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):	2,5,7,10,11,14-hexaoxa-1,6-distibabicyclo[4.4.4]tetradecane
EC Number:	249-820-2
CAS Number:	29736-75-2
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

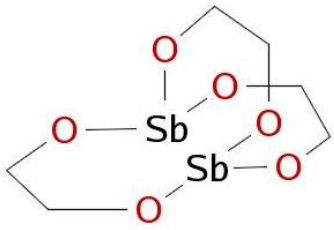
1.1 Other identifiers of the substance

Table: Other Substance identifiers

EC name (public):	2,5,7,10,11,14-hexaoxa-1,6-distibabicyclo[4.4.4]tetradecane
IUPAC name (public):	2,5,7,10,11,14-Hexaoxa-1,6-distibabicyclo[4.4.4]tetradecane
Index number in Annex VI of the CLP Regulation:	
Molecular formula:	C6H12O6Sb2
Molecular weight or molecular weight range:	423.68 g/mol
Synonyms:	Diantimony tris (ethylene glycolate) Antimony triglycolate Antimony glycolate Antimony tris(ethylene glycoxide)

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)		
051-003-00-9	antimony compounds with the exception of the tetroxide (Sb_2O_4), pentoxide (Sb_2O_5), trisulphide (Sb_2S_3), pentasulphide (Sb_2S_5) and those specified elsewhere in this Annex			Acute Tox. 4 * Acute Tox. 4 * Aquatic Chronic 2	H302 H332 H411		

3.1.2 Self classification

- In the registration (number of notifiers in brackets):

  Aquatic Chronic 2 H411 (13)

  Acute Tox. 4 H302, H332 (13)

- The following hazard classes are in addition notified among the aggregated self classifications in the C&L Inventory:
  - Skin Irrit. 2 H315 (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

[2] *The dissemination site was accessed January 2018.*

Part 2:

	Use(s)
Uses as intermediate	
Formulation	This substance is used in the following products/activities related to: - formulation of polymers. - transfer of chemicals. - formulation in materials, in the production of articles and as processing aid.
Uses at industrial sites	This substance is used in the following products/activities - polymers. - manufacture of plastic products - transfer of chemicals - low energy manipulation of substances bound in materials or articles. Production/use of long-life materials (e.g. metal, wooden and plastic construction and building materials) and indoor use in long-life materials (e.g. flooring, furniture, toys, construction materials, curtains, foot-wear, leather products, paper and cardboard products, electronic equipment)
Uses by professional workers	This substance is used in the following activities or processes at workplace: the low energy manipulation of substances bound in materials or articles. Use of long-life materials (e.g. metal, wooden and plastic construction and building materials) and indoor use in long-life materials (e.g. flooring, furniture, toys, construction materials, curtains, foot-wear, leather products, paper and cardboard products, electronic equipment).
Consumer Uses	
Article service life	The substance is used in the following articles used by consumers: Fabrics, textiles and apparel, leather articles, paper articles, plastic articles

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

Diantimony tris (ethylene glycolate) is a white crystalline powder which decomposes slowly in contact with air by reaction with moisture, liberating n-butanol vapour and antimony oxide fume (https://euon.echa.europa.eu/lt/web/guest/registration-dossier/-/registered-dossier/13268/9; http://www.gelest.com/wp-content/uploads/PAN-040-_PolyANTIMONY-ETHYLENE-GLYCOXIDE_GHS-US_English-US.pdf). Toxic effects of antimony glycolate 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 antimony glycolate particles is inhalable. The Sb-containing decomposition products are likely to be inhalable.

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 diantimony tris (ethylene glycolate) (as well as its transformation products), contain III-valent Sb, indicating a similar toxicological profile. With regard to opther Sb containing compounds, 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 different III-valent Sb compounds have similar toxicological properties. Thus, similar toxicological properties of diantimony tris (ethylene glycolate) are also plausible. 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). Again, these information support the assumption that different III-valent Sb compounds have similar toxicological properties. Accordingly, there is also a concern for potential developmental effects of diantimony tris (ethylene glycolate).

In addition to this, several chronic inhalation studies with Sb2O3 resulted in lung toxicity in rats (e.g., impaired lung clearance, inflammation, fibrosis, increased lung weights) and inflammatory reactions in the lungs were also observed in an acute toxicity inhalation study. Thus, there is a concern for specific target organ toxicity which might require further action.

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 diantimony tris (ethylene glycolate) may also have cancerogenic and developmental effects.

References:

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 diantimony tris (ethylene glycolate) may also have cancerogenic and developmental effects. Information on toxicological properties is needed in order to assess the read across.

If the substance evaluation reveals that risks for workers, further information on exposure and uses has to be provided.

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 might be necessary.