

Committee for Risk Assessment
RAC

Annex 2

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

Disodium octaborate tetrahydrate

EC number: 234-541-0
CAS number: 12280-03-4

CLH-O-0000003655-70-03/F

Adopted
14 March 2014

ANNEX 2 - COMMENTS AND RESPONSE TO COMMENTS ON CLH PROPSAL ON DISODIUM OCTABORATE, TETRAHYDRATE

COMMENTS AND RESPONSE TO COMMENTS ON CLH: PROPOSAL AND JUSTIFICATION

Comments provided during public consultation are made available in this table as submitted by the webform. Please note that some attachments received may have been copied in the table below. The attachments received have been provided in full to the dossier submitter and RAC.

ECHA accepts no responsibility or liability for the content of this table.

ECHA has received confidential comments or attachments during public consultation. They have been responded by the dossier submitter and the RAC and have been taken into account for the opinion development. However, they will not be published on ECHA website after the adoption of the opinion and background documents.

Substance name: disodium octaborate, tetrahydrate

EC number: 234-541-0

CAS number: 12280-03-4

Dossier submitter: The Netherlands

GENERAL COMMENTS

Date	Country	Organisation	Type of Organisation	Comment number
06.06.2013	United Kingdom		MemberState	1
Comment received				
We believe that it is currently inappropriate to develop a harmonised classification for disodium octaborate hexahydrate whilst the dataset on boric acid is also under consideration in the harmonised classification and labelling process.				
Dossier Submitter's Response				
We agree that the classification for disodium octaborate <u>tetrahydrate</u> should be discussed together with the classification for boric acid.				
RAC's response				
The evaluation of Boric Acid was made in parallel with the DOT and DOA by RAC. For more reasoning, please see the RAC opinion.				

Date	Country	Organisation	Type of Organisation	Comment number
04.06.2013	United Kingdom		Company-Downstream user	2
Comment received				
There is recent high-quality research which supports a lower classification for reproductive toxicity.				
Dossier Submitter's Response				
We do not agree. See response to comment 39.				
RAC's response				
RAC evaluated all the data available for reproductive toxicity. Based on the total weight of evidence, toxicity data from four different species (mice, rats, rabbits and dogs) provide clear evidence of an adverse effect on sexual function, fertility, and development in the absence of other toxic effects. No evidence of reproductive toxicity was observed in the epidemiological studies but they were designed to cover only male fertility effects and had methodological limitations. Therefore, the epidemiological studies do not give reasons to challenge the relevance of the animal toxicity data to humans at similar				

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dose levels as causing toxicity in experimental animals. The human data does not contradict the animal data. Therefore, there is no evidence that the effects observed in animals are not relevant to humans.

In conclusion, based on the adverse developmental and fertility effects of borates in rats and rabbits RAC agreed with the dossier submitter (the Netherlands) to assign a harmonised classification as a substance which may damage fertility and the unborn child (Repr. 1B; H360FD), according to Regulation EC 1272/2008. The RAC opinion includes the derivation of the GCL based on the new Guidance (Version 4.0 – November 2013, section 3.7.2.5. Setting of specific concentration limits). Using the new guidance, as the substance is a medium potency reproductive toxicant, the generic concentration limit of 0.3% (w/w) is applicable and there is thus no need for a SCL. The Committee also concluded that classification into other hazard classes was not warranted.

For more reasoning, please see the RAC opinion.

Date	Country	Organisation	Type of Organisation	Comment number
31.05.2013	United Kingdom	Safeguard Europe Ltd.	Company-Manufacturer	3
Comment received				
<p>Whilst the desire for harmonised classification is understandable this consideration should not eclipse the ECHA's responsibility to take into account all current evidence when deciding on substance classifications - including evidence that has come to light since other borates were classified under ATP.</p> <p>The ECHA would be failing in its duty if it were to ignore the evidence put forward by Poland in its dossier on the classification of boric acid when deciding on an appropriate classification for DOT.</p> <p>On a related note, I was very surprised to read of the decision not to name the "experts" at the IPSRA meeting (October 5-6 2004) at which it was decided to classify borates as Repr Cat. 2 (See CLH Report for Disodium Octaborate, page 68). This makes it impossible for the outside observer to judge the credentials or impartiality of the experts in question. In the interests of open government, I hope that the current consultation takes a less secretive approach.</p>				
Dossier Submitter's Response				
<p>We have taken the new information into account but still conclude that classification as Repr. 1B is appropriate. For an elaborate discussion of the new information, see our response to comment 39.</p>				
RAC's response				
<p>Please see the response to comment 2.</p>				

Date	Country	Organisation	Type of Organisation	Comment number
14.06.2013	Austria		Company-Downstream user	4
Comment received				
<p>Our above mentioned companies are downstream users of boron compounds. The European Borates Association (EBA) has provided a consolidated response on behalf of the European borate Manufacturers and Importers and on behalf of the REACH consortium for borates. As a consequence, we fully support and endorse with the above mentioned companies the</p>				

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comments submitted to this consultation by the EBA.
Dossier Submitter's Response
See response to comment 39.
RAC's response
Please see the response to comment 2.

Date	Country	Organisation	Type of Organisation	Comment number
14.06.2013	United Kingdom	Advanced Chemical Specialties Ltd	Company-Downstream user	5
Comment received				
Advanced Chemical Specialties Ltd is a downstream user of boron compounds. The European Borates Association (EBA) has provided a consolidated response on behalf of the European borate Manufacturers and Importers and on behalf of the REACH consortium for borates. As a consequence, Advanced Chemical Specialties Ltd fully supports and endorses the comments submitted to this consultation by the EBA.				
Dossier Submitter's Response				
See response to comment 39.				
RAC's response				
Please see the response to comment 2.				

Date	Country	Organisation	Type of Organisation	Comment number
14.06.2013	Italy	ASSOVETRO	Industry or trade association	6
Comment received				
Assovetro, Associazione di categoria aderente a Confindustria che rappresenta le Aziende italiane produttrici e trasformatrici di vetro, associa Vetrerie che sono utilizzatrici a valle di composti di boro. L'Associazione Europea dei borati (EBA) ha fornito una risposta consolidata per conto dei fabbricanti e degli importatori europei di borati e per conto del consorzio REACH per borati. Assovetro supporta pienamente e fa proprie le osservazioni presentate a questa consultazione dall'EBA.				
Dossier Submitter's Response				
See response to comment 39.				
RAC's response				
Please see the response to comment 2.				

Date	Country	Organisation	Type of Organisation	Comment number
14.06.2013	France		MemberState	7
Comment received				
FR agrees with the proposed classification.				
Dossier Submitter's Response				
Thank you for the support				
RAC's response				
Noted.				

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Date	Country	Organisation	Type of Organisation	Comment number
14.06.2013	United Kingdom	Property Care Association	Industry or trade association	8
Comment received				
The Property Care Association represents downstream users of Boron compounds. The EBA has provided a consolidated report on behalf of the European Borate manufacturers and importers and on behalf of the REACH consortium for Borates. As a consequence the Property Care Association fully supports and endorses the comments submitted for this consultation by the ECA.				
Dossier Submitter's Response				
See response to comment 39.				
RAC's response				
Please see the response to comment 2.				

Date	Country	Organisation	Type of Organisation	Comment number
14.06.2013	Austria		MemberState	9
Comment received				
The Austrian CA supports the Dutch classification proposal of disodium octaborate, tetrahydrate as Repr 1B H360FD.				
Dossier Submitter's Response				
Thank you for the support				
RAC's response				
Noted.				

Date	Country	Organisation	Type of Organisation	Comment number
14.06.2013	France	Arch Water Products France, group Lonza	Company-Downstream user	10
Comment received				
Arch Water Products France (group LONZA) is a downstream user of boron compounds. The European Borates Association (EBA) has provided a consolidated response on behalf of the European borate Manufacturers and Importers and on behalf of the REACH consortium for borates. As a consequence, Arch Water Products France (group LONZA) fully supports and endorses the comments submitted to this consultation by the EBA.				
Dossier Submitter's Response				
See response to comment 39.				
RAC's response				
Please see the response to comment 2.				

Date	Country	Organisation	Type of Organisation	Comment number
14.06.2013	United Kingdom	British Adhesives and Sealants Association	Industry or trade association	11
Comment received				
BASA members are downstream users of boron compounds. The European Borates Association (EBA) has provided a consolidated response on behalf of the European borate Manufacturers and Importers and on behalf of the REACH consortium for borates. As a				

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consequence, our members fully support and endorse the comments submitted to this consultation by the EBA.
Dossier Submitter's Response
See response to comment 39.
RAC's response
Please see the response to comment 2.

Date	Country	Organisation	Type of Organisation	Comment number
14.06.2013	Belgium	European Domestic Glass Committee	Industry or trade association	12
Comment received				
Companies members of EDG, the European Domestic Glass Committee , are downstream users of boron compounds . The European Borates Association (EBA) has provided a consolidated response on behalf of the European borate Manufacturers and Importers and on behalf of the REACH consortium for borates. As a consequence, EDG fully supports and endorses the comments submitted to this consultation by the EBA.				
Dossier Submitter's Response				
See response to comment 39.				
RAC's response				
Please see the response to comment 2.				

Date	Country	Organisation	Type of Organisation	Comment number
13.06.2013	Spain	National Association of Frits, Glazes and Inorganic Pigments (ANFFECC)	Industry or trade association	13
Comment received				
The companies members of ANFFECC are downstream user of boron compounds. The European Borates Association (EBA) has provided a consolidated response on behalf of the European borate Manufacturers and Importers and on behalf of the REACH consortium for borates. As a consequence, ANFFECC fully supports and endorses the comments submitted to this consultation by the EBA.				
Dossier Submitter's Response				
See response to comment 39.				
RAC's response				
Please see the response to comment 2.				

Date	Country	Organisation	Type of Organisation	Comment number
13.06.2013	Spain	Frit Consortium	Industry or trade association	14
Comment received				
The companies of the Frit Consortium are downstream user of boron compounds. The European Borates Association (EBA) has provided a consolidated response on behalf of the European borate Manufacturers and Importers and on behalf of the REACH consortium for borates. As a consequence, the Frit Consortium fully supports and endorses the comments submitted to this consultation by the EBA.				
Dossier Submitter's Response				

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See response to comment 39.
RAC's response
Please see the response to comment 2.

Date	Country	Organisation	Type of Organisation	Comment number
13.06.2013	Germany		Company-Downstream user	15
Comment received				
Dossier does not consider information on epidemiological studies of workers in China and Turkey exposed to Boric Acid. (Read Across approach to Boric acid has been considered to be valid due to similar properties of substances). Therefore the decision on the harmonised classification on disodium octaborate, tetrahydrate should be put on hold, until decision on re-classification dossier for Boric acid has been taken.				
Dossier Submitter's Response				
We did (although shortly) consider the epidemiological studies, however, since the results of these studies are not contradictory to the results of the animal studies, we see no reason to downgrade the classification to Repr. 2. The workers are exposed to concentrations that are lower than the doses that cause reproductive effects in laboratory animals. It can therefore not be excluded that in humans higher doses would also result in reproductive effects. For a more elaborate discussion of the epidemiological studies, see response to comment 19. In addition, we agree that the classification for disodium octaborate tetrahydrate should be discussed together with the classification for boric acid.				
RAC's response				
Please see the response to comment 2.				

Date	Country	Organisation	Type of Organisation	Comment number
13.06.2013	United Kingdom		Company-Importer	16
Comment received				
This importer is an importer of boron compounds. The European Borates Association (EBA) has provided a consolidated response on behalf of the European borate Manufacturers and Importers and on behalf of the REACH consortium for borates. As a consequence, this importer fully supports and endorses the comments submitted to this consultation by the EBA.				
Dossier Submitter's Response				
See response to comment 39.				
RAC's response				
Please see the response to comment 2.				

Date	Country	Organisation	Type of Organisation	Comment number
13.06.2013	Germany		MemberState	17
Comment received				
The classification and SCL proposed for disodiumoctaborate tetrahydrate reflects that of the related borates according to Commission Regulation (EC) No 790/2009 of 10 August 2009 and the conversion table provided in the CLH report. The proposal is fully supported. Currently there is also a proposal for reduced C&L of boric acid as Repr. 2, H361d rather than Repr. 1B, H360FD (version 2, 23/04/2013) by PL. We do, however, not think that a				

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decision about harmonized classification for DOT should be delayed until an opinion is adopted about reduced classification for boric acid.
Dossier Submitter's Response
Thank you for the support
RAC's response
Noted.

Date	Country	Organisation	Type of Organisation	Comment number
13.06.2013	Belgium	European Federation of Corrugated Board Manufacturers	Industry or trade association	18
Comment received				
<p>The European Federation of Corrugated Board Manufacturers (FEFCO), is a downstream user of boron compounds. The European Borates Association (EBA) has provided a consolidated response on behalf of the European borate Manufacturers and Importers and on behalf of the REACH consortium for borates. As a consequence, FEFCO fully supports and endorses the comments submitted to this consultation by the EBA.</p> <p><i>(ECHA note: The attachment "Detailed comments on DOT CLH Report" is copied under Comment number 39)</i></p>				
Dossier Submitter's Response				
See response to comment 39.				
RAC's response				
Please see the response to comment 2.				

Date	Country	Organisation	Type of Organisation	Comment number
13.06.2013	Netherlands	PPG Industries Fiber Glass bv	Company-Downstream user	19
Comment received				
<p>organisation is a downstream user of boron compounds. The European Borates Association (EBA) has provided a consolidated response on behalf of the European borate Manufacturers and Importers and on behalf of the REACH consortium for borates. As a consequence, name of your organisation fully supports and endorses the comments submitted to this consultation by the EBA.</p>				
Dossier Submitter's Response				
See response to comment 39.				
RAC's response				
Please see the response to comment 2.				

Date	Country	Organisation	Type of Organisation	Comment number
13.06.2013	Germany		Company-Downstream user	20
Comment received				
<p>This Company-Downstream user is a downstream user of boron compounds. The European Borates Association (EBA) has provided a consolidated response on behalf of the European</p>				

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borate Manufacturers and Importers and on behalf of the REACH consortium for borates. As a consequence, this Company-Downstream user supports and endorses the comments submitted to this consultation by the EBA.
Dossier Submitter's Response
See response to comment 39.
RAC's response
Please see the response to comment 2.

Date	Country	Organisation	Type of Organisation	Comment number
13.06.2013	Norway		MemberState	21
Comment received				
<p>Norway would like to thank the Netherlands for the proposal for harmonised classification and labeling of Disodiumoctaborate, tetrahydrate, cas no. 12280-03-4.</p> <p>We support the proposal to classify Disodiumoctaborate, tetrahydrate for reproductive toxicity with Repr. 1B - H360FD based on a read across to boric acid. Disodium octaborate tetrahydrate will predominantly exist as undissociated boric acid in physiological conditions. Therefore, the toxicological properties of borates are expected to be similar and a read across approach would be justified.</p> <p>This proposal is also in line with already existing classifications of borates included in Annex VI.</p>				
Dossier Submitter's Response				
Thank you for the support				
RAC's response				
Noted.				

Date	Country	Organisation	Type of Organisation	Comment number
13.06.2013	Belgium	Glass Alliance Europe	Industry or trade association	22
Comment received				
<p>Glass manufacturers support the REACH Regulation and believe that a reduction of the risk associated with worker exposure and the environmental impact of dangerous substances is welcome in the EU Market.</p> <p>Glass Alliance Europe (GAE) welcomes the opportunity to provide its contribution to the public consultation on the ECHA public consultation on the CLH report for disodium octaborate tetrahydrate (DOT) as a downstream user of boron compounds</p> <p>GAE cannot provide any further scientific evidence on the issue. However, the European Borates Association (EBA) has provided a consolidated response on behalf of the European borate Manufacturers and Importers and on behalf of the REACH consortium for borates. As a consequence, GAE fully supports and endorses the comments submitted to this consultation by the EBA.</p> <p>Considering all available information, GAE has already supported the proposed Category 2 classification for boric acid. GAE believes as well that the classification of boric acid as a Category 2 toxic for reproduction should be apply also to the other classified borates and particularly to DOT.</p>				

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Finally GAE would like to underline that boron is of great importance for the glass industries and that boron compounds are consumed in the production glass process and no longer present in the final article. These products are definitely safe as in the case of borosilicate glass articles, as, for example, pharmaceutical containers and laboratory ware, which are produced using boron compounds, and are today considered as the most inert material from chemical point of view.

(ECHA note: The content of the attachment provided "Consultation on disodium borate (DOT)" is the same as in the comment above. Therefore the attachment is not copied in the table)

Dossier Submitter's Response

See response to comment 39.

RAC's response

Please see the response to comment 2.

Date	Country	Organisation	Type of Organisation	Comment number
13.06.2013	France		Industry or trade association	23

Comment received

This Industry or trade association is a downstream user of boron compounds. The European Borates Association (EBA) has provided a consolidated response on behalf of the European borate Manufacturers and Importers and on behalf of the REACH consortium for borates. As a consequence, this Industry or trade association fully supports and endorses the comments submitted to this consultation by the EBA.

Dossier Submitter's Response

See response to comment 39.

RAC's response

Please see the response to comment 2.

Date	Country	Organisation	Type of Organisation	Comment number
13.06.2013	Slovenia		Company-Downstream user	24

Comment received

This Company-Downstream user is a downstream user of boron compounds. The European Borates Association (EBA) has provided a consolidated response on behalf of the European borate Manufacturers and Importers and on behalf of the REACH consortium for borates. As a consequence, this Company-Downstream user fully supports and endorses the comments submitted to this consultation by the EBA

Dossier Submitter's Response

See response to comment 39.

RAC's response

Please see the response to comment 2.

Date	Country	Organisation	Type of Organisation	Comment number
12.06.2013	United Kingdom	Johnson Matthey plc	Company-Downstream user	25

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Comment received
Johnson Matthey plc (and several of its affiliate companies) is a downstream user of boron compounds. The European Borates Association (EBA) has provided a consolidated response on behalf of the European borate Manufacturers and Importers, and on behalf of the REACH consortium for borates. Johnson Matthey plc fully supports and endorses the comments submitted to this consultation by the EBA in respect of the technical basis for classification, and the appropriate classification outcome.
Dossier Submitter's Response
See response to comment 39.
RAC's response
Please see the response to comment 2.

Date	Country	Organisation	Type of Organisation	Comment number
12.06.2013	France	Michelin	Company-Downstream user	26

Comment received
Michelin is a downstream user of boron compounds. The European Borates Association (EBA) has provided a consolidated response on behalf of the European borate Manufacturers and Importers and on behalf of the REACH consortium for borates. As a consequence, Michelin fully supports and endorses the comments submitted to this consultation by the EBA.
Dossier Submitter's Response
See response to comment 39.
RAC's response
Please see the response to comment 2.

Date	Country	Organisation	Type of Organisation	Comment number
12.06.2013	Belgium		Company-Downstream user	27

Comment received
We believe it is currently inappropriate to develop a harmonised classification for disodium octaborate anhydrate/tetrahydrate whilst a different classification of boric acid is also under consideration and is based on new information.
Dossier Submitter's Response
We agree that the classification for disodium octaborate anhydrous should be discussed together with the classification for boric acid.
RAC's response
Please see the response to comment 1.

Date	Country	Organisation	Type of Organisation	Comment number
12.06.2013	Germany	I&P Europe - Imaging and Printing Association e.V.	Industry or trade association	28

Comment received
I&P Europe – Imaging and Printing Association is a European association of product

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manufacturers and technology providers for the imaging and printing industry. I&P Europe members' products include conventional and digital materials and their processing solutions.

Some of our member companies are downstream user of boron compounds. The European Borates Association (EBA) has provided a consolidated response on behalf of the European borate Manufacturers and Importers and on behalf of the REACH consortium for borates. As a consequence, I&P Europe fully supports and endorses the comments submitted to this consultation by the EBA.

Dossier Submitter's Response

See response to comment 39.

RAC's response

Please see the response to comment 2.

Date	Country	Organisation	Type of Organisation	Comment number
11.06.2013	France	AIR LIQUIDE WELDING	Company-Downstream user	29

Comment received

AIR LIQUIDE WELDING is a downstream user of boron compounds. The European Borates Association (EBA) has provided a consolidated response on behalf of the European borate Manufacturers and Importers and on behalf of the REACH consortium for borates. As a consequence, AIR LIQUIDE WELDING fully supports and endorses the comments submitted to this consultation by the EBA.

Dossier Submitter's Response

See response to comment 39.

RAC's response

Please see the response to comment 2.

Date	Country	Organisation	Type of Organisation	Comment number
11.06.2013	Sweden	Jerbol System AB	Company-Downstream user	30

Comment received

Jerbol System AB is a downstream user of boron compounds. The European Borates Association (EBA) has provided a consolidated response on behalf of the European borate Manufacturers and Importers and on behalf of the REACH consortium for borates. As a consequence, Jerbol System AB fully supports and endorses the comments submitted to this consultation by the EBA.

Dossier Submitter's Response

See response to comment 39.

RAC's response

Please see the response to comment 2.

Date	Country	Organisation	Type of Organisation	Comment number
11.06.2013	Denmark	Osmose Denmark A/S	Company-Downstream user	31

Comment received

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Osmose is a downstream user of boron compounds. The European Borates Association (EBA) has provided a consolidated response on behalf of the European borate Manufacturers and Importers and on behalf of the REACH consortium for borates. As a consequence, Osmose fully supports and endorses the comments submitted to this consultation by the EBA.
Dossier Submitter's Response
See response to comment 39.
RAC's response
Please see the response to comment 2.

Date	Country	Organisation	Type of Organisation	Comment number
11.06.2013	United Kingdom		Company-Downstream user	32
Comment received				
This Company-Downstream user is a downstream user of boron compounds. The European Borates Association (EBA) has provided a consolidated response on behalf of the European borate Manufacturers and Importers and on behalf of the REACH consortium for borates. As a consequence, this Company-Downstream user fully supports and endorses the comments submitted to this consultation by the EBA.				
Dossier Submitter's Response				
See response to comment 39.				
RAC's response				
Please see the response to comment 2.				

Date	Country	Organisation	Type of Organisation	Comment number
11.06.2013	Belgium	Fertilizers Europe	Industry or trade association	33
Comment received				
Fertilizers Europe represents the downstream users of boron compounds. Boron can be added to fertilizers as micro-nutrient, essential for sustaining plant growth. The European Borates Association (EBA) has provided a consolidated response on behalf of the European borate manufacturers and importers and on behalf of the REACH consortium for borates. As a consequence, Fertilizers Europe fully supports and endorses the comments submitted to this consultation by the EBA.				
Dossier Submitter's Response				
See response to comment 39.				
RAC's response				
Please see the response to comment 2.				

Date	Country	Organisation	Type of Organisation	Comment number
11.06.2013	Belgium	European Precious Metals Federation aisbl	Industry or trade association	34
Comment received				
The members of the EPMF are downstream users of boron compounds. The European Borates Association (EBA) has provided a consolidated response on behalf of the European borate Manufacturers and Importers and on behalf of the REACH consortium for borates and				

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the EPMF fully supports and endorses the comments submitted to this consultation by the EBA.
Dossier Submitter's Response
See response to comment 39.
RAC's response
Please see the response to comment 2.

Date	Country	Organisation	Type of Organisation	Comment number
11.06.2013	Netherlands		Company-Downstream user	35
Comment received				
This Company-Downstream user is a downstream user of boron compounds. The European Borates Association (EBA) has provided a consolidated response on behalf of the European borate Manufacturers and Importers and on behalf of the REACH consortium for borates. As a consequence, this Company-Downstream user fully supports and endorses the comments submitted to this consultation by the EBA.				
Dossier Submitter's Response				
See response to comment 39.				
RAC's response				
Please see the response to comment 2.				

Date	Country	Organisation	Type of Organisation	Comment number
10.06.2013	Belgium	European Borates Association (EBA)	Industry or trade association	36
Comment received				
<p>About the European Borates Association (EBA): The EBA is the representative body of the European borates industry and is a member of IMA-Europe, the Industrial Minerals Association. The EBA membership represents all of manufactures and importers of disodium octaborate tetrahydrate in Europe. The IMA-Europe Secretariat is the Borates REACH Consortium Coordinator for disodium octaborate tetrahydrate as well as boric acid (EC 233-139-2). These comments represent the view of member companies.</p> <p>1. p10, Part A: Section 1.3, Table 3: "5.1 Hazardous to the ozone `data lacking`" The REACH registration dossier for this substance states the reason for no classification is "conclusive but not sufficient for classification".</p> <p>2. p18, Part B, Section 2.2: In addition to the identified use as a wood preservative, disodium octaborate tetrahydrate is also use in construction materials, fertilisers, paints and coatings.</p> <p>3. p54 Part B, Section 4.11.6: "Therefore, read across to disodium octaborate tetrahydrate is applied." This should read "Therefore, read across to boric acid is applied."</p> <p>4. p64 Part B, Section 6: reference is made to Directive 91/414/EEC; the correct reference is to Directive 98/8/EC.</p>				
Dossier Submitter's Response				
1. Noted				

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2. Noted 3. Noted 4. Noted
RAC's response
Noted.

Date	Country	Organisation	Type of Organisation	Comment number
05.06.2013	Germany		Company-Downstream user	37

Comment received

(ECHA note: The comment below was provided as a separate attachment)

**The case for a Category 2 Toxic to Reproduction classification for Borates
New and Previously Not Considered Scientific Data Justify Reclassification**

Position Paper of the European Borates Association

4 June 2013

Introduction

The European Chemicals Agency (ECHA) has invited interested parties to comment on a dossier proposing the re-classification of boric acid as a Category 2 reproductive toxicant under the EU's Classification, Labelling and Packaging Regulation (CLP). The proposal, which was submitted by Poland and cleared ECHA's customary accordance check, is based on scientific evidence from studies conducted on Chinese and Turkish borate mine workers with the highest exposures, which have yet to be considered by ECHA's Risk Assessment Committee. The dossier proposes to remove the classification for fertility effects and down-grade the current Category 1B classification of boric acid to Category 2 for developmental effects. The Polish proposal is supported by the European Borates Association (EBA).

ECHA has also requested comments on a proposal to classify disodium octaborate and disodium octaborate tetrahydrate (DOT) as a Category 1B reproductive toxicant. The reason for this proposal follows the inclusion of DOT as an active substance in Annex I of the Biocidal Products Directive (1998/8/EC) and the rules set out in CLP. The EBA does not support this proposal and is of the opinion that the data and evidence that justify a re-classification of boric acid to Category 2 apply equally to DOT which therefore leads to the logical conclusion that DOT should also be classified as a Category 2 reproductive toxicant.

The EBA anticipates that re-classification dossiers shall be submitted by Poland in due course for diboron trioxide and disodium tetraborates in accordance with the information in the ECHA Registry of Intentions. As with boric acid, these borates are currently classified as Category 1B reproductive toxicants and the forthcoming proposals to down-grade them to Category 2 would achieve a regulatory alignment for all relevant borates. As such, these future re-classifications would also be supported by the EBA.

Chinese and Turkish Worker Studies - new and previously not considered data

Chinese Study

Potential adverse male reproductive health effects among boron mine industry workers in the province of Liaoning in northeast China were investigated by a Chinese and US research teamⁱ. The project was led by principal investigators W.A. Robbins and Fusheng Wei, with funding from the U.S. National Institute of Occupational Safety and Health (NIOSH) and the China National Environmental Monitoring Station. Although the study was conducted in the period 2002-2004, it was not readily accessible, given that a large amount of the results had only been published in Chinese language journals. Consequently, the peer-reviewed and translated results of the study only became available in one place for review after the EU's 2008 decision published as the 30th ATPⁱⁱ to classify borates as Category 1B reproductive toxicants. Indeed the 30th ATP recognizes this fact as it contains a Recital which states that '*special attention should be paid to further results of epidemiological studies on the Borates concerned by this*

ANNEX 2 - COMMENTS AND RESPONSE TO COMMENTS ON CLH PROPSAL ON DISODIUM OCTABORATE, TETRAHYDRATE

Directive including the ongoing study conducted in China.¹

Boron measurements included concentrations in the workplace, soil, water, food, urine, blood and semen. The boron workers experienced very high boron exposures, exceeding the WHO recommended upper safe limit (13 mg B/day) by more than three-times and the highest exposed group was exposed to over 100-times more than the average daily exposure of the general European population. Despite these high exposures, no adverse reproductive effects were found.

Turkish study

A study of workers in Turkeyⁱⁱⁱ was conducted in 2009 by a Turkish and German research team to investigate the reproductive effects of boron exposure in workers employed in a boric acid production plant in Bandirma, Turkey. The project was led by principal investigator Prof. Dr., Yalçın Duydu, Ankara University, Department of Toxicology with funding from the National Boron Research Institute (BOREN) and Eti Mine Works.

Boron concentrations were determined in biological samples (blood, urine, semen), in workplace air, in food, and in water sources. The mean calculated daily boron exposure of the highly exposed group was 14.45 ± 6.57 (3.32–35.62) mg B/day. As with the Chinese study, there were no negative effects observed for boron exposure on the reproductive toxicity indicators (concentration, motility, morphology of the sperm cells and blood levels of follicle stimulating hormone (FSH), luteinizing hormone (LH), and total testosterone).

Recognising the weight of evidence for Category 2

CLP describes the weight of evidence determination where all available information relating to hazard is considered together, including relevant animal data, information on mechanism and human data. The importance of applying expert judgement in such weight of evidence cases is also conveyed for determining the most realistic conclusion on the hazard category.

For boric acid, it is known that the studies on laboratory animals clearly demonstrate fertility and developmental effects. However other available information relating to intrinsic properties considered as part of a weight of evidence assessment is summarised by the bullets below.

Human studies

- The China and Turkey worker studies represent the most sensitive studies that have been carried out on humans to date. They included sperm analysis, which is the most sensitive test for testicular toxicity in humans. These studies found no adverse reproductive toxic effects from high exposures to boron. The exposure of the workers in China is 100-times higher than the general European population.
- The Chinese and Turkish workers studies further support the argument that humans are not more sensitive to the effects of boric acid than laboratory animals demonstrated by the low rat NOAEL^v (17.5 mg B/kg/day) to human NOAEL (2.08 mg B/kg) ratio of 8.75. This ratio is over 10 times lower than the default safety factor of 100 often used in risk assessments.
- There is no evidence of developmental effects in humans attributable to boron. Three epidemiological studies evaluating high environmental exposures to boron and developmental effects in humans have been conducted and have shown an absence of effects.
- The highly exposed male Turkish workers did not show any adverse effects on hormone levels (FSH levels, LH levels and total testosterone). These results are in agreement with tests on laboratory animals that boric acid does not have an endocrine-related mechanism for the fertility and developmental effects because boric acid and its compounds are not Endocrine Disruptors. Furthermore, the U.S. Environmental Protection Agency (US EPA) did an evaluation of the endocrine disrupting potential of compounds where boric acid received the lowest score among the 309 chemicals evaluated indicating extremely low potential for endocrine-related toxicity^{iv}.

Mode of action

- Recent studies provide possible mechanisms of boric acid related developmental effects in laboratory animals, including histone deacetylase inhibition (HDACi)^{vi} and effects of boric acid on expression of Hox genes^{vii}. A major difference between laboratory animals and humans is the large zinc stores in bone and soft tissues in humans compared to laboratory animals. Zinc has been shown to be protective against the

ANNEX 2 - COMMENTS AND RESPONSE TO COMMENTS ON CLH PROPSAL ON DISODIUM OCTABORATE, TETRAHYDRATE

acute toxicity and male fertility effects of boron^{viii}.

- Studies that are underway that will provide more information on the role zinc plays in developmental and fertility effects of boric acid include:
 - Embryonic stem cell test (June 2013),
 - *In vitro* spermatogenesis assay (June 2013),
 - Developmental toxicity dose range finder study of zinc borate (June 2013),
 - 90-day oral toxicity study of zinc borate (October 2013),
 - Developmental toxicity study of zinc borate (to be completed in 2014).

Nutrient essentiality

- Boron is regarded as an essential nutrient to maintaining optimal human health and has demonstrated beneficial effects in several animal models. In 2001, the U.S. Food and Nutrition Board published a Tolerable Upper Intake Level for boron of 20mg per day, confirming its biological importance. In 2002, the U.K. Expert group on Vitamins and Minerals also ratified boron's benefits. Other epidemiological studies indicate that increased dietary boron exposure is associated with lower incidences of prostate, lung, cervical and esophageal cancer^{ix}.

In accordance with the CLP legislation and guidance, EBA considers that based on a weight of evidence evaluation of these studies, other investigations and considerations, there is sufficient evidence leading to the conclusion that it is improbable that boric acid will cause reproductive or developmental effects in humans, thereby questioning the relevance of the animal studies to humans.

Read across

The classification of boric acid as a Category 2 toxic for reproduction should also apply to the other classified borates and DOT. This is because in aqueous solutions at physiological and acidic pH, low concentrations of simple inorganic borates such as boric acid, disodium tetraborates, diboron trioxide and DOT will predominantly exist as undissociated boric acid. Accordingly, the boric acid data is also relevant to these other borates as they too can be considered to exist as undissociated boric acid under the same conditions. It would therefore be appropriate for the classification of these borates to be aligned.

Existing regulatory controls

The borate industry acknowledges that the proposed Category 2 classification would still require hazard communication for products containing boric acid. Further, compliance with EU legislation for classified substances would ensure humans are adequately protected.

Conclusion

The EBA recognises there is a reproductive effect of boron compounds in laboratory animals under test conditions. However, the latest studies and scientific evidence demonstrate that such effects are not found in humans, even when exposed to high levels. Therefore considering all available information, EBA supports the proposed Category 2 classification for boric acid.

The EBA urges all stakeholders, scientific experts and regulatory officials in ECHA, the European Commission and the Member States to support these facts as the re-classification proposals are debated and progress through the EU's regulatory process.

ⁱ Scialli AR, Bonde JP, Brüske-Hohlfeld, Culver DB, Li Y & Sullivan FM. (2010). An overview of male reproductive studies of boron with an emphasis on studies of highly exposed Chinese workers. *Reproductive Toxicology* 29: 10 – 24

ⁱⁱ COMMISSION DIRECTIVE 2008/58/EC of 21 August 2008 amending, for the purpose of its adaptation to technical progress, for the 30th time, Council Directive 67/548/EEC on the approximation of the laws, regulations and administrative provisions relating to the classification, packaging and labelling of dangerous substances

ⁱⁱⁱ Duydu Y, Başaran N, Ustündağ A, Aydın S, Undeğer U, Ataman OY, Aydos K, Düker Y, Ickstadt K, Waltrup BS, Golka K, Bolt HM. (2011). Reproductive toxicity parameters and biological monitoring in occupationally and environmentally boron-exposed persons in Bandırma, Turkey. *Arch Toxicol.* 2011 Jun;85(6):589-600. PMID:21424392.

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^{iv} No Observed Adverse Effect Level

^v Reif DM, Martin MT, Tan SW, Houck KA, Judson RS, Richard AM, Knudsen TB, Dix DJ, Davlock RJ (2010) Endocrine Profiling and Prioritization of Environmental Chemicals Using ToxCast Data. Environ Health Perspect 118:1714–1720.

^{vi} Di Renzo et al. (2007). Boric acid inhibits embryonic histone deacetylases: A suggested mechanism to explain boric acid-related teratogenicity. Tox. and Applied Pharm. 220:178-185.

^{vii} Narotsky MG, Wery N, Hamby BT, Best DS, Pacico N, Picard JJ, Gofflot F, and Kavlock J (2004). Effects of Boric Acid on Hox Gene Expression and the Axial Skeleton in the Developing Rat. From: The Skeleton: Biochemical, Genetic, and Molecular Interactions in Development and Homeostasis Edited by: E. J. Massaro and J. M. Rogers, Humana Press Inc., Totowa, NJ, pp 361-372.

^{viii} Ball, W and Harrass, M (2013) Weight of Evidence Considerations for Developmental Toxicity Classification of Boric Acid. The Toxicologist. PS:1021, p.218..

^{ix} Nielsen, FH, and Meacham, SL. (2011) Growing Evidence for Human Health Benefits of Boron. J Evidence-Based Complementary & Alternative Medicine. 9 May 2011 [Epub ahead of print].

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Dossier Submitter’s Response

See response to comment 39.

RAC’s response

Please see the response to comment 2.

TOXICITY TO REPRODUCTION

Date	Country	Organisation	Type of Organisation	Comment number
13.06.2013	Germany		Company-Downstream user	38

Comment received

New human studies of workers in China and Turkey exposed to Boric Acid are available and provide new and previously not considered data. In addition to that, further studies on the developmental and fertility effects of boric acid are underway and should be used for read-across purpose. Read Across approach to Boric acid has been considered to be valid due to similar properties of substances. Therefore the decision on the harmonised classification on disodium octaborate, tetrahydrate should be put on hold, until decision on re-classification dossier for Boric acid has been taken.

Dossier Submitter’s Response

Since the results of these studies are not contradictory to the results of the animal studies, we see no reason to downgrade the classification to Repr. 2. The workers are exposed to concentrations that are lower than the doses that cause reproductive effects in laboratory animals. It can therefore not be excluded that in humans higher doses would also result in reproductive effects. For a more elaborate discussion of the epidemiological studies, see response to comment 39.

In addition, we agree that the classification for disodium octaborate tetrahydrate should be discussed together with the classification for boric acid.

RAC’s response

Please see the response to comment 2.

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Date	Country	Organisation	Type of Organisation	Comment number
10.06.2013	Belgium	European Borates Association (EBA)	BehalfOfAnOrganisation	39
Comment received				
See confidential RCOM				
See confidential RCOM				
RAC's response				
See confidential RCOM				

Date	Country	Organisation	Type of Organisation	Comment number
31.05.2013	United Kingdom	Safeguard Europe Ltd.	Company-Manufacturer	40
Comment received				
<p>The current Repr Cat. 2 classification for borates (which is also being proposed for DOT) is too harsh and will have a disproportionate effect on the use of borates as wood preservatives. It will make it extremely difficult to register new borate formulations and application methods under BPR. This is unfortunate as borates are an extremely useful category of wood preservatives, particularly for preserving large dimension timbers in historic buildings - reducing the need for historic timbers to be replaced.</p> <p>The dossier submitted by Poland on the classification of boric acid makes a strong and convincing case that the Repr Cat. 2 classification is disproportionate and this is also true for DOT.</p>				
Dossier Submitter's Response				
<p>According to Regulation 1272/2008 classification should be based on hazard. The effects for industry should not be part of the discussion whether or not classification is necessary. Based on the information on hazards, we conclude that classification as Repr. 1B is appropriate.</p>				
RAC's response				
Noted.				

Date	Country	Organisation	Type of Organisation	Comment number
04.06.2013	United Kingdom		Company-Downstream user	41
Comment received				
<p>Chinese Study</p> <p>Potential adverse male reproductive health effects among boron mine industry workers in the province of Liaoning in northeast China were investigated by a Chinese and US research team . The project was led by principal investigators W.A. Robbins and Fusheng Wei, with funding from the U.S. National Institute of Occupational Safety and Health (NIOSH) and the China National Environmental Monitoring Station. Although the study was conducted in the period 2002-2004, it was not readily accessible, given that a large amount of the results had only been published in Chinese language journals. Consequently, the peer-reviewed and translated results of the study only became available in one place for review after the EU's 2008 decision published as the 30th ATP to classify borates as Category 1B</p>				

ANNEX 2 - COMMENTS AND RESPONSE TO COMMENTS ON CLH PROPSAL ON DISODIUM OCTABORATE, TETRAHYDRATE

reproductive toxicants. Indeed the 30th ATP recognizes this fact as it contains a Recital which states that 'special attention should be paid to further results of epidemiological studies on the Borates concerned by this Directive including the ongoing study conducted in China.'

Boron measurements included concentrations in the workplace, soil, water, food, urine, blood and semen. The boron workers experienced very high boron exposures, exceeding the WHO recommended upper safe limit (13 mg B/day) by more than three-times and the highest exposed group was exposed to over 100-times more than the average daily exposure of the general European population. Despite these high exposures, no adverse reproductive effects were found.

Turkish study

A study of workers in Turkey was conducted in 2009 by a Turkish and German research team to investigate the reproductive effects of boron exposure in workers employed in a boric acid production plant in Bandirma, Turkey. The project was led by principal investigator Prof. Dr., Yalçın Duydu, Ankara University, Department of Toxicology with funding from the National Boron Research Institute (BOREN) and Eti Mine Works.

Boron concentrations were determined in biological samples (blood, urine, semen), in workplace air, in food, and in water sources. The mean calculated daily boron exposure of the highly exposed group was 14.45 ± 6.57 (3.32–35.62) mg B/day. As with the Chinese study, there were no negative effects observed for boron exposure on the reproductive toxicity indicators (concentration, motility, morphology of the sperm cells and blood levels of follicle stimulating hormone (FSH), luteinizing hormone (LH), and total testosterone).

CLP describes the weight of evidence determination where all available information relating to hazard is considered together, including relevant animal data, information on mechanism and human data. The importance of applying expert judgement in such weight of evidence cases is also conveyed for determining the most realistic conclusion on the hazard category. For boric acid, it is known that the studies on laboratory animals clearly demonstrate fertility and developmental effects. However other available information relating to intrinsic properties considered as part of a weight of evidence assessment is summarised by the bullets below.

Human studies

- The China and Turkey worker studies represent the most sensitive studies that have been carried out on humans to date. They included sperm analysis, which is the most sensitive test for testicular toxicity in humans. These studies found no adverse reproductive toxic effects from high exposures to boron. The exposure of the workers in China is 100-times higher than the general European population.
- The Chinese and Turkish workers studies further support the argument that humans are not more sensitive to the effects of boric acid than laboratory animals demonstrated by the low rat NOAEL (17.5 mg B/kg/day) to human NOAEL (2.08 mg B/kg) ratio of 8.75. This ratio is over 10 times lower than the default safety factor of 100 often used in risk assessments.
- There is no evidence of developmental effects in humans attributable to boron. Three epidemiological studies evaluating high environmental exposures to boron and developmental effects in humans have been conducted and have shown an absence of effects.
- The highly exposed male Turkish workers did not show any adverse effects on hormone levels (FSH levels, LH levels and total testosterone). These results are in agreement with tests on laboratory animals that boric acid does not have an endocrine-related mechanism for the fertility and developmental effects because boric acid and its compounds are not Endocrine Disruptors. Furthermore, the U.S. Environmental Protection Agency (US EPA) did an evaluation of the endocrine disrupting potential of compounds where boric acid received

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the lowest score among the 309 chemicals evaluated indicating extremely low potential for endocrine-related toxicity .

Mode of action

- Recent studies provide possible mechanisms of boric acid related developmental effects in laboratory animals, including histone deacetylase inhibition (HDACi) and effects of boric acid on expression of Hox genes . A major difference between laboratory animals and humans is the large zinc stores in bone and soft tissues in humans compared to laboratory animals. Zinc has been shown to be protective against the acute toxicity and male fertility effects of boron .
- Studies that are underway that will provide more information on the role zinc plays in developmental and fertility effects of boric acid include:
 - o Embryonic stem cell test (June 2013),
 - o In vitro spermatogenesis assay (June 2013),
 - o Developmental toxicity dose range finder study of zinc borate (June 2013),
 - o 90-day oral toxicity study of zinc borate (October 2013),
 - o Developmental toxicity study of zinc borate (to be completed in 2014).

Nutrient essentiality

- Boron is regarded as an essential nutrient to maintaining optimal human health and has demonstrated beneficial effects in several animal models. In 2001, the U.S. Food and Nutrition Board published a Tolerable Upper Intake Level for boron of 20mg per day, confirming its biological importance. In 2002, the U.K. Expert group on Vitamins and Minerals also ratified boron's benefits. Other epidemiological studies indicate that increased dietary boron exposure is associated with lower incidences of prostate, lung, cervical and esophageal cancer .

In accordance with the CLP legislation and guidance, EBA considers that based on a weight of evidence evaluation of these studies, other investigations and considerations, there is sufficient evidence leading to the conclusion that it is improbable that boric acid will cause reproductive or developmental effects in humans, thereby questioning the relevance of the animal studies to humans.

Read across

The classification of boric acid as a Category 2 toxic for reproduction should also apply to the other classified borates and DOT. This is because in aqueous solutions at physiological and acidic pH, low concentrations of simple inorganic borates such as boric acid, disodium tetraborates, diboron trioxide and DOT will predominantly exist as undissociated boric acid. Accordingly, the boric acid data is also relevant to these other borates as they too can be considered to exist as undissociated boric acid under the same conditions. It would therefore be appropriate for the classification of these borates to be aligned.

Existing regulatory controls

The borate industry acknowledges that the proposed Category 2 classification would still require hazard communication for products containing boric acid. Further, compliance with EU legislation for classified substances would ensure humans are adequately protected.

Conclusion

The EBA recognises there is a reproductive effect of boron compounds in laboratory animals under test conditions. However, the latest studies and scientific evidence demonstrate that such effects are not found in humans, even when exposed to high levels. Therefore considering all available information, EBA supports the proposed Category 2 classification for boric acid.

The EBA urges all stakeholders, scientific experts and regulatory officials in ECHA, the European Commission and the Member States to support these facts as the re-classification proposals are debated and progress through the EU's regulatory process.

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Dossier Submitter's Response
See response to comment 39.
RAC's response
Please see the response to comment 2.

Date	Country	Organisation	Type of Organisation	Comment number
14.06.2013	Poland		MemberState	42

Comment received

The proposed classification and labelling of disodium octaborate tetrahydrate for reproductive toxicity is based on read-across from other tested borates e.g. boric acid.

PL CA accepts that there is a reproductive effect of boron compounds in laboratory animals under test conditions; however, it questions the relevancy of these data to consider disodium octaborate tetrahydrate as meeting the classification and labeling criteria of Category 1B as is proposed in this CLH Report.

Although the CLH Report has given some consideration to data not previously reviewed at the time of the original harmonized classification of boric acid in 2008, some key information has been omitted. Secondly, the CLP Regulation acknowledges that weight of evidence can be used to determine the category of classification.

A weight-of-evidence evaluation of numerous independent epidemiology, worker exposure and mechanistic studies raises doubt about the relevance in humans of the developmental and reproductive effects of boric acid observed in laboratory animals:

No evidence of developmental effects in humans attributable to boron has been observed in studies of populations in China, Turkey and Chile with high exposures to boron. While boron has been shown to adversely affect male reproduction in laboratory animals, studies of highly exposed boron industry workers consistently show no reproductive effects attributable to boron. Workers in boron mining and processing industries represent the maximum possible human exposure.

- The highest exposed workers in China were exposed to about 5 mg B/kg/day, which is more than 100 times greater than the average daily exposure of the general population.
- In the Turkish studies, the mean calculated daily boron exposure of the highly exposed group was 14.45 ± 6.57 (3.32–35.62) mg B/day. As with the Chinese study, there were no negative effects observed for boron exposure on the reproductive toxicity indicators (concentration, motility, morphology of the sperm cells and blood levels of follicle stimulating hormone (FSH), luteinizing hormone (LH), and total testosterone).
- The Chinese and Turkish semen studies in highly exposed workers are a major source of information as to human reproductive toxicity. Not only are these the most exposed workers with exposures measured directly from food, drink and inhalation, but the Chinese and Turkish workers studies are the most sensitive studies that have been carried out as semen analysis was performed, a very sensitive detection system for testicular damage.
- These studies show that humans are not more sensitive to fertility toxic effects than rodents.

Based on the total weight of evidence, the data show that it is improbable that boric acid will cause reproductive or developmental effects in humans. Repr. Category 2 H361d:

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<p>suspected of damaging the unborn child, is considered the appropriate classification for the following reasons: Extensive evaluations of sperm parameters in highly exposed workers have demonstrated no effects on male fertility justifying the removal of the fertility classification; and no developmental effects have been seen in highly exposed populations. However, epidemiological studies of developmental effects are not as robust as the fertility studies, warranting the Category 2 H361d. This classification accommodates for both the positive findings in laboratory animals and the absence of significant effects in humans.</p>
<p>Dossier Submitter's Response</p> <p>We did (although shortly) consider the epidemiological studies, however, since the results of these studies are not contradictory to the results of the animal studies, we see no reason to downgrade the classification to Repr. 2. The workers are exposed to concentrations that are lower than the doses that cause reproductive effects in laboratory animals. It can therefore not be excluded that in humans higher doses would also result in reproductive effects. It should be noted that classification should be based on hazard, not on risk. Maximal exposure (under normal circumstances) in workers is therefore no criterium for downgrading the classification. For a more elaborate discussion of the epidemiological studies, see response to comment 39.</p>
<p>RAC's response</p> <p>Please see the response to comment 2.</p>

Date	Country	Organisation	Type of Organisation	Comment number
14.06.2013	Denmark		MemberState	43
Comment received				
<p>Denmark supports the proposal for classification with Repr. 1B; H360FD and agrees that read-across to boric acid and other tested borates is fully justified. This is based on the well-established reproductive toxicity of the boron ion in different species and the fact that disodiumoctaborate, tetrahydrate primarily exists as undissociated boric acid in aqueous solution at physiological and acidic pH. As mentioned in the CLH report, read-across for borate substances has also recently been deemed acceptable by the European Court of Justice.</p> <p>The epidemiological studies in humans have not demonstrated effects on either fertility or development. However, the exposure levels in these studies did not reach the levels leading to adverse effects in animal studies. The toxicokinetics of boric acid are similar for animals and humans and there is no mechanistic information supporting that humans should be less susceptible to borates than the animal models used. Furthermore, it can be questioned whether the human data are adequate and representative. Hence, the epidemiological studies in humans are considered insufficient to demonstrate an absence of adverse effects on reproduction.</p> <p>With regard to the suggested SCL we can accept the approach for the reason of consistency in relation to the already established SCL for boric acid and several other borates. As the Guidance to the CLP regulation recently has introduced a novel approach to assess the potency of reproductive toxicants based on the ED10 value, we however suggest that the SCLs for all the borates in CLP Annex VI should be looked over and re-evaluated at a given opportunity.</p>				

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Dossier Submitter's Response
Thank you for the support. We agree that, considering the novel approach for SCLs, the SCLs for all borates should be re-considered.
RAC's response
Please see the response to comment 2.

Date	Country	Organisation	Type of Organisation	Comment number
14.06.2013	France		MemberState	44

Comment received
<p>Fertility :</p> <p>Studies in rats, mice and dogs show that boric acid and tetraborates target the male reproductive system. The effects, which manifest as histological changes in the testes, impaired spermiation and sperm quality, result in a partial reduction in fertility or complete sterility, depending on the dose administered. Moreover, these effects occur at doses that do not induce any strong signs of toxicity.</p> <p>In the epidemiological studies on exposed human workers, no robust effect was identified on the male reproduction. However, these studies suffer methodological weaknesses such as imprecise or absent definition of fertility criteria (Chang 2006), socioeconomic factors not adjusted or different between groups (Sayli 2003 and 2004, Chang 2006), absence of consideration of potential co-exposure (Chang 2006, Sayli 2003 and 2004, Duydu 2011) and analysis of mean sperm parameters that do not reflect heterogeneity of individual sperm count (Robbins 2008 and 2010). Besides, the small size of the cohorts resulted in a limited statistical power. Only large impact could be identified, in the range of a 30 to 40% reduction in sperm concentration in Robbins 2008 and 2010 and in the range of a 50 to 60% reduction in sperm cell concentration in Duydu 2011. These studies were unable to rule out potential, less subtle effects that may contribute to low fertility in humans. Besides, it is noted that due to differences in exposure levels, the human data do not contradict with animal data and do not allow concluding that humans are not sensitive to the toxicity of borates on the male reproductive system that was identified in rats, mice and dogs.</p> <p>FR therefore supports the proposal to classify disodiumoctaborate (anhydrate and tetrahydrate) in category 1B for fertility consistently with the classification of boric acid and tetraborates.</p> <p>Development:</p> <p>Exposure to boric acid during gestation causes reduced foetal weight, and malformations of the cardiovascular system, ribs and brain in rats, mice and rabbits. The rat is the most sensitive species and developmental effects are observed at a dose that induces only limited maternal toxicity and which cannot explain the effects observed in offspring.</p> <p>A few epidemiological studies are available for assessing the effects of boric acid on fertility in exposed workers. Some indicators measured in these studies may be relevant for identifying effects on development (e.g., miscarriages) but in addition to their methodological deficiencies, these studies were conducted on groups of exposed workers mainly composed of men and are not considered to be relevant for an adequate assessment of the developmental effects of boric acid. The case-control study on congenital abnormalities by Acs (2006) reports an association between treatment with boric acid during pregnancy and neural tube defects as well as skeletal system abnormalities. This result was however based on a very small number of exposed controls and cases and exposure was imprecisely characterised. This study is therefore considered insufficiently robust to draw a firm conclusion but overall, human data do not provide an evidence of an</p>

ANNEX 2 - COMMENTS AND RESPONSE TO COMMENTS ON CLH PROPSAL ON DISODIUM OCTABORATE, TETRAHYDRATE

absence of effect in humans nor challenge the human relevance for the effects identified in animals. FR therefore supports the proposal to classify disodiumoctaborate (anhydrate and tetrahydrate) in category 1B for development consistently with the classification of boric acid and tetraborates.
Dossier Submitter's Response
Thank you for the support
RAC's response
Noted.

OTHER HAZARDS AND ENDPOINTS – Hazardous to the Aquatic Environment

Date	Country	Organisation	Type of Organisation	Comment number
13.06.2013	Germany		MemberState	45
Comment received				
p. 59 ff: The German CA supports the proposal not to classify disodium octaborate tetrahydrate with respect to hazards to the aquatic environment. However, we would like to mention, that the Competent Authority Report (CAR) for this substance according to Directive 98/8 EEC was finalized in June 2008. The data referenced in the CLH dossier refer to the draft CAR from 2006. Thus, not all key studies for aquatic toxicity identified in the final CAR from 2008 are referenced in the CLH Dossier (e.g. <i>Brachydanio rerio</i> : ELS-test; 34d-NOEC _{growth} = 1.8 mg B/L)). It would be helpful to add the final CAR from June 2008 to the CLH dossier.				
Dossier Submitter's Response				
Thank you for your support and comments. As suggested, the finalized CAR of Disodium octaborate tetrahydrate (2008) has been taken into account (Product-type 8 (Wood preservative) Annex I, 20 February 2009, NL). As for the ELS study in <i>Brachydanio rerio</i> (34d-NOEC _{growth} = 1.8 mg B/L), the established NOEC value is higher than the NOEC value of 0.7 mg B/L obtained in <i>Oncorhynchus mykiss</i> and will not change the outcome of the assessment.				
RAC's response				
Noted.				

Date	Country	Organisation	Type of Organisation	Comment number
14.06.2013	Belgium	European Borates Association (EBA)	Industry or trade association	46
Comment received				
The CLH Report's proposal of 'no classification' for the environmental endpoint is correct, however, the data selection from the extensive database of ecotoxicological studies on boric acid and other borates appears to be based on the classical techniques applied for data-poor organic chemicals and not the specific metal guidance presented in Chapter 4 of the CLP guidance. For example, it seeks the lowest value among studies rated with Klimisch scores 1 and 2. Where multiple studies with the same species were available, the CLH Report provides only the single lowest value. For data-rich chemicals, such as inorganics and metals, means of the test results with the same species or a species-sensitivity-distribution (SSD) are widely used, as is done in REACH as well as CLP. The CLH Report does not appear to have involved any independent review of the original study reports or publications to				

ANNEX 2 - COMMENTS AND RESPONSE TO COMMENTS ON CLH PROPSAL ON DISODIUM OCTABORATE, TETRAHYDRATE

ascertain the relevance to classification and labeling.

Most relevant is that acute marine data were used to conduct a long-term hazard assessment, ignoring the availability of long-term hazard data for freshwater organisms. This issue has been debated in the past when other metals were assessed for environmental hazard classification, concluding that for data rich substances, standard freshwater data should preferably be used if extensive freshwater data sets are available, therefore limiting the need for read across from salt water data. Other accepted practices for assessing metal and inorganic substances were also ignored, such as correction for background and application of a weight-of-evidence approach.

Detailed comments have been submitted in response to the CLH Report for "disodium octaborate anhydrate" for which the approach taken in the CLH Report does have an impact on the classification under Directive 67/548/EEC.

Dossier Submitter's Response

We are of the opinion that the studies provided in the CLH, are all relevant for the classification and labelling of the substance. As stated in the CLH report, only studies indicated in the CAR as being reliable have been included in this CLH report. Additional good quality aquatic toxicity studies (equivalent to Klimisch score 1 and 2) and reported in the EU RAR and the REACH registration dossier were included if the results obtained in these studies were lower than those reported in the CAR. We further note that CLP (e.g. Annex I 4.1.1.2.2) allows use of marine species for hazard assessment as the goal of the Regulation is to protect the entire aquatic environment. Although the DSD is less explicit on this issue, we consider that DSD (e.g. Annex VI sections 1.6.1 (b) and 1.7.2) also allows "non-standard" species and "non-standard" tests.

RAC's response

The RAC analysed all the available data (equivalent to Klimisch score 1 and 2) and is of the view that the data do not fulfil the criteria for classification, neither under DSD or CLP, and that DOT should not be classified for environmental hazards. For more reasoning, please see the RAC opinion.

Date	Country	Organisation	Type of Organisation	Comment number
14.06.2013	France		MemberState	47
Comment received				
We agree with the current proposal for consideration by RAC: disodium octaborate tetrahydrate does not need to be classified with respect to hazards to the aquatic environment according to Regulation EC no 1272/2008 and Directive 67/548/EEC.				
Dossier Submitter's Response				
Thank you for your support and comments.				
RAC's response				
Noted.				

ATTACHMENTS RECEIVED

- 1. Detailed comments on DOT CLH Report** (Filename: DOT CLH report_EBA detailed comments_HH), submitted on 13.06.2013, by the European Federation of Corrugated Board Manufacturers, and on 10.06.2013 by the European Borates Association (EBA) (ECHA note: the attachment is copied under Comment 39)

ANNEX 2 - COMMENTS AND RESPONSE TO COMMENTS ON CLH PROPSAL ON DISODIUM OCTABORATE, TETRAHYDRATE

2. **Consultation on disodium borate (DOT)** (Filename: Boron compounds Disodium Borate DOT - GAE answer on consultation.pdf), submitted on 13.06.2013, by Glass Alliance Europe
3. **The case for a Category 2 Toxic to Reproduction classification for Borates. New and Previously Not Considered Scientific Data Justify Reclassification. Position Paper of the European Borates Association. 4 June 2013** (Filename: EBA position paper reclassification_3 June2013.docx), submitted on 05.06.2013 by a Company-Downstream user from Germany (*ECHA note: The attachment is copied under Comment 37*)