Committee for Risk Assessment

RAC

Annex 2
Response to comments document (RCOM)
to the Opinion proposing harmonised classification and labelling at EU level of

dipotassium octaborate

EC Number: -
CAS Number: 12008-39-8

CLH-O-0000007417-70-01/F

Adopted

14 March 2024

COMMENTS AND RESPONSE TO COMMENTS ON CLH: PROPOSAL AND JUSTIFICATION

Comments provided during consultation are made available in the table below as submitted through the web form. Any attachments received are referred to in this table and listed underneath, or have been copied directly into the table.

All comments and attachments including confidential information received during the consultation have been provided in full to the dossier submitter (Member State Competent Authority), the Committees and to the European Commission. Non-confidential attachments that have not been copied into the table directly are published after the consultation and are also published together with the opinion (after adoption) on ECHA's website. Dossier submitters who are manufacturers, importers or downstream users, will only receive the comments and non-confidential attachments, and not the confidential information received from other parties. Journal articles are not confidential; however they are not published on the website due to Intellectual Property Rights.

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Substance name: dipotassium octaborate
EC number: -
CAS number: 12008-39-8
Dossier submitter: Sweden

TOXICITY TO REPRODUCTION

Date	Country	Organisation	Type of Organisation	Comment number
20.04.2023	Germany		MemberState	1
Comment received				
Fertility The proposed classification of dipotassium octaborate as Repr. 1B, H360F, with a GCL due to medium potency is supported. No studies with dipotassium octaborate itself are available Available read-across studies for this endpoint include studies with boric acid and disodium tetraborate decahydrate (borax), both already classified as Repr. 1B, H360FD. The studies in different species indicate that boron severely impairs sexual function and fertility predominantly through an effect on the testes (e.g. testes atrophy, reduced sperm count, viability and motility). In addition, more recent studies confirm these effects. The available human data, which do not show adverse effects, do not contradict the animal data, because the daily exposure to boron was far below the NOAEL/LOAEL in animal studies. Development The proposed classification of dipotassium octaborate as Repr. 1B, H360D, with a GCL due to medium potency is supported. As with the fertility endpoint, no studies with dipotassium octaborate itself are available. The classification is solely based on the read-across to boric acid and borax. These substances induced developmental abnormalities (malformations) in different species and are already classified as Repr. 1B, H360D.				

A recent PNDT study with boric acid (Pleus, 2018) showed a reduction in mean foetal body weight. However, this study has only been evaluated as an additional study. The doses resulting in significant lower foetal weights are below the LOAEL for developmental abnormalities observed in other studies, however, they do support the GCL derived from previous studies.

Therefore, criteria for classification of dipotassium octaborate as Repr. 1B, H360FD, are considered fulfilled.

The GCL of 0.3 % is based on read-across from boric acid (lowest ED10/LOAEL) and adjusted for boron equivalents.

In addition, there is agreement with no classification for adverse effects on or via lactation.

Dossier Submitter's Response
Thank you for your support.
RAC's response
Noted and agreed.

Date	Country	Organisation	Type of Organisation	Comment number
05.05.2023	Belgium	European Borates Association	Industry or trade association	2

Comment received

The European Borates Association (EBA) accepts that there is a reproductive effect of certain boron compounds in laboratory animals under test conditions and that read across between boric acid and the substance is applicable. However, the EBA questions the relevancy of these data to consider the substance as meeting the classification and labelling criteria of Category 1B as is proposed in this CLH Report. The EBA is of the view that a Repr. Category 2 H361d classification is more justified than a Category 1B H 360 FD. Secondly, the CLP Regulation provides that weight of evidence should be used to determine the category of classification, and this evaluation is missing from the CLH Report. Finally, we agree with the proposal from the Dossier Submitter to assign the note 11 (additivity note) to the substance.

See the attachment for more detailed comments

ECHA note – An attachment was submitted with the comment above. Refer to public attachment EBA comments on 10 CLH boron compounds.pdf

Dossier Submitter's Response

Thank you for your comments and for supporting the grouping of the boron compounds as well as the addition of note 11 on additivity for reproductive toxicity.

The EBA comments that the CLP Regulation provides that weight of evidence should be used to determine the category of classification, and that this evaluation is missing from the CLH Report. In response to this the dossier submitter would like to emphasize that the primary basis for the proposed classification in the current proposal is the data on boric acid and borates in a read-across approach. This data has been assessed by RAC and the classification concluded in a **total weight of evidence determination** for adverse effects on sexual function and fertility as well as adverse effects on the development of the offspring (RAC opinions on boric acid, disodium tetraborate anhydrate and disodium

octaborate tetrahydrate; ECHA, 2014). The data comprised animal data from several species as well as data from human studies. The additional studies included in this proposal, assessed by RAC in opinions of sodium per(oxo)borates (ECHA, 2021) and of trimethyl borate (ECHA, 2021), do not present any conclusive data and the findings do not contradict the data previously assessed by RAC in earlier opinions. The study by Duydu et al. (2018) mentioned in the attachement from EBA was assessed by RAC in the opinions of barium diboron tetraoxide (ECHA, 2020) and on the revision of concentration limits for reproductive toxicity of boric acid and a number of borates (ECHA, 2019), sodium per(oxo)borates (ECHA, 2021) and of trimethyl borate (ECHA, 2021) and was found negative but with significant limitations and not considered to contradict the positive animal data.
With regards to mechanistic studies that EBA states raises doubts about the relevance for humans we are not aware of such studies and the EBA is not making any specific references to publications in their comments or attachment. Hence, we cannot assess or respond to the relevance of this statement.

RAC's response

RAC notes that read across to data on boric acid and borax, and the additivity of the hazard with the use of note 11 is supported in the comment from the Industry association.
The commenter on the other hand disagrees with the proposed classification, stressing that the weight of evidence evaluation should rely on the human evidence and questionning the relevance of the animal data for humans.
RAC is not aware of scientific data supporting the doubts of the commenter on the relevance for humans of the animal data.
RAC notes that all human evidence included in this dossier has already been evaluated by RAC in previous opinions (e.g. that on peroxoborates, 2022).
RAC further notes that the exposure levels used in the human studies are much lower than that used in the animal studies available, e.g. in the Duydu *et al.*, 2019 study, the the extreme Daily Boron Exposure values (DBE) was 0.64 ± 0.26 mg B/kg bw/day, with a maximum individual DBE (i.e. 106.8 mg B/day) that converts to 1.52 mg B/kg bw/day. For comparison the LOAEL and NOAEL in the rat for fertility in male rats were 58.5 mg B/kg bw/day and 17.5 mg B/kg bw/day respectively.
Based on these considerations the committee considered that the human evidence supplemented the animal data, but that the human data could not be used to negate the consistent findings of adverse effects to fertility and sexual function or on development.

As a general consideration RAC underlines that the classification criteria under CLP do not include the assessment of exposure in different uses of a substance, the probability of the occurrence of an effect, nor any risk assessment in relation to different uses. Rather, classification under CLP is based on the identification evaluation of the inherent toxicological properties of the substances.

PUBLIC ATTACHMENTS
1. EBA comments on 10 CLH boron compounds.pdf [Please refer to comment No. 2]