Justification for the selection of a substance for CoRAP inclusion

Substance Name (Public Name):	Sodium dithionite
Chemical Group:	--
EC Number:	231-890-0
CAS Number:	7775-14-6
Submitted by:	AT
Date:	17/03/2015

Note

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

Contents

1 IDENTITY OF THE SUBSTANCE

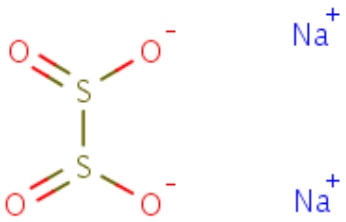
1.1 Other identifiers of the substance

Table 1: Substance identity

EC name:	Sodium dithionite
IUPAC name:	disodium dithionite
Index number in Annex VI of the CLP Regulation	016-028-00-1
Molecular formula:	$H_2O_4S_2$ 2Na
Molecular weight or molecular weight range:	174.108
Synonyms/Trade names:	*Disodium dithionate, Disodium dithionite, Dithionous acid, disodium salt, Sodium dithionate, Sodium hydrosulfite, Disodium hydrosulfite, Dithionous acid, disodium salt, Sodium sulfoxylate, Hydrosulfite R Conc, Blankit, V-Brite B, Vatrolite*

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

Structural formula:



1.2 Similar substances/grouping possibilities

Examples of similar substances are listed in Table below:

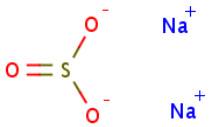
Table: Examples of similar substances

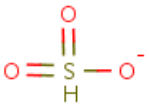
Public name:	*Sodium sulphite*	*Sodium hydrogen-sulphite*	*Sodium metabisulphite (Disodium disulfite)***
EC No.	*231-821-4*	*231-548-0*	*231-673-0*
CAS No.	*7757-83-7*	*7631-90-5*	*7681-57-4*
Index number in Annex VI of the CLP Regulation	*--*	*016-064-00-8*	*016-063-00-2*
Molecular formula:	*$H_2O_3S.2Na$*	*$HO_3S.Na$*	*$H_2O_5S_2.2Na$*
Molecular weight (range)	*126.043*	*104.061*	*190.107*

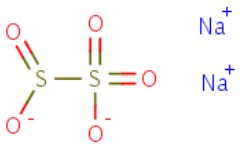
***CoRAP 2014 (Hungary)*

Structural formula:

Sodium sulphite: *Sodium hydrogen sulphite:* *Sodium metabisulphite:*







2 CLASSIFICATION AND LABELLING

2.1 Harmonised Classification in Annex VI of the CLP

The harmonised classification of sodium dithionite according to the entry in table 3.1 in Annex VI of CLP is given in Table 2.

Table 2: 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)		
016-028-00-1	sodium dithionite sodium hydrosulphite	231-890-0	7775-14-6	Self-heat. 1 Acute Tox. 4 *	H251 H302 EUH031*	--	--

*Supplementary hazard statement code

2.2 Self classification

- In the registration

  The substance has been self-classified as follows:

  Xi; R36 Irritant; Irritating to eyes (Directive 67/548/EEC criteria), Eye Irrit. 2; H319 (GHS)

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

  Following self classifications were identified in the C&L Inventory not covered by the harmonized classification (GHS).

  Eye Irrit. 2; H319

  Skin Irrit. 2, H315

  Aquatic Chronic 3, H412

2.3 Proposal for Harmonised Classification in Annex VI of the CLP

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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
☐ <1 . . . . . >+ tpa (e.g. 10+ ; 100+ ; 10,000+ tpa)		☐ Confidential

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

The substance is used in the photographic, pharmaceutical, textile/leather, rubber/plastic, paper and pulp industry (bleaching), food industry, mining, and metal industry. Furthermore, the substance is used for water and surface treatment.

Following consumer uses have been registered: consumer use of textile cleaning products; consumer use of ink eraser containing sodium dithionite

Examples of technical function of the substance are:
Food processing aid, bleaching agents, processing aid, plating agents and metal surface treating agents, pH-regulating agents

The substance is used in following articles: rubber articles, plastic articles, fabrics, textiles and apparel, leather articles, paper articles.

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)	

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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[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)

[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

Sodium dithionite has strong reducing properties and is chemically unstable in the presence of water and oxygen. The substance decomposes rapidly especially under acidic conditions to sulfite, SO_2 and sodium thiosulfate. Therefore, the registrants applied a read across approach in order to close data gaps and took into consideration toxicological data of e.g., sodium sulfite (CAS Nr. 7757-83-7), sodium hydrogen sulfite (CAS Nr. 7631-90-5) and disodium disulfite (synonym: sodium metabisulfite; CAS Nr. 7681-57-4).

Applicability of the read across approaches needs to be assessed potentially in detail.

Acute Toxicity, Irritation & sensitization properties

An oral acute toxicity test is available for sodium dithionite and a LD50 value of about 2500 mg/kg bw was determined. No dermal or inhalative study for sodium dithionite has been submitted by the registrants. A read across approach to sodium sulfite (CAS: 7757-83-7) has been applied. For dermal toxicity an LD50 > 2000 mg/kg bw has been deduced and for the inhalative route an LC50 value of > 5.5 mg/l has been determined.

Read across approach with sodium sulfite and potassium sulfite has been applied to fill the data gap for the **skin irritating** properties. The registrants concluded based on the read across approach that sodium dithionite does not possess skin irritation properties. However, in the OECD SIDS (2004) a study has been referenced in which mild skin irritation properties of 80% aqueous suspension of sodium dithionite was observed. The study has been evaluated to be reliable with restrictions (Klimisch 2). The registrant submitted two in vivo studies with New Zealand White rabbits, which are guideline conform. Sodium dithionite possesses irritation properties to the eyes and sodium thionite is self-classified by the registrants with Eye Irrit. 2 based on CLP criteria. The appropriate classification of **irritating effects shall be verified within substance evaluation**, also taking into account the study cited in the OECD SIDS (2004).

A local lymph node assay according to guideline OECD Guideline 429 (Skin Sensitisation: Local Lymph Node Assay - LLNA) has been submitted, which indicates that sodium dithionite has no sensitizing properties. No animal data regarding respiratory sensitizing properties have been reported. Sodium dithionite might be decomposed to sulfur dioxide, which induces respiratory irritation and also leads to bronchospasm in exposed humans. The hypersensitivity reaction is known as "sulfite asthma". It has been stated that about 10 % of asthmatic humans are reportedly sulfite- or SO2-sensitive. There are no reports available on the respiratory sensitisation properties of sodium dithionite, but an allergic potential for allergoid reactions in sensitive individuals following oral or inhalation exposure has been assumed (OECD SIDS, 2004).

Therefore, the sensitization properties should also be determined in the highlight of decomposition products (sulfite) and human data reported in the OECD SIDS (OECD SIDS, 2004). It has to be verified, if workers or consumers are exposed to sulfite (and in which magnitude) and toxicological data on the decomposition product should be considered in the evaluation.

Mutagenicity and Carcinogenicity

In vitro & in vivo mutagenicity studies

The registrants submitted *in vitro* bacterial gene mutation assay (AMES assay), with sodium dithionite and two with the read across substance (disodium disulfite). No mutagenic activity has been detected in the bacterial reverse mutation assay.

An *in vitro* cell gene mutation assay has been conducted with the read across substance disodium disulfite. There have been ambiguous test results within the first experiment, whereas the subsequent experiments with identical test conditions did not indicate any adverse outcome.

In vivo chromosome aberration test (micronucleus assay), in which sodium sulfite has been administered with sodium sulfite in mice has been carried out. No chromosomal aberration has been detected. There has been no indication for mutagenic effects.

However, study outcome from a study carried out in 2002 (not mentioned by registrants) demonstrates that a mixture 1:3 of sodium hydrogen sulfite (CAS: 7631-90-5) and sodium sulfite (CAS: 7757-83-7) in saline was positive in a bone-marrow mouse micronucleus assay after intraperitoneal injection. (Meng, Sang and Zhang, 2002).

Carcinogenicity studies

Three carcinogenicity studies are included carried out with dipotassium disulfide (two studies carried out with rats) and disodium disulfide (carried out with mice). Test substances have been applied in drinking water or feed in concentrations up to 2%. No carcinogenic effects are reported due to substance exposure.

There is evidence from *in vivo* animal experiments carried out with read across substances (dipotassium disulfide and potassium sulfite) that these substances have tumor promoting effects (e.g., for glandular stomach carcinogenesis).

Moreover, there is also evidence from human studies (pulp and paper mill workers) that sulfite and sulfate exposure correlates with an increased risk for stomach cancer. Higher incidence of leukemia and soft tissue sarcomas, kidney, rectal cancer, pancreas cancer, lymphosarcoma, Hodgkin disease, as well as brain tumors was observed in individual studies.

A further in-depth evaluation of the human studies together with evidence of *in vivo* animal experiments with the read across substance has to be carried out. It should be evaluated if the substance possesses tumor promoting effects.

Evidence for carcinogenicity from repeated dose toxicity has been indicated by the scenario code Sev HH 62 (IT Screening Approach ECHA). The repeated dose toxicity study indicates a hyperplastic and inflammatory changes in the fore-stomach and gastric lesions. The studies have been carried out with read across substances. For most of the repeated dose toxicity studies no NOAEL or NOAEC could be identified. The appropriate NOAEL for repeated dose toxicity should be identified within substance evaluation, upon careful reviewing the studies. Furthermore, it has to be clarified, if the observed adverse adverse effects on the gastric system warrants classification and if these lesions and changes might also be part of the tumorigenic (tumour promoting) effects of the substance.

The IARC concluded in 1992 that degradation products of dithionite (such as sulfites, hydrogen sulfites and metabisulfites, and sulfur dioxide) are not classifiable for their carcinogenicity to huamas (group 3). Newer studies have not been considered in the IARC evaluation of 1992.

Developmental toxicity

Several studies with read across substances have been submitted. The applied read across should be verified and also the reliability of these studies. Due to the registrant's statement, no adverse effects have been observed within these studies.

DNEL derivation approach

The DNEL derivation approach seems to be elaborated and the applied assessment factors justified. It has to be verified within the substance evaluation if the proper point of departure has been chosen, depending also on the evaluation of the hazard properties of sodium dithionite.

Environmental Hazard/risk assessment

In the C&L inventory 28 notifiers (> 6% of notifiers) notified sodium dithionite with an Aquatic Chronic Cat. 3 classification. The registrants do not classify for this endpoint and provide no basis for such a classification in their provided data. A check regarding the potential availability of data proving an aquatic classification does seem warranted.

The assessment of transformation products like sulphur dioxide is currently scarcely reflected in the registration dossier. Here, potentially more data should be included into the dossier.

Exposure

Sodium dithionite is manufactured and used in many sectors and at high tonnages. Many industrial, professional and consumer uses exist. Referring to the harmonized classification and the self classification given in the registration dossiers, this substance is considered to be minor toxic. Therefore, corresponding exposure and risk assessments are based on this idea of handling a low hazardous chemical. As severe toxicological effects are identified as potential concerns, it needs to be assessed, if uses are safe, risk management measures are sufficient, if toxicological concerns are substantiated substance during evaluation of this substance. More data on exposure will be required in this case.

Conclusion:

Sodium dithionite as a candidate substance to be included in the CoRAP list, because of properties related to human health hazards (tumour promoter effects of read across substances, higher cancer incidences in sulphite/sulfate exposed workers, irritant effects, sulfite asthma).

References:

OECD SIDS (2004). Sodium dithionite. CAS 7775-14-6. Initial Assessment Report for SIAM 19. Berlin, Germany, 19-22 October 2004

Meng Z., Sang, N., and Zhang B. (2002). Effects of derivates of sulfur dioxide on micronuclei formation in mouse bone marrow cells in vivo, Bull. Environm. Contam. Toxicol. 69, 257-264

IARC, 1992: Occupational exposures to mists and vapours from strong inorganic acids and other industrial chemicals. IARC Monographs on the evaluation of carcinogenic risks to humans. Vol. 54, 131-188, International Agency for Research on Cancer, Lyon.

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)

5.5 Potential follow-up and link to risk management

☒ Harmonised C&L	☐ Restriction	☒Authorisation	☒ Other (provide further details)
In the case the above mentioned concerns are confirmed a harmonized C&L or an authorization might be required.			