SUBSTANCE EVALUATION

CONCLUSION DOCUMENT

as required by REACH Article 48

for

Disodium disulphite

EC No 231-673-0

CAS No 7681-57-4

Evaluating Member State(s): Hungary

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Evaluating Member State Competent Authority

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Year of evaluation in CoRAP: 2014

Member State concluded the evaluation without the need to ask further information from the registrants under Article 46(1) decision.

Please find (search for) further information on registered substances here:

http://echa.europa.eu/web/guest/information-on-chemicals/registered-substances

DISCLAIMER

The Conclusion document has been prepared by the evaluating Member State as a part of the substance evaluation process under the REACH Regulation (EC) No 1907/2006. The information and views set out in this document are those of the author and do not necessarily reflect the position or opinion of the European Chemicals Agency or other Member States. The Agency does not guarantee the accuracy of the information included in the document. Neither the Agency nor the evaluating Member State nor any person acting on either of their behalves may be held liable for the use which may be made of the information contained therein. Statements made or information contained in the document are without prejudice to any further regulatory work that the Agency or Member States may initiate at a later stage.

Foreword

Substance evaluation is an evaluation process under REACH Regulation (EC) No. 1907/2006. Under this process the Member States perform the evaluation and ECHA secretariat coordinates the work.

In order to ensure a harmonised approach, ECHA in cooperation with the Member States developed risk-based criteria for prioritising substances for substance evaluation. The list of substances subject to evaluation, the Community rolling action plan (CoRAP), is updated and published annually on the ECHA web site[1].

Substance evaluation is a concern driven process, which aims to clarify whether a substance constitutes a risk to human health or the environment. Member States evaluate assigned substances in the CoRAP with the objective to clarify the potential concern and, if necessary, to request further information from the registrant(s) concerning the substance. If the evaluating Member State concludes that no further information needs to be requested, the substance evaluation is completed. If additional information is required, this is sought by the evaluating Member State. The evaluating Member State then draws conclusions on how to use the existing and obtained information for the safe use of the substance.

This Conclusion document, as required by the Article 48 of the REACH Regulation, provides the final outcome of the Substance Evaluation carried out by the evaluating Member State. In this conclusion document, the evaluating Member State shall consider how the information on the substance can be used for the purposes of identification of substances of very high concern (SVHC), restriction and/or classification and labelling. With this Conclusion document the substance evaluation process is finished and the Commission, the registrants of the substance and the competent authorities of the other Member States are informed of the considerations of the evaluating Member State. In case the evaluating Member State proposes further regulatory risk management measures, this document shall not be considered initiating those other measures or processes.

[1] http://echa.europa.eu/regulations/reach/evaluation/substance-evaluation/community-rolling-action-plan

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1. CONCERNS SUBJECT TO EVALUATION

Disodium disulphite was originally selected for substance evaluation in order to clarify these suspected risks:

- There is a study available on the substance that suggests mutagenic property. In the in vitro study the substance induced chromosome aberration and sister chromatid exchange in human lymphocytes dose-dependently.
- The self-classification in the C&L inventory suggests that the substance also has sensitising properties.
- Taking into consideration certain hazard classes given as self-classification in the C&L Inventory, certain ways of exposure may raise a concern. In particular the new hazard classes and some of the uses ground the concern of environmental exposure and the possible exposure of sensitive population.

During the evaluation also other concerns were identified. The additional concerns were:

- Self-classification notified in the C&L Inventory suggests that the substance may indicate that the current harmonized classification of the substance as Acute tox. 4 is not correct, but more severe classification may be justified.
- Self-classification notified in the C&L Inventory indicated that more detailed evaluation of the possible irritating properties is necessary.
- The hazard class of STOT RE 1; H372: Causes damage to organs has been notified among the aggregated self-classifications in the C&L Inventory, and the evaluating Member State considered that this raised some concern about this endpoint.
- Considering the above specified concern on mutagenicity, the evaluating Member State decided to have a prudent approach and examine in more detail also the carcinogenicity of disodium disulphite.
- The issue of reproductive toxicity was also raised as an additional concern for disodium disulphite. Several fertility studies are available, and some indications were present that suggested some potential effects of the substance and warranted a thorough inspection of the submitted data.
  Developmental toxicity studies have also been evaluated in detail to identify any further potential effects of disodium disulphite.

2. CONCLUSION OF SUBSTANCE EVALUATION

The available information on the substance and the evaluation conducted has led the evaluating Member State to the following conclusions, as summarised in the table below.

Conclusions	**Tick box**
Need for follow up regulatory action at EU level	
Need for Harmonised classification and labelling	x
Need for Identification as SVHC (authorisation)	
Need for Restrictions	
Need for other Community-wide measures	
No need for regulatory follow-up action	

3. JUSTIFICATION FOR THE CONCLUSION ON THE NEED OF REGULATORY RISK MANAGEMENT

3.1. NEED FOR FOLLOW UP REGULATORY ACTION AT EU LEVEL

3.1.1. Need for harmonised classification and labelling

Based upon the substance evaluation the evaluating Member State concludes that the results of two inhalation toxicity studies support the existence of local cytotoxic effect of a structurally closely related substance, sodium sulphite. According to the Guidance on CLP, respiratory tract irritation (RTI) covers two different effects: "sensory irritation" and "local cytotoxic effects", and classification as STOT SE 3 is generally limited to this latter effect. Consequently, the evaluating Member State considers that the classification of disodium disulphite into STOT SE Category 3 for RTI may be warranted.

The current proposal is an update of an existing harmonised classification because disodium disulphite has an entry in CLP-Annex VI (Index no.: 016-063-0, classified as Acute Tox. 4(*) and Eye Dam. 1) but it should be amended.

Considering the high (aggregated) tonnage and the wide dispersive use of disodium disulphite a harmonised classification is the most appropriate risk management option at EU level.

3.1.2. Need for Identification as a substance of very high concern, SVHC (first step towards authorisation)

There is no need to identify disodium disulphite as a substance of very high concern because taking into account the results of the substance evaluation the substance does not fulfil the criteria set out in article 57 of the REACH Regulation.

3.1.3. Need for restrictions

The manufacture, placing on the market or use of a substance on its own, in a mixture or in an article does not pose a risk to human health or the environment that is not adequately controlled therefore restriction is not needed.

3.1.4. Proposal for other Community-wide regulatory risk management measures

There is no need for other Community-wide regulatory risk management measures.

3.2. NO FOLLOW-UP ACTION NEEDED

The concern could be removed because	**Tick box**
Hazard and /or exposure was verified to be not relevant and/or *For endpoints not addressed in 3.1. above*	***X***
Hazard and /or exposure was verified to be under appropriate control and/or	
The registrant modified the applied risk management measures.	
other:	

-Exposure to the environment:

The evaluating Member State carefully assessed the information submitted by the Registrant with regard to various environmental endpoints and also several other available and relevant publications. The following was concluded:

Disodium disulphite has low bioaccumulation potential, further to this, under environmental conditions sulphate rapidly forms from sulphite. The evaluating Member State concludes that the secondary poisoning is an unlikely exposure pathway.

Data on short-term and long-term toxicity to the aquatic environment was available with either disodium disulphite or structurally related substances, with a key study on disodium disulphite on *Daphnia magna*, which was considered by the evaluating Member State as the most sensitive species. None of the data in the relevant studies warranted classification of disodium disulphite as toxic to the aquatic environment.

Due to the salt-character and physico-chemical properties (negligible vapour pressure, very high solubility and dissociation in water), the Henry constant is near to zero, and therefore disodium disulphite as well as its dissociation products are not volatile from aqueous solutions. Relevant adsorption onto soils, sediments or suspended matter is not to be expected.

In water and in other aqueous media disodium disulphite is present in dissociated forms. Although these have a strong anionic nature, sulphite substances in the presence of water do not show any quantitatively relevant adsorption to the soil, sediment or suspended material.

Consequently, based on the fate and toxicity properties of the substance it appears that the substance is not a concern for the environment and therefore it is not considered necessary to further investigate the releases and exposure to the environment.

-Mutagenicity:

There are both positive and negative results of *in vivo* and *in vitro* mutagenicity tests on sulphites which raised concern. Detailed analysis revealed that some publications are not reliable because of methodological and reporting deficiencies. Two *in vivo* micronucleus and two chromosome aberration assays with sulphite on bone marrow cells were negative and one micronucleus assay on bone marrow cells of mice was positive. Two dominant lethal tests on rats and mice also gave negative results.

The evaluating Member State is of the opinion that there is very vague and inconsistent evidence of induction of genetic toxicity with relevance to humans for sulphites, and considers, based upon the available information, that the concern for mutagenicity is no longer substantiated. Thus also classification for mutagenicity seems not warranted.

-Sensitisation:

Based on the evaluated literature data it is unlikely that disodium disulphite is a skin sensitiser or induces respiratory sensitization but may enhance symptoms of asthma in sensitive individuals. The information related to the skin and respiratory sensitising properties of the disodium disulphite presented by the Registrant is sufficient for evaluation. Based on the available data the evaluating Member State concludes that there is no concern for respiratory sensitisation. With regard to skin sensitisation the conclusion is also supported by the review of the available study performed by the German MAK Commission in 2014, who also concluded that in view of the widespread use of disodium disulphite, and therefore the numerous possibilities for contact in everyday life and the occupational field, the number of persons dermally sensitised is, however, very small.

-Irritation:

Several reliable and relevant studies with structurally similar substances indicated no skin irritation when applied as aqueous solution (substance as such are not existent in dry form). Erythema and oedema scores were zero after 24, 48 and 72h for all test substances. The evaluating Member State considered these studies as sufficient to establish that there is no concern for skin irritation.

- Repeated dose toxicity:

Based upon the physo-chemical properties of disodium disulphite, and especially the particle size of it (the median particle size of the disodium disulphite is 66.8 µm, so the particles are most likely to deposit in the upper respiratory tract and they are excreted with mucus), and considering also the above mentioned respiratory tract irritation, as well as the fact that disodium disulphite is not used in sprays, the evaluating Member State considers that the concern about the inhalation toxicity of disodium disulphite after repeated exposure can be disregarded.

-Carcinogenicity:

No reliable study suggested that disodium disulphite has any carcinogenic activity *in vitro*. One study suggests that disodium disulphite has tumour promoting activity, however it was a single-dose study, and long-term studies did not indicate carcinogenic activity *in vivo.* In the relevant cohort study due to the lack of exposure information the contribution of disodium disulphite in the increase of tumour incidences was not verified.

-Toxicity for reproduction:

-Fertility

In the key study on disodium disulphite no effects were seen on fertility or reproduction, thus the NOAEL for these effects was above the highest treatment dose of 2.0% for all generations. Another study also did not reveal any reproductive effects of disodium disulphite.

Two other submitted studies on disodium disulphite were not considered relevant or reliable for the evaluation.

The available studies did not follow any guidelines and several parameters were not examined (e.g. sperm parameters, estrous cyclicity, offspring pathology, etc.), nevertheless the weight of evidence from these data showed no concern for the endpoint of fertility.

-Developmental toxicity

No effects suggesting any teratogenic potential were seen in the submitted studies. The available tests were provided based on read-across from sulphites, metabisulphites, hydrogensulphites and thiosulphates. In a study performed on rats fetotoxicity (reduced fetal body weight) was observed only at maternally toxic doses, suggesting a secondary effect that may have been caused by maternal malnutrition. In another study slight reduced fetal body weight was observed at all treatment doses, even below the maternal NOAEL, however these effects were not dose-dependent and were not present in the live-birth part of the study. Other studies did not reveal any fetotoxic or teratogenic effects. Based on the available information the evaluating Member State considers that there is no concern for developmental toxicity.

4. TENTATIVE PLAN FOR FOLLOW-UP ACTIONS (IF NECESSARY)

Indication of a tentative plan is not a formal commitment for the evaluating Member State. A formal commitment to prepare a REACH Annex XV dossier (SVHC, restrictions) and/or CLP Annex VI dossier shall be made via the Registry of Intentions.

Follow-up action	**Date for intention**	**Actor**
CLP Annex VI dossier	10/2016	Hungary