

Committee for Risk Assessment
RAC

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

Boric acid,
Diboron trioxide,
Tetraboron disodium heptaoxide hydrate,
Disodium tetraborate anhydrous,
Orthoboric acid sodium salt,
Disodium tetraborate decahydrate and
Disodium tetraborate pentahydrate

CLH-O-0000001412-86-300/F

Adopted
20 September 2019

COMMENTS AND RESPONSE TO COMMENTS ON CLH: PROPOSAL AND JUSTIFICATION

Comments provided during public 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 public 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 public 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.

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Chemical names, EC/CAS numbers:

Boric acid [1] [2]: EC 233-139-2 [1], EC 234-343-4 [2]; CAS 10043-35-3 [1], CAS 11113-50-1 [2]

Diboron trioxide: EC 215-125-8; CAS 1303-86-2

Tetraboron disodium heptaoxide hydrate [1], disodium tetraborate anhydrous [2], orthoboric acid, sodium salt [3]: EC 235-541-3 [1], 215-540-4 [2], 237-560-2 [3]; CAS 12267-73-1 [1], 1330-43-4 [2], 13840-56-7 [3]

Disodium tetraborate decahydrate: EC 215-540-4; CAS 1303-96-4

Disodium tetraborate pentahydrate: EC 215-540-4; CAS 12179-04-3

Dossier submitter: Sweden

GENERAL COMMENTS

Date	Country	Organisation	Type of Organisation	Comment number
22.02.2019	Spain	Frit Consortium	Industry or trade association	1
Comment received				
The Frit Consortium supports the comments submitted by EBA (European Borates Association) regarding the CLH proposal for the following substances: - Boric acid (CAS# 10043-35-3, 11113-50-1) - Diboron trioxide (CAS# 1303-86-2) - Tetraboron disodium heptaoxide, hydrate (CAS# 12267-73-1) - Disodium tetraborate, anhydrous (CAS# 1330-43-4) - Orthoboric acid sodium salt (CAS# 13840-56-7) - Disodium tetraborate decahydrate (CAS# 1303-96-4) - Disodium tetraborate pentahydrate (CAS# 12179-04-3)				
Dossier Submitter's Response				
Noted. Please see responses to comments number 8 and 19.				
RAC's response				
Please see the response to the comments from EBA (comments 8 and 19).				

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Date	Country	Organisation	Type of Organisation	Comment number
22.02.2019	Germany		MemberState	2
Comment received				
The German CA supports the proposed C&L (=removal of SCLs).				
Dossier Submitter's Response				
Thank you for the support.				
RAC's response				
Noted.				

Date	Country	Organisation	Type of Organisation	Comment number
22.02.2019	Belgium	European Cellulose Insulation Association	Industry or trade association	3
Comment received				
<p>The existing Specific Concentrations Limits (SCLs) for boron substances are health-based driven and the SCL values are set according to the boron content of the substances. The SCLs of boron substances were calculated using the "Limit Dose" method [Schneider et al. 2007] and concentration limits in preparations are derived by applying § 4.2.3.3 of Annex VI of Directive 2001/59/EC to preparations analogously. The current SCLs are appropriate to prevent risks to human health. Human studies on highly exposed populations and boron industry workers in United States, Turkey and China did not show reproductive health effects as observed in animals supporting a very low potency hazard for boron substances.</p> <p>The change of the concentration limit will have a strong impact on the borates supply chain if the limit will be dropped from e.g. 5.5% to 0.3% for boric acid. Mixtures containing borates in quantity equal or higher than 0.3% (w/w) will have to be classified and labelled as Reprotox. 1B and the usual restrictions linked to classification (e.g. ban from the consumer market) will apply. This is very unconsidered development taking into account that the risk with current SCL is proven to be negligible. For the mentioned reasons the GCL of 0,3% should not be applied for boric acid.</p>				
Dossier Submitter's Response				
Thank you for the comment.				
<p>Regarding the human data, it was found that the estimated daily boron exposure levels of "highly exposed" individuals are well below the LOAELs in animal studies. There is no evidence of toxicokinetic differences between animals and humans. It can therefore not be excluded that reproductive effects would occur in humans if they were exposed to boron levels corresponding to the LOAELs. In addition, it is not possible to assess the exposure potential for the different B substances in different uses. It should be noted that exposure is not taken into consideration in the classification, since classification is based solely on the intrinsic hazardous properties of the substance. Moreover, there are no exposure considerations for setting specific concentrations limits according to CLP Article 10(1) and following CLP guidance in section 3.7.2.6.</p> <p>RAC understands the impact of the change of an SCL into a GCL. However, classification including the setting of SCLs or applying the GCL is based on the hazardous properties of a substance and does not taken into account the exposure and risks or the social economic consequences of the classification.</p>				

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RAC's response
 Classification including the setting of SCLs or applying the GCL is based on the hazardous properties of a substance and does not taken into account the exposure and risks or the social economic consequences of the classification. RAC understands the impact of the change of an SCL into a GCL. However, the impact may be more properly adressed in the relevant downstream legislation.

Date	Country	Organisation	Type of Organisation	Comment number
22.02.2019	Germany	<confidential>	Company-Downstream user	4

Comment received

We are an SME and produce mainly foliar fertilizers, which are distributed in over 70 countries all over the world. Our main business is located outside of Europe. Nearly all of our products (over 90%) contain boric acid in a range of 0,01 % to 7 % Boron (0,06% to 40% boric acid). Up to 50% of our total turnover is made by products which contain more than 1% B (≥ 5,5% boric acid).

Boron is essential for plant growth. Boron deficiency is one of the most widespread deficiencies among plant micronutrients in agriculture and one of the major constraints to crop production. For this reason the use of boric acid in manufacture of foliar fertilizers is fundamental.

Boron is an essential nutrient for plants and most organisms, and is acquired from aqueous solution as boric acid. Boron in soil solution is mainly present as boric acid or borate. Boric acid, a charge-neutral molecule, is the major chemical form of B taken up by plants (Marschner, 1995). More than 98% of the free boron in the cell sap is found in the form of boric acid (B(OH)₃ and less than 2% as borate (B(OH)₄⁻ (Marschner, P, 2012). Boron is essential for the structure of plants. Its activity depends on its presence as borate ion H₄BO₄⁻ with the capacity to form bonds with molecules such as polysaccharides.

In foliar nutrition a nutrient such as Boron must be fully soluble in order of being absorbed through the wax cuticle into the leaf (Fernandez, V.et.al. "Foliar fertilization" Scientific principles and field practices, 2013). Disodium tetraborate pentahydrate and decahydrate and disodium octaborate tetrahydrate have been most commonly used for soil application, while sodium borate and boric acid for foliar fertilization. Water insoluble compounds of boron such as boron frits or calcium borates are not suitable for foliar nutrition as they cannot penetrate through the cuticular membrane in an acceptable period of time. Therefore water soluble boric acid and borates not least as they are natural compounds of plants remain the optimal boron substances for foliar fertilization.

It follows that there is no real substitute for the naturally used boron compounds Boric acid and Borates. As the evolutionary process in plants throughout the last 400 Mio years was not able to develop new Boron compounds for metabolism instead of Boric acid and Borates, human driven research and development will take many decades to synthesize alternatives if it will be successful at all!

If the common generic limit of 0,3% boric acid will be assigned, a great part of our product range is affected and the classification an labelling need to be changed. Furthermore because of the restriction 30 for substances classified as Repr. 1B, for a great product range it would not be possible to sell them on the consumer market.

Replacing the existing SCL by a common generic concentration limit would have also consequences if boric acid would be included into Annex XIV. In the worst case if only an authorization for a use under the concentration limit is granted, we would lose a lot of

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market share.
Dossier Submitter's Response
<p>Thank you for the comment and information provided. The dossier submitter reminds that exposure is not taken into consideration in the classification, since classification is based on the intrinsic hazardous properties of the substance. In addition, socio-economic consequences are not taken into consideration in classification that is solely based on the intrinsic hazardous properties of the substance.</p> <p>The DS recognizes the potential negative impact on the borate supply chain due to revised concentration limits for the borates included in the classification proposal. However, this issue would be more appropriately dealt with independently through other European legal instruments and this issue is not within the scope of the current public consultation.</p>
RAC's response
<p>RAC understands the impact of the change of an SCL into a GCL. However, classification including the setting of SCLs or applying the GCL is based on the hazardous properties of a substance and does not taken into account the exposure and risks or the social economic consequences of the classification.</p>

Date	Country	Organisation	Type of Organisation	Comment number
22.02.2019	Belgium	Cerame-Unie	Industry or trade association	5

Comment received
<p>Please see attached document.</p> <p>ECHA note – An attachment was submitted with the comment above. Refer to public attachment 19 02 22 Cerame Unie reply to public consultation - Borates.pdf</p>

Dossier Submitter's Response
<p>Thank you for the comments.</p> <p>The DS would like to point out that the proposal to remove SCLs for boric acid and the borates is based on the toxicity of boron and hence boron equivalent ED10 values were calculated for each substance included in the proposal. These are given in Table 30 of the CLH-report and allocated the borates to the medium potency group. Moreover, the derivation of boron equivalent ED10 values for boric acid and the borates in the present proposal uses the same approach as was applied for disodium octaborate, anhydrous and disodium octaborate tetrahydrate (EC No. 234-541-0, Index No. 005-020-00-3), on which the RAC concluded in March 2014 as Repr. 1B (H360FD) with a GCL of 0.3% w/w.</p> <p>Regarding the human data it was concluded in the dossier that the lack of evidence on adverse health effects in "highly exposed" humans could not negate the positive findings from animal studies. In addition, we have had no possibility to assess the exposure potential for the different B substances in different uses. The dossier submitter reminds that exposure and socio-economic consequences is not taken into consideration in the classification, since classification is based on the intrinsic hazardous properties of the substance.</p> <p>Comments on the, by Member States agreed, methodology or approach to derive concentration limits are outside of the scope of this CLH-proposal.</p> <p>For response to EBAs comments, we refer to comment number 8 and 19.</p>

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RAC's response
<p>The suggestion to consider deriving a boron based GCL instead of a substance specific GCL will be discussed within the opinion and the background document.</p> <p>We do not agree that the absence of effects in humans indicates a low potency as the human exposure was clearly below the ranges for low potency (above 400 mg/kg bw/day). Regarding your support of the comments from EBA, please see the response to the comments from EBA (comments 8 and 19).</p>

Date	Country	Organisation	Type of Organisation	Comment number
20.02.2019	Denmark	KRS ApS	Company-Downstream user	6

Comment received
<p>Please see attached file.</p> <p>ECHA note – An attachment was submitted with the comment above. Refer to public attachment Proposed future entry - signed.pdf</p>

Dossier Submitter's Response
<p>Thank you for the information provided.</p> <p>The DS recognizes the potential negative impact on the borate supply chain due to revised concentration limits for the borates included in the classification proposal. However, this issue would be more appropriately dealt with independently through other European legal instruments and is not within the scope of the current public consultation.</p> <p>The dossier submitter also reminds that classification is based on the intrinsic hazardous properties of the substance. Potential negative environmental or socio-economic effects due to revised concentration limits for boric acid and the borates are hence not taken into consideration.</p>

RAC's response
<p>RAC understands the impact of the change of an SCL into a GCL. However, classification including the setting of SCLs or applying the GCL is based on the hazardous properties of a substance and does not taken into account the exposure and risks or the social economic consequences of the classification.</p>

Date	Country	Organisation	Type of Organisation	Comment number
14.02.2019	Germany	Verband Schmierstoff-Industrie e.V.	Industry or trade association	7

Comment received
<p>Boric acid is used for decades without any observed adverse effect on humans. Current SCL are somehow acceptable for formulators of high performing metal working fluids. Replacement of those chemicals would very likely lead to serious disadvantages for production of metal parts in the EU while having very likely no effect on health, safety and environment.</p>

Dossier Submitter's Response
<p>Thank you for the comment. The DS recognizes the potential negative impact on the borate supply chain due to revised concentration limits for the borates included in the classification proposal. However, this issue would be more appropriately dealt with independently</p>

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through other European legal instruments and is not within the scope of the current public consultation.

RAC's response

RAC understands the impact of the change of an SCL into a GCL. However, classification including the setting of SCLs or applying the GCL is based on the hazardous properties of a substance and does not taken into account the exposure and risks or the social economic consequences of the classification.

Date	Country	Organisation	Type of Organisation	Comment number
14.02.2019	Belgium	European Borates Association (EBA)	Industry or trade association	8

Comment received

A low potency category – i.e. a GCL of 3% (w/w) – for boron substances is warranted based on the consistent and repeated absence of health effects in humans highly exposed to boron and the inconsistencies in the ECHA methodology where applied to boron substances. The GCL should be applied as a boron-based concentration limit – i.e. a GCL of 3% (w/w as boron) – for boron substances as justified by the toxicology and toxicokinetics of boron-substances.

Our detailed comments are available in the attachment

ECHA note – An attachment was submitted with the comment above. Refer to public attachment EBA Comments on CLH Report_14-02-2019.pdf

Dossier Submitter's Response

Thank you for the comments.

The DS would like to point out that the proposal to remove SCLs for boric acid and the borates is based on the toxicity of boron, calculated on a boron-equivalent basis, using the same methodology that was applied in two previous RAC-opinions on boron substances, classified as Repr. 1B, H360FD with GCLs of 0.3% w/w (disodium octaborate, anhydrous and disodium octaborate tetrahydrate, EC No. 234-541-0, Index No. 005-020-00-3).

The DS has followed the current Guidance on the Application of the CLP criteria to conclude on potency group for boric acid and the borates. The EBA suggests there is a skewness of the distribution of ED10 values used as input to derive the dose cut-offs (> 4 mg/kg bw/day, and < 400 mg/kg bw/day) for the medium potency group, that place the ED10 values for boric acid closer to the upper cut-off of the medium potency group than what would be expected from a normally shaped distribution of ED10-values. Regardless of the alleged skewness, according to the Guidance on the Application of the CLP criteria the ED10 values for boric acid fall in the middle or lower span of the dose interval of the medium potency group and in the DS's view they could therefore not be considered borderline.

All the epidemiological data on boron referenced by EBA was included in the present dossier as additional information. All the studies were found to be lacking in some or several aspects, as described in the dossier. Overall, the DS concluded that the lack of evidence on adverse health effects in humans could not negate the positive findings from the animal studies. The proposal to remove the SCLs is therefore based on evidence of adverse effects in animals.

Regarding the human data, the estimated daily boron exposure levels of "highly exposed" individuals are well below the LOAELs in animal studies, as are corresponding blood levels. We have had no possibility to assess the exposure potential for the different B substances

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in different uses. Also, it should be noted that exposure is not taken into consideration in the classification, since classification is based on the intrinsic hazardous properties of the substance. Moreover, there are no exposure considerations for setting specific concentrations limits according to CLP Article 10(1) and following CLP guidance in section 3.7.2.6.

There is no evidence that the toxicokinetic (tk) behavior (i.e. the absorption, distribution, metabolism and elimination) of boric acid differs between species. Since epidemiological studies lack controlled external exposure conditions, they cannot be used to draw conclusions about the toxicokinetic behaviour of chemical substances. Hence, the DS is of the opinion that the epidemiological studies for boron cannot, as suggested by the EBA, be used as an input for a toxicokinetic modifying factor for the purpose of moving boric acid and the borates to the low potency group.

Comments on the, by Member States agreed, methodology or approach to derive concentration limits are outside of the scope of this CLH-proposal.

RAC's response

RAC does not agree that a low potency is warranted based on the absence of effects in humans as the exposure level in humans is clearly below the below the ranges for low potency (above 400 mg/kg bw/day).

The methodology for deriving a GCL or a SCL is considered reasonable.

The suggestion to consider deriving a boron based GCL instead of a substance specific GCL will be discussed within the opinion and the background document.

RAC did not assess the study by Igra *et al.* (2016) and the provided comments as the interpretation of this study does not affect the derivation of the GCL or SCL as indicated by the DS.

Date	Country	Organisation	Type of Organisation	Comment number
14.02.2019	Finland		MemberState	9

Comment received

The dossier submitter has put forward a proposal to remove current specific concentration limits of various substances with a boron moiety under Article 36 of EC 1272/2008 whereby the existing specific concentration limits for reproductive toxicity category 1B (H360D) would be replaced by the generic concentration limit of 0.3% w/w.
The substances covered in the current proposal have harmonised classifications for reproductive toxicity category 1B, H360DF (May damage the unborn child. Suspected of damaging fertility) with specific concentration limits of 3.1% - 8.5% w/w corresponding to their boron content.

Dossier Submitter's Response

Noted.

RAC's response

Noted.

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Date	Country	Organisation	Type of Organisation	Comment number
22.02.2019	Italy	CEWEP	Industry or trade association	10
Comment received				
<p>In mixtures containing water it is impossible to distinguish between the different boron compounds, and therefore the most toxic must be taken into account, for the precautionary principle. Removing the specific concentration limit (SCL) to all the boron compounds, and applying instead the same generic concentration limit (GLC), will lead to a misleading classification of mixtures, and not to a level playing field. Proposal: keep the current existing SCLs or define new appropriate SCLs</p>				
Dossier Submitter's Response				
<p>Thank you for the comment. The proposal to remove the SCLs was based on the derivation of boron equivalent ED10 values for boric acid and the borates in the present proposal using the same approach as was applied for disodium octaborate, anhydrous and disodium octaborate tetrahydrate (EC No. 234-541-0, Index No. 005-020-00-3), on which the RAC concluded in March 2014 as Repr. 1B (H360FD) with GCLs of 0.3% w/w. The reference to a level playing field made by the DS refers to using the same methodology to derive concentration limits for all borates on Annex VI.</p>				
RAC's response				
<p>The problem that in mixtures containing water it is impossible to distinguish between different boron compounds is also applicable to the current SCLs. Deriving a boron based SCL or GCL, which could potentially solve this problem, will be discussed within the opinion and the background document.</p>				

Date	Country	Organisation	Type of Organisation	Comment number
22.02.2019	France		MemberState	11
Comment received				
<p>P3-9: degree of purity stated in 1.2 should be reported in the different tables instead of "not relevant".</p> <p>P9 table 4 (disodium tetraborate, anhydrous): the molecular weight is 201.22g/mol instead of 202.22g/mol.</p> <p>To be noted that validated physico-chemical properties of the substances: boric acid, disodium tetraborate anhydrous, disodium tetraborate pentahydrate, disodium tetraborate decahydrate and diboron trioxide are available in the biocidal CAR of the difference active substances.</p>				
Dossier Submitter's Response				
<p>Thank you for the comment.</p> <p>The degree of purity of boric acid and the borates was found not to be relevant for the entry in Annex VI, and was therefore not given in section 1.2.</p> <p>We agree that the molecular weight of disodium tetraborate, anhydrous in section 1.1.3. Table 4, should read 201.22 g/mol.</p>				
RAC's response				
Noted.				

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Date	Country	Organisation	Type of Organisation	Comment number
22.02.2019	Poland	Polish Association of Cosmetic and Detergent Industry	Industry or trade association	12
Comment received				
<p>Boron compounds are inorganic chemical compounds of natural origin with low toxicity and many medical applications. These substances (mainly boric acid and disodium tetraborate, pentahydrate) are also active substances in PT8 (wood protection) biocidal products as well as essential components of fireproof mixtures.</p> <p>Boron compounds are cheap and easily obtainable substances, suitable for wood protection products.</p> <p>During biocidal product authorization, for products that have been granted biocidal product authorization for the Polish market, the environmental and human impacts were tested (toxicological and ecotoxicological tests of products), and the studies confirmed that the products do not pose a threat.</p> <p>For over 20 years the availability of these products on the Polish market there were no complaints to manufacturers of these products due to adverse health effects, environmental or even damage to property.</p> <p>A limitation of up to 0.3% will prevent access to products to the general public but also to professional customers.</p> <p>It is not possible to provide an effective protection for wood at a concentration of 0,3% boron compounds.</p> <p>There are no alternative substances with equally good wood protection effectiveness and a similar good toxicological profile.</p> <p>A limitation of the concentration will result in the loss of opportunities for cheap and safe wood protection. This will involve the necessity of using more toxic alternatives.</p>				
Dossier Submitter's Response				
<p>Thank you for the comment and the information provided. The dossier submitter reminds that exposure or exposure is not taken into consideration in the classification, since classification is based on the intrinsic hazardous properties of the substance. In addition, socio-economic consequences are not taken into consideration in classification that is solely based on the intrinsic hazardous properties of the substance.</p> <p>The DS recognizes the potential negative impact on the borate supply chain due to revised concentration limits for the borates included in the classification proposal. However, this issue would be more appropriately dealt with independently through other European legal instruments and this issue is not within the scope of the current public consultation.</p>				
RAC's response				
<p>RAC understands the impact of the change of an SCL into a GCL. However, classification including the setting of SCLs or applying the GCL is based on the hazardous properties of a substance and does not taken into account the exposure and risks or the social economic consequences of the classification.</p>				

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Date	Country	Organisation	Type of Organisation	Comment number
22.02.2019	Germany	Oemeta Chemische Werke GmbH	Company-Downstream user	13
Comment received				
<p>However, boric acid has contributed to a better health and safety of humans and the environment. The biocidal effect leads to a significant decrease of biocides. A ban of boric acid from the market (possible as long as it is on the candidate list) would lead to the opposite trend.</p> <p>ECHA note – An attachment was submitted with the comment above. Refer to public attachment Boric acid public consultation 01-2019 Öff.doc ECHA note – An attachment was submitted with the comment above. Refer to confidential attachment Boric acid public consultation 01-2019 NÖff (2).doc</p>				
Dossier Submitter’s Response				
<p>Thank you for the comment and the information provided. The dossier submitter reminds that exposure is not taken into consideration in the classification, since classification is based on the intrinsic hazardous properties of the substance. In addition, socio-economic consequences are not taken into consideration in classification that is solely based on the intrinsic hazardous properties of the substance.</p> <p>The DS recognizes the potential negative impact on the borate supply chain due to revised concentration limits for the borates included in the classification proposal. However, this issue would be more appropriately dealt with independently through other European legal instruments and this issue is not within the scope of the current public consultation.</p>				
RAC’s response				
<p>RAC understands the impact of the change of an SCL into a GCL. However, classification including the setting of SCLs or applying the GCL is based on the hazardous properties of a substance and does not taken into account the exposure and risks or the social economic consequences of the classification.</p>				

TOXICITY TO REPRODUCTION

Date	Country	Organisation	Type of Organisation	Comment number
22.02.2019	Spain	Frit Consortium	Industry or trade association	14
Comment received				
<p>This CLH proposal includes removing the existing SCLs and applying the generic concentration limit (GCL) of 0.3% w/w by substance (not based on boron content of the substance), thus considering boron substances as “medium potency” reprotoxicants.</p> <p>For substances toxic to reproduction, it is assumed there exists a threshold below which the substance exerts no such activity. According to the available studies demonstrating the absence of adverse health effects on highly exposed populations, these boron compounds should be considered as “low potency” reprotoxicants, as has been justified in the comments submitted by EBA.</p> <p>Moreover, given that SCLs, NOAELs, LOAELs as well as the toxicology and toxicokinetics of borates based on boron equivalency, the GCL should be applied as a boron-based concentration limit with appropriate conversions of each borate based on the fraction of</p>				

boron in each substance, on a molecular weight basis.

In addition, throughout different scientific opinions and EU Directives limit values as well as the existing analytical methods for measuring exposure levels to boron substances have been referenced and set on boron, and not on borate substances

In conclusion, we support the application of a GCL of 3% (w/w as boron content) for boron substances, as low potency substances.

Dossier Submitter's Response

Thank you for the comments. The DS would like to point out that the proposal to remove SCLs for boric acid and the borates is based on the toxicity of boron and hence boron equivalent ED10 values were calculated for each substance included in the proposal. These are given in Table 30 of the CLH-report and were used to allocate the borates to the medium potency category, by following current CLP guidance.

Moreover, the derivation of boron equivalent ED10 values for boric acid and the borates in the present proposal uses the same approach as was applied for disodium octaborate, anhydrous and disodium octaborate tetrahydrate (EC No. 234-541-0, Index No. 005-020-00-3), on which the RAC concluded in March 2014 as Repr. 1B (H360FD) with a GCL of 0.3% w/w.

Regarding the human data, it was concluded in the present dossier that the lack of evidence of adverse health effects in humans could not negate the positive findings from the animal studies. We have had no possibility to assess the exposure potential for the different B substances in different uses. The dossier submitter also reminds that exposure is not taken into consideration in the classification, since classification is based on the intrinsic hazardous properties of the substance.

RAC's response

The suggestion to consider deriving a boron based GCL instead of a substance specific GCL will be discussed within the opinion and the background document.

We do not agree that the absence of effects in humans indicates a low potency as the human exposure was clearly below the ranges for low potency (above 400 mg/kg bw/day).

Date	Country	Organisation	Type of Organisation	Comment number
22.02.2019	Germany	<confidential>	Company-Downstream user	15

Comment received

We are an SME and produce mainly foliar fertilizers, which are distributed in over 70 countries all over the world. Our main business is located outside of Europe. Nearly all of our products (over 90%) contain boric acid in a range of 0,01 % to 7 % Boron (0,06% to 40% boric acid). Up to 50% of our total turnover is made by products which contain more than 1% B (≥ 5,5% boric acid).

Boron is essential for plant growth. Boron deficiency is one of the most widespread deficiencies among plant micronutrients in agriculture and one of the major constraints to crop production. For this reason the use of boric acid in manufacture of foliar fertilizers is fundamental.

Boron is an essential nutrient for plants and most organisms, and is acquired from aqueous solution as boric acid. Boron in soil solution is mainly present as boric acid or borate. Boric acid, a charge-neutral molecule, is the major chemical form of B taken up by plants (Marschner, 1995). More than 98% of the free boron in the cell sap is found in the form of

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boric acid (B(OH)₃ and less than 2% as borate (B(OH)₄⁻ (Marschner, P, 2012). Boron is essential for the structure of plants. Its activity depends on its presence as borate ion H₄BO₄⁻ with the capacity to form bonds with molecules such as polysaccharides.

In foliar nutrition a nutrient such as Boron must be fully soluble in order of being absorbed through the wax cuticle into the leaf (Fernandez, V. et.al. "Foliar fertilization" Scientific principles and field practices, 2013). Disodium tetraborate pentahydrate and decahydrate and disodium octaborate tetrahydrate have been most commonly used for soil application, while sodium borate and boric acid for foliar fertilization. Water insoluble compounds of boron such as boron frits or calcium borates are not suitable for foliar nutrition as they cannot penetrate through the cuticular membrane in an acceptable period of time.

Therefore water soluble boric acid and borates not least as they are natural compounds of plants remain the optimal boron substances for foliar fertilization.

It follows that there is no real substitute for the naturally used boron compounds Boric acid and Borates. As the evolutionary process in plants throughout the last 400 Mio years was not able to develop new Boron compounds for metabolism instead of Boric acid and Borates, human driven research and development will take many decades to synthesize alternatives if it will be successful at all!

If the common generic limit of 0,3% boric acid will be assigned, a great part of our product range is affected and the classification and labelling need to be changed. Furthermore because of the restriction 30 for substances classified as Repr. 1B, for a great product range it would not be possible to sell them on the consumer market.

Replacing the existing SCL by a common generic concentration limit would have also consequences if boric acid would be included into Annex XIV. In the worst case if only an authorization for a use under the concentration limit is granted, we would lose a lot of market share.

Dossier Submitter's Response

Thank you for the comment. The dossier submitter reminds that exposure is not taken into consideration in the classification, since classification is based on the intrinsic hazardous properties of the substance. In addition, socio-economic consequences are not taken into consideration in classification that is solely based on the intrinsic hazardous properties of the substance.

The DS recognizes the potential negative impact on the borate supply chain due to revised concentration limits for the borates included in the classification proposal. However, this issue would be more appropriately dealt with independently through other European legal instruments and this issue is not within the scope of the current public consultation.

RAC's response

RAC understands the impact of the change of an SCL into a GCL. However, classification including the setting of SCLs or applying the GCL is based on the hazardous properties of a substance and does not taken into account the exposure and risks or the social economic consequences of the classification.

Date	Country	Organisation	Type of Organisation	Comment number
22.02.2019	Belgium	Cerame-Unie	Industry or trade association	16

Comment received

Please see attached document.

ANNEX 2 - COMMENTS AND RESPONSE TO COMMENTS ON CLH PROPOSAL ON BORIC ACID AND BORATES

ECHA note – An attachment was submitted with the comment above. Refer to public attachment 19 02 22 Cerame Unie reply to public consultation - Borates.pdf

Dossier Submitter’s Response

Thank you for the comments. The proposal to remove SCLs for boric acid and the borates is based on the toxicity of boron and hence boron equivalent ED10 values were calculated for each substance included in the proposal. These are given in Table 30 of the CLH-report and were used to allocate boric acid as well as the borates to the medium potency group, by following current CLP Guidance.

Moreover, the derivation of boron equivalent ED10 values for boric acid and the borates in the present proposal uses the same approach as was applied for disodium octaborate, anhydrous and disodium octaborate tetrahydrate (EC No. 234-541-0, Index No. 005-020-00-3), on which the RAC concluded in March 2014 as Repr. 1B (H360FD) with a GCL of 0.3% w/w.

Regarding the human data it was found in the CLH-dossier that the lack of evidence on adverse health effects in humans could not negate the positive findings from the animal studies. We have had no possibility to assess the exposure potential for the different B substances in different uses. The dossier submitter reminds that exposure is not taken into consideration in the classification, since classification is based on the intrinsic hazardous properties of the substance. In addition, socio-economic consequences are not taken into consideration in classification that is solely based on the intrinsic hazardous properties of the substance.

Comments on the, by Member States agreed, methodology or approach to derive concentration limits are outside of the scope of this CLH-proposal.

For responses to EBAs comments, we refer to comment number 8 and 19.

RAC’s response

Please see the RAC response to comment 5.

Date	Country	Organisation	Type of Organisation	Comment number
21.02.2019	Germany	Verband der Deutschen Feuerfest-Industrie e. V.	Industry or trade association	17

Comment received

The Verband der Deutschen Feuerfest-Industrie e. V. welcomes the possibility to submit comments on the CLH report of the Swedish Chemical Agency. The proposal includes removing the specific concentration limits (SCLs) of the boron substances and applying the generic concentration limit (GCL) of 0.3% w/w by substance. As the Swedish Chemical Agency mentioned in the Dossier, the current SCLs, NOAELs and LOAELs for the boron substances are based on the content of boron. Therefore the proposed GCL should also be based on boron. This is common practice in EU directives, e.g. Safety of toys, and the German occupational exposure limit value for inorganic boron substances. The GCL should be applied as a boron-based concentration limit – i.e. a GCL (w/w as boron) – for boron substances.

Dossier Submitter’s Response

Thank you for the comments. The DS would like to point out that the proposal to remove SCLs for boric acid and the borates is based on the toxicity of boron and hence boron equivalent ED10 values were calculated for each substance included in the proposal. These

ANNEX 2 - COMMENTS AND RESPONSE TO COMMENTS ON CLH PROPOSAL ON BORIC ACID AND BORATES

are given in Table 30 of the CLH-report and allocated boric acid and the borates to the medium potency group, by following current CLP Guidance.

In addition, the derivation of boron equivalent ED10 values for boric acid and the borates in the present proposal uses the same approach as was applied for disodium octaborate, anhydrous and disodium octaborate tetrahydrate (EC No. 234-541-0, Index No. 005-020-00-3), on which the RAC concluded in March 2014 as Repr. 1B (H360FD) with a GCL of 0.3% w/w.

RAC's response

The suggestion to consider deriving a boron based GCL instead of a substance specific GCL will be discussed within the opinion and the background document.

Date	Country	Organisation	Type of Organisation	Comment number
21.02.2019	United Kingdom	Orthene Chemicals ltd	Company-Downstream user	18

Comment received

Having looked at the data we would fully endorse the comments sent to you by the European Borates association.

Dossier Submitter's Response

Noted. Please see response to comment 8 and 19.

RAC's response

Please see the response to the comments from EBA (comments 8 and 19).

Date	Country	Organisation	Type of Organisation	Comment number
21.02.2019	Belgium	European Borates Association (EBA)	Industry or trade association	19

Comment received

EBA wishes to share with the RAC some supplementary comments related to the modifying factors of the potency categories (see enclosed attachment).

ECHA note – An attachment was submitted with the comment above. Refer to public attachment EBA suppl. Comments on CLH Report_20-02-2019.pdf

Dossier Submitter's Response

Thank you for the comment.

Epidemiological data:

There is no scientific evidence to suggest that humans are less sensitive than animals to the adverse effects of boron on reproduction. The estimated daily boron exposure levels of "highly exposed" individuals are well below the LOAELs in animal studies. The blood boron levels of such highly exposed individuals are also reported to be below the blood levels in animals at which reproductive effects have been demonstrated. There is no evidence of toxicokinetic differences between animals and humans. It can therefore not be excluded that reproductive effects would occur in humans if exposed to boron levels corresponding to the LOAELs. It should also be noted that exposure is not taken into consideration in the classification, since classification is based on the intrinsic hazardous properties of the substance. Moreover, there are no exposure considerations for setting specific concentrations limits according to CLP Article 10(1) and following CLP guidance in section 3.7.2.6. Modifying the potency group based on the epidemiological data for boron would therefore not be appropriate.

Type of effect/severity:

Classification for developmental effects of boric acid (and similarly, disodium octaborate, anhydrous and disodium octaborate, tetrahydrate) is according to the RAC opinions based primarily on increased incidences of several malformations, mainly in rats, of which the most common ones were:

- Enlargement of lateral ventricles in the brain of rats. (5.4% of the foetuses at 58 mg B/kg bw/day and 26.4% of the foetuses at 94 mg B/kg bw/day vs 0% of control groups, respectively). Heindel et. al. 1992.
- Agenesis of rib XIII in rats. (6.2% and 12.5% of foetuses, at 58 and 94 mg B/kg bw/day, respectively vs 0.2% and 0% of controls). Heindel et. al. 1992.
- Shortening of rib XIII in rats. Significantly increased incidence at 13.3 mg B/kg bw/day. Price et al. 1996.

Additional evidence of embryotoxicity in rats was significantly decreased fetal body weights in absence of maternal toxicity, starting from 13.3 mg B/kg bw/day (4%) with increased severity (12%) in high dose (25 mg B/kg bw/day) (Price et al. 1996).

Evidence of anomalies of the eyes, i.e. displaced eyes (5.1%) and convoluted retina/microphthalmia (6.6%) in total 11% of rat foetuses at 94 mg B/kg bw/day vs. 0% for controls (Heindel et. al. 1992), as well as anomalies of the cardiovascular system in rabbit (major cardiovascular malformations in 72% of foetuses vs 3% for controls) at doses equivalent to 44 mg B/kg bw (Heindel et al. 1994) also forms the basis for the RAC-opinions.

The SCLs for boric acid and other borates were therefore derived, by RAC, from the overall NOAEL for embryotoxic/teratogenic effects of 9.6 mg B/kg bw/day, based on a reduction in mean fetal body weight/litter and an increased incidence in short rib XIII at 76 mg/kg bw/day (13.3 mg B/kg bw/day) (Price at al., 1996).

The DS recognise that shortening of rib XIII usually is considered as variations; however, together with the agenesis of rib XIII they signal an increased teratogenic effect on the axial skeleton and in summation with anomalies of the eyes, effects on the central nervous system and the cardiovascular system there is an increased generalized dysmorphogenic effect. No new animal data relevant for classification of boric acid and the borates has been published since the RAC-opinions on disodium octaborate, anhydrous and disodium octaborate tetrahydrate in 2014. Therefore, the DS find no reason to challenge the LOAEL-value used by RAC to set concentration limits for development for these substances (i.e. 13.3 mg B/kg bw/day, based on shortening of rib XIII and decreased fetal weight). The LOAEL of 13.3 mg B/kg bw/day is therefore used to determine concentration limits for classification in the present CLH-proposal for boric acid and borates, on a boron equivalent basis.

Male fertility effects:

The LOAELs for fertility in male rats based on a 2 year feeding study with boric acid (BA) (Weir 1966; Weir and Fisher, 1972) is reported to be 334 (58.5) mg BA (B)/kg bw day. At this dose level 100% (10/10) of the rats had testicular atrophy. In a similar study with borax (Weir 1966; Weir and Fisher, 1972) the same frequency of atrophy is reported at the LOAEL (516 (58.5) mg borax (B)/kg bw/day). The 90-day studie with BA by Paynter (1962) also reports that all male rats (10/10) had testicular atrophy at dosing at the LOAEL (i.e. 500 mg BA/kg bw/day). Due to the unfortunate dosing intervals in these studies, the LOAEL is not appropriate to use for potency determination. In addition, due to the poor reporting of these studies, an ED10 is also difficult to derive. At the end of the treatment in

ANNEX 2 - COMMENTS AND RESPONSE TO COMMENTS ON CLH PROPOSAL ON BORIC ACID AND BORATES

the 2-year studies (24 months), the incidence of testicular atrophy was 30%, 10%, 40% and 100% at 0, 5.9, 17.5 and 58.5 mg B/kg bw/day, respectively, with both BA and borax as test material. An increase of 10% compared to control would give an ED10 of 17.5 mg B/kg bw/day, which is similar to the NOAEL reported from these studies. Using instead the reported NOAEL (17.5 B/kg bw/day) as a starting point, linear extrapolation give an ED10 of approximately 26 mg B/kg bw/day (normalising incidences to the NOAEL would give 0/10 animals and 6/10 animals with testicular atrophy at 17.5 and 58.5 mg B/kg bw/day, respectively). 26 mg B/kg bw/day is also a dose which has been reported as the LOAEL for mildly inhibited spermiation in rats (grade 1, i.e. 25 – 50 % tubules at stages below the inhibited spermiation and stage IX with retained spermatids, 0% tubules with germ cell exfoliation and 0% atrophic tubules) (Ku et al. 1993) and that has been associated with significantly decreased sperm motility in mice (i.e. 26.6 mg B/kg bw/day) (Fail at al. 1996). However, using 17.5 or 26 mg B/kg bw/day as the ED10 will make no difference when it comes to potency group, since the substances included in the CLH-proposal fall within the dose interval of the medium potency group for fertility regardless. Hence, the GCL (0.3%) would apply for fertility.

RAC's response

RAC agrees with the Dossier Submitter that there is no evidence that suggests a difference in sensitivity between humans and animals or evidence that suggests that there is no difference. Therefore, the default assumption of comparable sensitivity has to be assumed. Therefore, there this modifying factor does not warrant a change in potency.

RAC agrees with the DS that the effects used to determine the ED10/LOAEL are consider severe.

Date	Country	Organisation	Type of Organisation	Comment number
20.02.2019	Belgium	FERTILIZERS EUROPE	Industry or trade association	20

Comment received

Fertilizers Europe supports the same arguments and conclusion of European Borates Association (EBA), asking for a Generic Concentration Limit (GCL) of 3% w/w to be applied as boron-based concentration limit for boron substances as justified by the toxicology and toxicokinetics of boron-substances. More detailed comments can be found in the attached document.

ECHA note – An attachment was submitted with the comment above. Refer to public attachment Fertilizers Europe position on Borates_19_02_2019.pdf

Dossier Submitter's Response

Thank you for the comment.

The justification for the proposal to remove the SCLs for boric acid and the borates is given in section 4 of the CLH-proposal. Since the borates covered by the present proposal were subject to harmonised classification, new recommendations on how to derive concentration limits for reproductive toxicity has been agreed upon by the Member States. The justification for the proposal is therefore "*Change in existing entry due to new evaluation of existing data*".

The reference to "a level playing field" made by the DS refers to using the same methodology to derive concentration limits for reproductive toxicity for all borates as well as other substances on Annex VI.

The available human epidemiological studies have been assessed and considered in the CLH-proposal. Due to deficiencies or lacks in design or execution, they are all regarded as

to provide only additional information. The proposal to remove the SCLs is based on adverse effects in animals.

The DS has followed the current Guidance on the Application of the CLP criteria (v.5 July 2017) to propose withdrawal of the specific concentration limits for boric acid and the borates included in the proposal. It states that substances classified as toxic to reproduction in category 1B should be allocated to one of three potency groups; the high potency group with ED10 values ≤ 4 mg/kg bw/day (SCL of 0.03% w/w); the medium potency group with 4 mg/kg bw/day $< ED10$ value < 400 mg/kg bw/day (GCL of 0.3% w/w) or the low potency group with ED10 values ≥ 400 mg/kg bw/day (SCL of 3% w/w).

The derivation of ED10 values by the DS is based on boron equivalent doses using the same approach as was applied in the CLH proposals for disodium octaborate, anhydrous and disodium octaborate tetrahydrate (EC No. 234-541-0 and Index No. 005-020-00-3). These substances were classified as Repr. 1B (H360FD) with a GCL of 0.3% w/w (RAC-opinion, March 2014).

Comments on the, by Member States agreed, methodology or approach to derive concentration limits are outside of the scope of this CLH-proposal.

The estimated daily boron exposure levels of “highly exposed” individuals are well below the LOAELs in animal studies. There is no evidence of toxicokinetic differences between animals and humans. It can therefore not be excluded that reproductive effects would occur in humans if they were exposed to boron levels corresponding to the LOAELs. In addition, it is not possible to assess the exposure potential for the different B substances in different uses. It should be noted that exposure is not taken into consideration in the classification, since classification is based on the intrinsic hazardous properties of the substance. Moreover, there are no exposure considerations for setting specific concentrations limits according to CLP Article 10(1) and following CLP guidance in section 3.7.2.6. Modifying the potency group based on the epidemiological data for boron would therefore not be appropriate.

For response to EBAs comments, we refer to comment number 8 and 19.

RAC’s response

Please see the response to the comments from EBA (comments 8 and 19).

The suggestion to consider deriving a boron based GCL instead of a substance specific GCL will be discussed within the opinion and the background document.

RAC does not agree that a low potency is warranted based on the absence of effects in humans as the exposure level in humans is clearly below the below the ranges for low potency (above 400 mg/kg bw/day).

Date	Country	Organisation	Type of Organisation	Comment number
20.02.2019	United Kingdom	<confidential>	Company-Downstream user	21

Comment received

Boric acid and other boron compounds have been assessed and have Specific Classification Limits assigned to them. This proposal seeks to reclassify these substances under a generic classification limit that has been developed since the original classification limits were set. The CLP Guidance 2017 contains areas related to reclassification, but they are limited to carcinogenic substances and substances harmful to the aquatic environment.

The evidence evaluated is a mixture of epidemiological human studies and daily intake rat studies. The rodent studies were available at the time of the original classification. None of the evidence on humans indicates reproductive toxicity from increased exposure to boron. It is noted that the Committee for Risk Assessment have previously seen that rats are more susceptible to boron related effects compared to rabbits (para 10.8.5.1) hence the direct transfer of risks to rats onto risks to humans seems to be a pessimistic stance not based on the evidence available.

The evidence put forth does not back up that using the new limits will result in improved safety or reduced incidence of harm to people. If current limits have provided safety to humans, then additional controls are unnecessary. The proposal states reclassification "will result in a level playing field in between borates as well as in relation to other classified substances". This statement lacks any quantifiable meaning and does not convey any benefit to reclassifying these substances. There is no way to measure this apparent benefit.

Therefore, I disagree with the proposal to reclassify the Boric Acid Specific Concentration Limit.

Dossier Submitter's Response

Thank you for the comment. The justification for the proposal to remove the SCLs for boric acid and the borates is given in section 4 of the CLH-proposal. Since the borates covered by the present proposal were subject to harmonised classification, new recommendations on how to derive concentration limits for reproductive toxicity has been agreed upon by the Member States. The justification for the proposal is therefore "*Change in existing entry due to new evaluation of existing data*".

The reference to "a level playing field" made by the DS refers to using the same methodology to derive concentration limits for reproductive toxicity for all borates as well as other substances on Annex VI.

There are no evidence to conclude that humans are less sensitive to boron related effects than rats, or that humans are more similar to rabbits. Availability of information on two species allows a more comprehensive evaluation of prenatal developmental toxicity.

The estimated daily boron exposure levels of "highly exposed" individuals are well below the LOAELs in animal studies. There is no evidence of toxicokinetic differences between animals and humans. It can therefore not be excluded that reproductive effects would occur in humans if they were exposed to boron levels corresponding to the LOAELs. In addition, it is not possible to assess the exposure potential for the different B substances in different uses. It should be noted that exposure is not taken into consideration in the classification, since classification is based on the intrinsic hazardous properties of the substance. Moreover, there are no exposure considerations for setting specific concentrations limits according to CLP Article 10(1) and following CLP guidance in section 3.7.2.6.

RAC's response

RAC understands the impact of the change of an SCL into a GCL. However, classification including the setting of SCLs or applying the GCL is based on the hazardous properties of a substance and does not taken into account the exposure and risks or the social economic consequences of the classification.

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Date	Country	Organisation	Type of Organisation	Comment number
20.02.2019	France	<confidential>	Company-Manufacturer	22
Comment received				
<p>We are a SME producing water treatment products for swimming pool. We use boric acid in two ways :</p> <ol style="list-style-type: none"> 1. With disodium tetraborate pentahydrate in liquid formulations as pH buffering agent 2. In chlorine based products (tablets) as release agent <p>The human studies showed no clear evidence of adverse effects on male fertility by boron. The latest study Duydu et al. (2018a) investigated the effects of boron in exposed workers. Even if boron exposure levels were well below the LOAELs from corresponding animal studies, there is no evidence that the effects observed in animals are relevant to humans.</p> <p>We use boric acid and disodium tetraborate pentahydrate as pH buffering acid in formulations in concentrations under SCLs but higher than 0.3% w/w. With this proposal to change SCL to GCL of 0.3% w/w, we would label our products with GHS 07 pictogram, which is very damaging for pool products.</p> <p>Pool products containing boric acid and/or borates are diluted when they are used in the swimming pool: swimmers exposure is extremely low and well below GCL but these products will have to be labeled with H360FD statement and corresponding pictogram.</p> <p>Moreover, we don't understand this position while boric acid and sodium borate are used in personal care products: solution of boric acid and sodium borate (respectively 1.8 g and 1.2 g per 100 ml) is used for ocular wash, 3 times per days. It is not mentioned it could have effects on fertility and not labeled with the GHS07 pictogram. This product is used since years and some people use it regularly and repeatedly.</p>				
Dossier Submitter's Response				
<p>Thank you for the comment. It has been noted.</p> <p>As stated in the comment, the estimated human exposure levels from epidemiological studies are well below the LOAEL from animal studies. It can therefore not be excluded that reproductive effects would occur in humans if exposed to boron levels corresponding to the LOAELs. Hence, the DS found that the lack of adverse health effects from human epidemiological studies did not contradict the positive findings from animal studies.</p> <p>CLP does not apply to substances and mixtures in the form of cosmetic products (as defined in Directive 76/768/EEC), which are in the finished state, intended for the final user (Article 1.5).</p>				
RAC's response				
<p>There borates are classified as toxic to reproduction in category1B meaning that the classification is based on animal data. The CLP criteria do not require evidence that the effects are relevant to humans.</p> <p>RAC agrees with the dossier submitter that CLP does not apply to cosmetic products.</p> <p>The proposed classification is not only relevant to swimmers but also to the consumer applying the pool products. The statement on the label is the only information that the product contains substances that have an effect on reproduction. RAC understands the impact of the change of an SCL into a GCL.</p>				

ANNEX 2 - COMMENTS AND RESPONSE TO COMMENTS ON CLH PROPOSAL ON BORIC ACID AND BORATES

Date	Country	Organisation	Type of Organisation	Comment number
20.02.2019	Austria	Environment Agency Austria/National Expert Institution	Academic institution	23
Comment received				
<p>The Environment Agency Austria supports the proposal to change the specific concentration limits (SCLs) currently part of the harmonised classification of the listed borates to generic concentration limits (GCLs). The reproductive potential, including developmental effects as well as effects on fertility, which is demonstrated in several animal species, clearly supports a classification as Repr 1B, H360DF. Read -across between the single boron compounds is clearly supported based on the fact that the boron content drives the reprotoxic potential of these compounds, which exist as un-dissociated boric acid under most physiological conditions (i.e. below pH 8). The ED10 / LOAELs derived for the single compounds all fall between 4 and 400 mg/kg bw/day, the medium potency group. According to the CLP guidance GCLs should be allocated to substances in that group. None of the modifying factors related to type or severity of effect, data availability, dose-response relationship, mode/mechanism of action, toxicokinetics or bioaccumulation applies.</p>				
Dossier Submitter's Response				
Thank you for the support.				
RAC's response				
Noted.				

Date	Country	Organisation	Type of Organisation	Comment number
20.02.2019	Austria		MemberState	24
Comment received				
<p>The AT CA supports the proposal to change the specific concentration limits (SCLs) currently part of the harmonised classification of the listed borates to generic concentration limits (GCLs). The reproductive potential, including developmental effects as well as effects on fertility, which is demonstrated in several animal species, clearly supports a classification as Repr 1B, H360DF. Read -across between the single boron compounds is clearly supported based on the fact that the boron content drives the reprotoxic potential of these compounds, which exist as un-dissociated boric acid under most physiological conditions (i.e. below pH 8). The ED10 / LOAELs derived for the single compounds all fall between 4 and 400 mg/kg bw/day, the medium potency group. According to the CLP guidance GCLs should be allocated to substances in that group. None of the modifying factors related to type or severity of effect, data availability, dose-response relationship, mode/mechanism of action, toxicokinetics or bioaccumulation applies.</p>				
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
12.12.2018	United Kingdom	<confidential>	Company-Downstream user	25
Comment received				
Will this removal of SCL affect all metal borates? Eg potassium borate				
Dossier Submitter's Response				
The proposal includes the following substances: Boric acid [1]; Diboron trioxide [2]; Tetraboron disodium heptaoxide, hydrate [3]; Disodium tetraborate, anhydrous [4]; Orthoboric acid sodium salt [5]; Disodium tetraborate decahydrate [6]; Disodium tetraborate pentahydrate [7], and CAS numbers: 10043-35-3 [1]; 11113-50-1 [1]; 1303-86-2 [2]; 12267-73-1 [3]; 1330-43-4 [4]; 13840-56-7 [5]; 1303-96-4 [6]; 12179-04-3 [7]. Potassium borate is not included.				
RAC's response				
RAC agrees with the dossier submitter that the proposal does not affect potassium borate and other borates not part of the proposal.				

Date	Country	Organisation	Type of Organisation	Comment number
14.02.2019	Germany	Verband Schmierstoff-Industrie e.V.	Industry or trade association	26
Comment received				
In recent epidemiological study was published on the effect of boron on human development [Duydu et al. 2018a], showing no effects from boron exposure on pregnancy outcomes. In addition, studies on occupational boron exposure were conducted in male workers employed in boron mining and production facilities in Turkey [Xing et al., 2008; Duydu et al., 2011, 2018b] with the absence of any adverse effects. The extremely high blood boron concentrations of males and females in published epidemiological studies reflects the heavy environmental and/or occupational exposure conditions (worst-case scenario). However, the mean blood boron concentrations of humans are still lower than the blood boron concentrations at the NOAELs for developmental and reproductive toxicity in rats. Under conditions of normal handling and use of boron compounds, it is very unlikely that humans could exceed blood boron concentrations corresponding to the NOAELs for developmental and reproductive toxicity in rats [Duydu et al, 2011, 2018a, 2018b]. Based on a critical review of Igra et al. and the absence of developmental effects of high exposure to boron during pregnancy, removal of SCLs and application of the more restrictive GCLs are not warranted.				
Dossier Submitter's Response				
The available human epidemiological studies have been assessed and considered in the CLH-proposal. All the studies were found to be lacking in some or several aspects, as described in the dossier. Overall, the DS concluded that the lack of evidence on adverse health effects in humans could not negate the positive findings from the animal studies. The proposal to remove the SCLs is therefore based on evidence of adverse effects in animals.				
The estimated daily boron exposure levels of "highly" exposed individuals in the epidemiological studies are well below the LOAELs in animal studies. The same applies to the respective blood boron levels. There is no evidence of toxicokinetic differences between animals and humans that could indicate species differences in toxicity. The teratogenicity of B is possibly caused by an altered hox gene expression, caused by inhibition of histone				

ANNEX 2 - COMMENTS AND RESPONSE TO COMMENTS ON CLH PROPOSAL ON BORIC ACID AND BORATES

deacetylases, a mechanism that is likely to be relevant also for humans (RAC opinion for boric acid 2014). It can therefore not be excluded that reproductive effects would occur in humans if they were exposed to boron levels corresponding to the LOAELs. In addition, it is not possible to assess the exposure potential for the different B substances in different uses. The dossier submitter reminds that exposure is not taken into consideration in the classification, since classification is based on the intrinsic hazardous properties of the substance.

RAC's response

The available epidemiologic data do not contradict the available animal data and do not warrant a different approach for deriving and SCL or GCL.

Date	Country	Organisation	Type of Organisation	Comment number
14.02.2019	Finland		MemberState	27

Comment received

The current Guidance on the Application of the CLP Criteria describes the possibilities for derivation of specific concentration limits for certain hazards according to Article 10(1) of the CLP legislation. In line with the guidance and for the endpoint in question, substances with ED10 values $4 \text{ mg/kg bw/day} < \text{ED}_{10} \text{ or LOAEL} < 400 \text{ mg/kg bw/day}$ belong to the medium potency category corresponding to a classification limit of 0.3% w/w. Existing key study data for boric acid and disodium tetraborate decahydrate indicate LOAEL values above 4 mg/kg bw/day and below 400 mg/kg bw/day for effects on fertility and development. Hence, these substances can be assigned medium potency accordingly. FI CA considers the removal of the current harmonised specific concentrations for the borates in question as justified in light of the data described in the CLH report.

Dossier Submitter's Response

Thank you for the support.

RAC's response

Noted.

Date	Country	Organisation	Type of Organisation	Comment number
22.02.2019	France		MemberState	28

Comment received

RAC provided in March 2014 an opinion that recommended the application of GCL for disodium octaborate and noted that SCL should not apply to boric acid. Indeed, ANSES agrees that these SCL were determined according to a previous non-validated methodology that is not in line with the current guidance to set SCL for reproductive toxicity. The present proposal to remove SCL for boric acid and borates is consistent with the previous RAC recommendation and follows appropriate guidance. FR agrees with the values of ED10 (for fertility) and LOAEL (for development) which include these borates in the medium potency group ($4 \text{ mg/kg bw/day} < \text{ED}_{10} < 400 \text{ mg/kg bw/day}$) and trigger an application of the GCL of 0.3% for both developmental effects and effects on sexual function and fertility (Table VI.8 of the CLP guidance).

New studies published since the 2014 RAC recommendation do not challenge the assessment of reproductive toxicity potency and the proposal to remove the SCL for boric acid and borates is supported.

The section 3.7.2.6.3 refers to the determination of the ED10 value. The appropriate reference should Table VI.8 of the CLP guidance. This should be amended.

ANNEX 2 - COMMENTS AND RESPONSE TO COMMENTS ON CLH PROPOSAL ON BORIC ACID AND BORATES

Dossier Submitter's Response
Thank you for your support. We agree that the reference to section 3.7.2.6.3 is incorrect, it should read 3.7.2.6.6. (Table 3.14).
RAC's response
Noted.

Date	Country	Organisation	Type of Organisation	Comment number
22.02.2019	Poland	Polish Association of Cosmetic and Detergent Industry	Industry or trade association	29

Comment received
toxicological and ecotoxicological studies of authorized products (BPR) confirmed that the products do not pose a threat - studies confirmed the safety of products with 3-20% Boron compounds
Dossier Submitter's Response
Thank you for the comment, it has been noted.
RAC's response
Noted.

Date	Country	Organisation	Type of Organisation	Comment number
22.02.2019	Germany		Individual	30

Comment received
<p>The classification of substances and mixtures is important not only within the application range of Regulation (EC) 1272/2008, but also e.g. for the classification of wastes or for application of Directive 2012/18/EU and others. Hence correct substances and mixtures classification is essential for the applicability of EU legal framework.</p> <p>If weighing of evidence necessarily results in category 1b reproduction toxicity for soluble boric oxides, boric acid and boric acid salts, I would like to draw attention to the outcome of omitting specific concentration limits:</p> <p>The reproduction toxicity of boric acid, of diboron trioxide and of the borates mentioned in the CLH report submitted by the Swedish Chemicals Agency in November 2018 bases on the same principle with boron the toxic component. There is broad agreement on the fact that boron exhibits reproduction toxicity in animal tests (ED10 = 13.3 mg/kg bw / day). Hence the toxic potency is sufficiently accounted for when ranking boron in potency group 2 (medium potency, ED10 ≥ 4 mg / kg bw / day and ≤ 400 mg / kg bw / day).</p> <p>The borates react rapidly with water, depending on concentration and pH value. Therefore, in mixtures containing water it will be impossible to distinguish between the boron compounds. If the component present in a mixture is unknown, the precautionary principle forces to assume the "most toxic" compound to be present.</p> <p>Boron has a very low atomic weight; hence the conversion factor when recalculating boron to boron compounds is high and varies a lot between different compounds. Therefore in the case of the borates, application of both a GCL and the precautionary principle will result in a significant overestimation of reproductive toxicity. For example assuming Na3BO3 as a mixture's component will give the same result as if boron had a high reproductive toxicity potential, i.e. a concentration limit of 0,03 % calculated on boron content would be applied (cf. column 10 of the table attached).</p> <p>I cannot imagine this is intended by the classification rules, so one should look at the motivation for changing from the present SCL values to the GCL:</p> <p>The justification that action is needed at Community level bases on two arguments</p> <p>a) new recommendations on how to derive concentration limits for reproductive toxicity have been agreed on</p>

b) "revising the SCL will result in a level playing field in between the borates as well as in relation to other classified substances."

Applying the same concentration limit (GCL) to all of the boron compounds mentioned, obviously will not lead to a level playing field in between the borates, but to a severe distortion regarding the classification of mixtures containing one of the boron compounds. Within the framework of Regulation (EC) 1272/2008 specific concentration limits (SCL) give the opportunity to take into account specific effects. In case of the borates, this should be used to achieve the level playing field in between the borates mentioned above.

Therefore I propose to either

- stick to the present SCL values although these may not be well reasoned any more or
- define new appropriate SCL or to
- switch from compound concentration base to element concentration base, if bridging is being applied for several compounds of a toxic element.

ECHA note – An attachment was submitted with the comment above. Refer to public attachment [Boron_CL_comparison_.pdf](#)

Dossier Submitter's Response

Thank you for the comment.

The DS has followed the current Guidance on the Application of the CLP criteria (v.5 July 2017) to propose withdrawal of the specific concentration limits for boric acid and the borates included in the proposal. It states that substances classified as toxic to reproduction in category 1B should be allocated to one of three potency groups; the high potency group with ED10 values ≤ 4 mg/kg bw/day (SCL of 0.03% w/w); the medium potency group with 4 mg/kg bw/day $<$ ED10 value < 400 mg/kg bw/day (GCL of 0.3% w/w) or the low potency group with ED10 values ≥ 400 mg/kg bw/day (SCL of 3% w/w).

The derivation of ED10 values by the DS is based on boron equivalent doses using the same approach as was applied in the CLH proposals for disodium octaborate, anhydrous and disodium octaborate tetrahydrate (EC No. 234-541-0 and Index No. 005-020-00-3). These substances were classified as Repr. 1B (H360FD) with a GCL of 0.3% w/w (RAC-opinion, March 2014).

The reference to a level playing field made by the DS refers to using the same methodology to derive concentration limits for all borates on Annex VI.

The DS notes the suggestion for recalculation of the concentration limits for boric acid and the borates. However, comments on the, by Member States agreed, methodology or approach to derive concentration limits are outside of the scope of this CLH-proposal.

RAC's response

The suggestion to consider deriving a boron based GCL instead of a substance specific GCL will be discussed within the opinion and the background document.

ANNEX 2 - COMMENTS AND RESPONSE TO COMMENTS ON CLH PROPOSAL ON BORIC ACID AND BORATES

Date	Country	Organisation	Type of Organisation	Comment number
22.02.2019	Germany	<confidential>	Company-Downstream user	31
Comment received				
<p>The existing specific concentration limits for boric acids (5.5 % w/w) should be maintained or a GCL of 3 % (w/w as boron) should be established.</p> <p>According to the „Guidance on the Application of the CLP Criteria“ modifying factors (even of a more qualitative nature) can be applied. In this instance the epidemiological human data have not been taken into account sufficiently.</p> <p>Despite extreme exposure conditions the mean blood boron concentrations of humans are still lower than the blood boron concentrations at the NOAELs in rats. Studies exist that conclude that reproductive and developmental effects are not relevant to human under feasible and realistic conditions of exposure to inorganic boron compound. The outcome of this studies should be used in the evaluation process of the potency classification.</p> <p>Studies exist (Muller et al, A regulatory approach to assess the potency of substances toxic to the reproduction. Regulatory Toxicology and Pharmacology, 63, 97-105, 2012) showing that ED10 values of boric acid are 123.5 mg/kg/d and 195 mg/kg/d for fertility and developmental effects respectively. As these values are near to the boundary of low potency group, classification of boric acid into the low potency group should be considered. It would lead to an GCL of 3 %, that should be applied as boron based concentration limit.</p>				
Dossier Submitter's Response				
<p>Thank you for the comment. The available human epidemiological data has been assessed and considered in the CLH-proposal. Overall, the DS concluded that the lack of evidence of adverse health effects in human epidemiological studies could not negate the positive findings from the animal studies, since the estimated daily boron exposure levels in humans were well below the LOAELs of the animal studies. The same observation was made for the measured levels of boron in blood.</p> <p>According to the Guidance of the application of the CLP criteria, the following factors are used as modifying factors:</p> <ul style="list-style-type: none"> • type or severity of effect • data availability • dose-response relationship • mode/mechanism of action • toxicokinetics and, • bioaccumulation <p>External exposure conditions may to our knowledge not be used as a modifying factor. It should be noted that exposure is not taken into consideration in the classification, since classification is based on the intrinsic hazardous properties of the substance.</p> <p>The ED10/LOAEL values for boric acid, as derived in the CLH-dossier are 103 and 78 mg/kg bw/day for fertility and development, respectively. The DS does not consider these values, or the ones proposed in the comment above to be borderline to the low potency group, for which the ED10-values should be ≥ 400 mg/kg bw/day, according to the CLP Guidance.</p>				
RAC's response				
<p>The available human data has been taken into account and do not show that the effects observed in animals are not relevant to humans nor show a difference in sensitivity.</p>				

ANNEX 2 - COMMENTS AND RESPONSE TO COMMENTS ON CLH PROPOSAL ON BORIC ACID AND BORATES

Therefore, this modifying factor does not warrant a deviation from the estimated medium potency. Further, RAC does not agree that the ED10 values derived by Muller et al. (2012) should be used for potency estimation. RAC considers the potency values proposed by the dossier submitter and in line with the previous assessment by RAC for two others borates appropriate.

PUBLIC ATTACHMENTS

1. Boric acid public consultation 01-2019 Öff.doc [Please refer to comment No. 13]
2. Boron_CL_comparison_.pdf [Please refer to comment No. 30]
3. 19 02 22 Cerame Unie reply to public consultation - Borates.pdf [Please refer to comment No. 5, 16]
4. EBA suppl. Comments on CLH Report_20-02-2019.pdf [Please refer to comment No. 19]
5. Fertilizers Europe position on Borates_19_02_2019.pdf [Please refer to comment No. 20]
6. Proposed future entry - signed.pdf [Please refer to comment No. 6]
7. EBA Comments on CLH Report_14-02-2019.pdf [Please refer to comment No. 8]

CONFIDENTIAL ATTACHMENTS

1. Boric acid public consultation 01-2019 NÖff (2).doc [Please refer to comment No. 13]