baua:
Bundesanstalt für Arbeitsschutz
und Arbeitsmedizin
Federal Institute for Occupational
Safety and Health

Justification Document for the Selection of a CoRAP Substance

Substance Name (public name):	Antimony trichloride
EC Number:	233-047-2
CAS Number:	10025-91-9
Authority:	Germany
Date:	20/03/2018

Cover Note

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

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1 IDENTITY OF THE SUBSTANCE

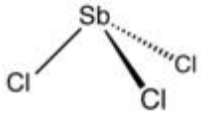
1.1 Other identifiers of the substance

Table: Other Substance identifiers

EC name (public):	Antimony trichloride
IUPAC name (public):	Antimontrichlorid
Index number in Annex VI of the CLP Regulation:	051-001-00-8
Molecular formula:	Cl_3Sb $SbCl_3$
Molecular weight or molecular weight range:	228.11 g/mol
Synonyms:	Antimony trichloride antimony(3+) ion trichloride antimony(3+) trichloride Antimony(III) chloride antimony-trichloride- trichlorostibane

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

Structural formula:



1.2 Similar substances/grouping possibilities

Substance	read-across applied by registant(s)
Reference: diantimony trioxide (Sb_2O_3); EC-No.: 215-175-0, CAS-No.: 1309-64-4	yes
antimony metal (Sb), EC-No.: 231-146-5, CAS-No.: 7440-36-0	no

2 OVERVIEW OF OTHER PROCESSES / EU LEGISLATION

Table: Completed or ongoing processes

RMOA	☐ Risk Management Option Analysis (RMOA)	
REACH Processes	Evaluation	☐ Compliance check, Final decision
		☐ Testing proposal
		☐ CoRAP and Substance Evaluation
	Authorisation	☐ Candidate List
		☐ Annex XIV
	Restric -tion	☐ Annex XVII[1]
Harmonised C&L	☒ Annex VI (CLP) (see section 3.1)	
Processes under other EU legislation	☐ Plant Protection Products Regulation Regulation (EC) No 1107/2009	
	☐ Biocidal Product Regulation Regulation (EU) 528/2012 and amendments	
Previous legislation	☒ Dangerous substances Directive Directive 67/548/EEC (NONS)	
	☒ Existing Substances Regulation Regulation 793/93/EEC (RAR/RRS)	
(UNEP) Stockholm convention (POPs Protocol)	☐ Assessment	
	☐ In relevant Annex	
Other processes / EU legislation	☒ Other (provide further details below)	

[1] Please specify the relevant entry.

Further details	**Cosmetics Regulation (EC) 1223/2009:** Entry 40: Antimony and its compounds listed in "LIST OF SUBSTANCES PROHIBITED IN COSMETIC PRODUCTS"

3 HAZARD INFORMATION (INCLUDING CLASSIFICATION)

3.1 Classification

3.1.1 Harmonised Classification in Annex VI of the CLP

Table: Harmonised classification

Index No	International Chemical Identification	EC No	CAS No	Classification		Spec. Conc. Limits, M-factors	Notes
				Hazard Class and Category Code(s)	Hazard statement code(s)		
051-001-00-8	Antimony trichloride	233-047-2	10025-91-9	Skin Corr. 1B Aquatic Chronic 2	H314 H411	STOT SE 3; H335: C≥5 %	

3.1.2 Self classification

- In the registration:

  Skin Corr. 1B H314
  Aquatic Chronic 2 H411

- The following hazard classes are in addition notified among the aggregated self classifications in the C&L Inventory (number of notifiers in brackets):

  Eye Dam. 1 H318 (1)
  STOT SE 3 H335 (lungs) (1)
  Muta. 2 H341 (1)
  Carc. 1B H350 (1)

3.1.3 Proposal for Harmonised Classification in Annex VI of the CLP

Currently, no proposal for harmonized classification and labelling is available.

4 INFORMATION ON (AGGREGATED) TONNAGE AND USES[2]

4.1 Tonnage and registration status

Table: Tonnage and registration status

From ECHA dissemination site *		
☒ Full registration(s) (Art. 10)	☐ Intermediate registration(s) (Art. 17 and/or 18)	
Tonnage band (as per 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
☐ <1 . . . . . >+ tpa (e.g. 10+ ; 100+ ; 10,000+ tpa)		☐ Confidential

*the total tonnage band has been calculated by excluding the intermediate uses, for details see the Manual for Dissemination and Confidentiality under REACH Regulation (section 2.6.11):

https://echa.europa.eu/documents/10162/22308542/manual_dissemination_en.pdf/7e0b87c2-2681-4380-8389-cd655569d9f0

4.2 Overview of uses

Table: Uses

Part 1:

☒ Manufacture	☐ Formulation	☒ Industrial use	☐ Professional use	☐ Consumer use	☐ Article service life	☐ Closed system

Part 2:

	Use(s)
Uses as intermediate	
Formulation	-

[2] *The dissemination site was accessed in November 2017.*

Uses at industrial sites	Industrial use of antimony trichloride in the production of antimony metal (PROC 22: Potentially closed processing operations with minerals/metals at elevated temperature)
Uses by professional workers	-
Consumer Uses	
Article service life	

5. JUSTIFICATION FOR THE SELECTION OF THE CANDIDATE CoRAP SUBSTANCE

5.1. Legal basis for the proposal

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

☒ Article 45(5) (Member State priority)

5.2. 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

5.3. 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[3]	
☐ 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)

[3] 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

Antimony trichloride is prone to hydrolytic transformation depending on the physiologica media and its properties (e.g., temperature, pH). In water, for example, $SbCl_3$ is transformed according to the following reaction: $SbCl_3 + H_2O \rightarrow SbOCl + 2\ HCl$. Due to the formation of HCl, $SbCl_3$ is classified as Skin Corr. 1b. Thus, local irritant/corrosive effects can be expected in the upper respiratory tract in inhalation experiments due to HCl. However, effects of $SbCl_3$ and/or of the III-valent transformation product antimony oxychloride (SbOCl) could occur below the threshold for corrosive effects. Toxic effects of SbOCl are likely, considering the toxicological profile of other III-valent antimony compounds, in particular diantimony trioxide. Part of the substance evaluation would be to decide whether a significant fraction of $SbCl_3$ particles is inhalable. According to Pubchem, exposure to fumes of antimony compounds originating from antimony trichloride is possible (https://pubchem.ncbi.nlm.nih.gov/compound/24814#section=Related-Compounds). Moreover, inhalation exposure of rats to antimony trichloride showed that primary sites of antimony deposition other than lung were whole blood, spleen, heart and other highly vascularized organs, demonstrating both, systemic bioavailability of antimony after inhalation of antimony trichloride as well as that antimony trichloride dust particles reach the lung (Clayton, 1994; https://pubchem.ncbi.nlm.nih.gov/compound/24814#section=Pharmacology-and-Biochemistry).

Currently, diantimony trioxide is classified as Carc. 2, H351. A new NTP study confirmed lung tumourigenic effects in mice and rats in a 2-year inhalation study (https://ntp.niehs.nih.gov/ntp/about_ntp/bsc/2016/december/meetingmaterials/draftantimonytrioxide_508.pdf) indicating that a reclassification for carcinogenicity may be necessary. Both, diantimony trioxide and antimony trichloride (as well as its transformation products), contain III-valent Sb, indicating a similar toxicological profile. *In vitro* studies indicate a potential for genotoxic effects of antimony trichloride similar to diantimony trioxide (both positive in the non-guideline rec assay and sister chromatide exchange assay – the latter equivalent to OECD TG 479; Huang et al. 1998, Kuroda et al. 1991). Furthermore, oral exposure of mice to antimony trichloride was associated with a dose-related increase of DNA-strand breaks and slowed DNA repair processes (https://toxnet.nlm.nih.gov/cgi-bin/sis/search2/r?dbs+hsdb:@term+@rn+@rel+10025-91-9). Increased incidence of DNA-strand breaks have also been observed in the NTP study after inhalation of diantimony trioxide. These information support the assumption that both compounds have similar toxicological properties. Since the III-valent Sb moiety and/or the Sb ion after dissolution is supposed to be responsible for reactivity as well as toxic effects of Sb containing compounds, a possible cumulative exposure to the toxicophore through various III-valent Sb compounds cannot be excluded.

Additionally, antimony metal caused embryotoxic effects in a developmental toxicity study (OECD TG 414, https://echa.europa.eu/registration-dossier/-/registered-dossier/16124/7/9/3/?documentUUID=e07399e8-ca2a-44f8-b66d-a6a8e6636e97). Antimony metal is oxidized to the III-valent diantimony trioxide under physiological conditions suggesting that III-valent Sb compounds are causing the observed effects. Additionally, oral antimony trichloride exposure of rats (both prenatal and postnatal) caused a significant reduction in body weight of pups at the higher dose level (10 mg/L in drinking water, Rossi et al. 1987). Another study indicates that prenatal and/or postnatal exposure of rats to antimony trichloride interferes with vasomotor reactivity development in rats (Marmo et al. 1987). Accordingly, there is also a concern for potential systemic developmental effects of antimony trichloride.

Therefore, in the substance evaluation it will be assessed if a read across to diantimony trioxide and/or antimony metal is justified and thus if antimony trichloride may also have cancerogenic and developmental effects.

Exposure

As indicated already above, exposure to fumes of antimony compounds originating from antimony trichloride is possible and inhalation exposure of rats to antimony trichloride showed that primary sites of antimony deposition other than lung were whole blood, spleen, heart and other highly vascularized organs, demonstrating both, systemic bioavailability of antimony after inhalation of antimony trichloride as well as that antimony trichloride dust particles reach the lung. Since the III-valent Sb moiety and/or the Sb ion after dissolution is supposed to be responsible for reactivity as well as toxic effects of Sb containing compounds, a possible cumulative exposure to the toxicophore through various III-valent Sb compounds cannot be excluded.

References:

Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New York, NY: John Wiley & Sons Inc., 1993-1994., p. 1905.

Huang, H., Shu, S.C., Shih, J.H., Kuo, C.J. and Chiu, I.D. (1998) Antimony trichloride induces DNA damage and apoptosis in mammalian cells. Toxicology 129(2-3), 113-123.

Kuroda, K., Endo, G., Okamoto, A., Yoo, Y.S. and Horiguchi, S. (1991) GENOTOXICITY OF BERYLLIUM, GALLIUM AND ANTIMONY IN SHORT-TERM ASSAYS. Mutation Research 264(4), 163-170.

Marmo, E., Matera, M.G., Acampora, R., Vacca, C., De Santis, D., Maione, S., Susanna, V., Chieppa, S., Guarino, V., Servodio, R., Cuparencu, B. and Rossi, F. (1987) Prenatal and postnatal metal exposure: Effect on vasomotor reactivity development of pups. Experimental research with antimony trichloride, thallium sulfate, and sodium metavanadate. Current Therapeutic Research - Clinical and Experimental 42(5), 823-838.

Rossi, F., Acampora, R., Vacca, C., Maione, S., Matera, M.G., Servodio, R. and Marmo, E. (1987) Prenatal and postnatal antimony exposure in rats: effect on vasomotor reactivity development of pups. Teratogenesis, Carcinogenesis, and Mutagenesis 7(5), 491-496.

5.4. 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)

In the substance evaluation it will be assessed if a read across to diantimony trioxide and/or antimony metal is justified and thus if antimony trichloride may also have cancerogenic and developmental effects. Information on toxicological properties is needed in order to assess the read across.

Due to the low tonnage only very limited information on the uses exist. If the substance evaluation indicates that risks for workers arise, further information on the uses might be necessary.

5.5. Potential follow-up and link to risk management

☒ Harmonised C&L	☐ Restriction	☐ Authorisation	☐ Other (provide further details)
Depending on the outcome of the substance evaluation and further studies a harmonized classification.			