] CMR/Sensitiser: known carcinogenic and/or mutagenic and/or reprotoxic properties/known sensitising properties (according to CLP harmonized or registrant self-classification or CLP Inventory)
Suspected CMR/Suspected sensitiser: suspected carcinogenic and/or mutagenic and/or reprotoxic properties/suspected sensitising properties (not classified according to CLP harmonized or registrant self-classification)Suspected PBT: Potentially Persistent, Bioaccumulative and Toxic

CMR evaluation:

Several bacterial reverse mutation assays (ames assays) have been conducted (partly under GLP), which do not indicate any positive results. The testing dosis was up to 3900 µg/plate and in one study all five tester strains (including TA 100) have been used.

Furthermore, three in vitro tests (two gene mutation, one chromosome aberration assay) do not demonstrate any adverse effects. An in vivo micronucleus assay used as key study by the registrant has not shown any genotoxic potential. Toxicity has been present only at the highest dosis tested (100mg/kg bw).

No data on carcinogenicity are available.

No neo-plastic lesions have been identified in the short term repeated dose toxicity study (sub-acute, 28 days, OECD Guideline 407) carried out with Wistar rats (male/female).

Regarding the enpoint reproductive toxicity a developmental screening test has been conducted according to the OECD testguideline 421. No effects on reproductive performance or fertility by administering 3-aminopropyldimethylamine (0, 10, 50, 200 mg/kg bw) have been identified.

No further reproductive toxicity tests have been performed.

Justification for the data waiving has been inter alia due to absence of significant exposure (no chronic exposure, no wide dispersive use for worker and consumer). For several applications, e.g. use of 3-aminopropyldimethylamine in coatings or in similar products, this statement of no significant exposure is considered to be questionable at this stage. Therefore, the justification for waiving and the concern on this endpoint needs to be clarified.

Additional concern: chronic aquatic toxicity

No data are currently available on chronic aquatic toxicity. The data for acute toxicity revealed an 48 h EC50 of 59.46 mg/l for Daphnia magna and a 96h LC50 value of 122 mg/L for freshwater fish.

In a 72-hour static test with the green alga Scenedesmus subspicatus according to the German Industrial Standard Test Guideline DIN 38412, an EbC50 of 53.5 mg/L was estimated for the biomass, related to the nominal concentration.

Using ECOSAR (v1.00; performed by evaluating MS) a QSAR value of 0.021 mg/l was obtained for chronic fish toxicity, giving some alert for this endpoint.

Exposure based concern

3-aminopropyldimethylamine has a wide dispersive use and is manufactured at high tonnages. Workers, as well professionals are expected to be exposed regarding the identified uses. Applications like the use as additive for coatings and cement/concrete imply potential relevant exposure of professionals and general public. Exposure of consumers was excluded by the registrants.

Nevertheless, it needs to be clarified, if products containing this substance like coatings (e.g., paints) or concrete/cement are only applied industrially or professionally or if relevant release of this substance from endproducts or treated articles might be a concern for the general public.

Dermal exposure:

The substance is classified as corrosive and as sensitizer. The assessment was done in a qualitative way by the registrants. It is mentioned inter alia that the substance requires a stringent use of appropriate chemical resistant gloves, protective clothing and suitable eye protection, if any skin/eye contact is foreseen. Based on that, the intensity of exposure was considered to be very low by the registrants. Regarding uses like use as additive for coatings (brush, roller, spraying) and cement/concrete, low dermal exposure is considered to be a questionable statement, as the provided exposure scenarios lack significant details for estimating the expected and realistic conditions (e.g., concentration of substance in products). Furthermore, it is questionable to expect that the proposed personal protective equipment exclude fully any relevant dermal exposure. Therefore, the potential concern of hazardous effects via dermal exposure requires clarification (e.g., via a quantitative assessment, specification of use pattern).

Inhalation exposure:

Regarding the provided human exposure assessment, ECETOC TRA was applied for deriving the corresponding exposure. ECETOC TRA is considered to be a conservative Tier 1 exposure estimation tool in principle tending rather to overestimate than to underestimate most exposure scenarios. The derived RCR values in the risk characterization section are all below one but some are near to one. Especially situations like use of coating (painting, brushing, spraying) or cement/concrete might differ significantly case by case. Therefore, more details and potential refinements are expected for substantiating that potential risk can be excluded under the defined conditions of use.

Environmental exposure:

The environmental exposure assessment was waived as the substance is not classified for aquatic toxicity. Neveretheless, no data are currently available on chronic aquatic toxicity. Using ECOSAR (v1.00; performed by evaluating MS) a QSAR value of 0.021 mg/l was obtained for chronic fish toxicity, providing some alert for this endpoint. Based on the outcome of the intended evaluation covering the fate & behavior and the ecotoxicological section, it will be assessed, if an environmental exposure assessment might be required for assessing the risk for the environment.

Conclusion:

During the substance evaluation it should be verified, if the applied risk management measures are sufficient to protect workers from sensitizing potential of 3-dimethylaminopropylamine. It has to be clarified, if consumers are also exposed and if further risk mitigation options have to be installed. Furthermore, it should be clarified during the SEV process, if further testing for the endpoint(s) repeated dose toxicity, developmental toxicity, carcinogenicity and/or chronic aquatic toxicity is needed.

References:

Knopp E; Watsky K. (2008) Eyelid dermatitis: contact allergy to 3-(dimethylamino)propylamine. Dermatitis. 2008 Nov-Dec; 19(6):328-33.

Hervella M. et al. (2006) Contact allergy to 3-dimethylaminopropylamine and cocamidopropyl betaine. Actas Dermosifiliogr. 2006, Apr; 97(3):189-95.

Moreau L, Sasseville D. (2004). Allergic contact dermatitis from cocamidopropyl betaine, cocamidoamine, 3-(dimethylamino)propylamine, and oleamidopropyl dimethylamine: co-reactions or cross-reactions? Dermatitis. 2004, Sep; 15(3):146-9.

4.4 Other completed / ongoing regulatory processes that may affect suitability for substance evaluation

☐ Compliance check, Final decision	☐ Dangerous substances Directive 67/548/EEC
☐ Testing proposal	☐ Existing Substances Regulation 793/93/EEC
☐ Annex VI (CLP)	☐ Plant Protection Products Regulation 91/414/EEC
☐ Annex XV (SVHC)	☐ Biocidal Products Directive 98/8/EEC ; Biocidal Product Regulation (Regulation (EU) 528/2012)
☐ Annex XIV (Authorisation)	☐ Other (provide further details below)
☐ Annex XVII (Restriction)	
Please provide further details when relevant.	

4.5 Preliminary indication of information that may need to be requested to clarify the concern

☒ Information on toxicological properties	☐ Information on physico-chemical properties
☐ Information on fate and behaviour	☒ Information on exposure
☒ Information on ecotoxicological properties	☒ Information on uses
☐ Information ED potential	☐ Other (provide further details below)

4.6 Potential follow-up and link to risk management

☒ Harmonised C&L	☐ Restriction	☐ Authorisation	☐ Other (provide further details)