Committee for Risk Assessment

RAC

Annex 2

Response to comments document (RCOM)

to the Opinion proposing harmonised classification and labelling at EU level of

perboric acid, sodium salt [1]; perboric acid, sodium salt, monohydrate [2]; perboric acid (HBO(O2)), sodium salt, monohydrate; sodium peroxoborate [3]; sodium perborate [4]

EC Number: 234-390-0 [1]; 234-390-0 [2]; 239-172-9 [4]
CAS Number: 11138-47-9 [1]; 12040-72-1 [2]; 10332-33-9 [3]; 15120-21-5 [4]

CLH-O-0000007164-77-01/F

Adopted

15 September 2022

ANNEX 2 - COMMENTS AND RESPONSE TO COMMENTS ON CLH PROPOSAL ON PERBORIC ACID, SODIUM SALT [1]; PERBORIC ACID, SODIUM SALT, MONOHYDRATE [2]; PERBORIC ACID (HBO(O2)), SODIUM SALT, MONOHYDRATE; SODIUM PEROXOBORATE [3]; SODIUM PERBORATE [4]

COMMENTS AND RESPONSE TO COMMENTS ON CLH: PROPOSAL AND JUSTIFICATION

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

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

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Substance name: perboric acid, sodium salt [1]; perboric acid, sodium salt, monohydrate [2]; perboric acid ($HBO(O_2)$), sodium salt, monohydrate; sodium peroxoborate [3]; sodium perborate [4]
EC number: 234-390-0 [1]; 234-390-0 [2]; 239-172-9 [4]
CAS number: 11138-47-9 [1]; 12040-72-1 [2]; 10332-33-9 [3]; 15120-21-5 [4]
Dossier submitter: Sweden

GENERAL COMMENTS

Date	Country	Organisation	Type of Organisation	Comment number
19.01.2022	Germany		MemberState	1
Comment received				
Due to the available toxicokinetic information for per(oxo)borates and boric acid, it is agreed that the read across to boric acid and per(oxo)borate tetrahydrate (PBS-4) is justified. There are several inconsistencies in Table 5: - "sodium peroxoborate" is neither present under "Retain" nor under "Remove", but in the Resulting Annex VI entry (last row). Please check if this term should be retained or removed and amend both rows accordingly. - According to Table 0, "sodium peroxometaborate" and the corresponding CAS number 7632-04-4 should be removed and thus are not present in the Resulting Annex VI entry. Please also add them under "Remove". - "[containing ≥ 0,1 % (w/w) of particles with an aerodynamic diameter of below 50 µm]" is not present in the Resulting Annex VI entry but neither listed under "Remove" nor "Retain". Please check and amend accordingly. Moreover, there is no information about physicochemical properties. The respective chapter 7 only deals with details about identity and molecular structure, so the heading is misleading.				
Dossier Submitter's Response				
Read-across Thank you for supporting the read-across from boric acid and per(oxo)borate tetrahydrate (PBS-4).				

Table 5

Thank you for pointing to the editorial mistakes in Table 5. The corrections can be seen highlighted in yellow below in table 5 in Appendix 1. In addition, similar to your comments on corresponding table 5 for PBS-4 and sodium peroxometaborate, also "dusts and mists" have been added for the acute tox classification.

Physicochemical properties

There is only a Reach registration available for Perboric acid, sodium salt, EC number: 234-390-0, CAS number: 11138-47-9 where there is some information on the physciochemical properties of PBS-1 and PBS-4. There is also some information from the *SCCS Opinion on sodium perborate and perboric acid* (2010) and the *European Risk Assessment Report on perboric acid, sodium salt (CAS 11138-47-9)*(2007) (both refences included in the CLH-reports) on the per(oxo)borates, including sodium peroxometaborate. The data, when found in all three information sources, appears to be consistent. Please see compiled relevant information on physicochemical properties of sodium peroxometaborate, PBS-1 and PBS-4 in the table below.

Substance name	Sodium peroxometaborate	perboric acid, sodium salt [1]; perboric acid, sodium salt, monohydrate [2]; perboric acid (HBO(O2)), sodium salt, monohydrate; sodium peroxoborate [3]; sodium perborate [4]	perboric acid (H3BO2(O2)), monosodium salt trihydrate [1]; perboric acid, sodium salt, tetrahydrate [2]; perboric acid (HBO(O2)), sodium salt, tetrahydrate; sodium peroxoborate, hexahydrate [3]
CAS number	7632-04-4	11138-47-9 [1]; 12040-72-1 [2]; 10332-33-9 [3]; 15120-21-5 [4]	13517-20-9 [1]; 37244-98-7 [2]; 10486-00-7 [3]
EC number	231-556-4	234-390-0 [1]; 234-390-0 [2]; 239-172-9 [4]	239-172-9 [1]; 234-390-0 [2]
Molecular formula	NaBO3	B2H4O8Na2	B2H4O8Na2.6H2O
Molecular weight	81.8 g/mol	199.6 g/mol	307.6 g/mol
Boron content	13,2%	10,8%	7,0%
Physical form	Solid white amorphous powder	Solid white crystal	Solid white crystal
Melting point	63 °C	Decompose >50 - >180°C	Ca 60-65,5 °C
Boiling point	no information available	decomposition	decomposition
Water solubility	21,5 g/L	15-16 g/L	23 g/L
Dissociation constant	Not applicable due to decomposition	Not applicable due to decomposition	Not applicable due to decomposition
Partition coefficient	no information available	Not applicable (analytical difficulties)	Not applicable (analytical difficulties)

RAC's response
RAC thanks the Dossier Submitter for correcting the editorial mistakes and for providing the phys chem properties of the substances. The adapted Table from the Annex is included in the draft opinion.

TOXICITY TO REPRODUCTION

Date	Country	Organisation	Type of Organisation	Comment number
20.01.2022	France		MemberState	2

Comment received

Perboric acid, sodium salt monohydrate (PBS-1) has a harmonised classification as toxic to reproduction for developmental effects and fertility effects: Repr. 1B (H360Df). Moreover, it has SCLs for adverse effects on sexual function and fertility and for adverse effects on the development of the offspring (at 9% and 6-9.5%, respectively) that were established based on the toxicity of the boron moiety (B) using an approach proposed by BauA (1998). This method has since been reassessed and the RAC removed the SCLs based from it and concluded on the harmonisation of GCL 0.3% w/w for boric acid and six sodium borates that have a harmonised classification as Repr. 1B in 2019.

FR agrees with the classification proposed and comes to the same conclusion about the allocation of potency of PBS-1 as medium, GCL of 0.3% for fertility based on read-across with boric acid and for development, based on read-across of data from developmental toxicity studies conducted with PBS-4.

Page 54, table 31: we cannot find the same ED10 for the developmental effects of PBS-4 presented in the table 31. Indeed, by applying the method presented in the CLP guidance (2017) page 409, section 3.7.2.6.3.3. we obtain different results :
Live foetus weight : ED10 = 271.72 mg PBS-4/kg bw/day
Litter weight : ED10 = 202.68 mg PBS-4/kg bw/day

Could you please re-check your calculations? These results do not change the allocation of potency expected for PBS-1.

Dossier Submitter's Response

Thank you for your support.

We agree that there are mistakes regarding ED10 in table 31 (please see corrections in the table below). As you point out, the corrected ED10 values (calculated according to CLP guidance (2017)) do not change the potency group allocation of PBS-1.

Developmental effects	**Dose levels (mg PBS-4/kg bw/day)**				**ED10 (linear interpolation of available doses)**		**Allocation of potency group***
	0	**100**	**300**	**1000**	**(mg PBS-4/kg bw/day)**	**mg B/kg bw/day**	
Live foetus weight (g)	3.69	3.57	3.28	2.4	~~127.5~~ 271.7	~~9~~ 19	Medium, GCL of 0.3%
Litter weight (g)	54.97	52.62	46.49	32.52	~~197.2~~ 202.7	~~13.8~~ 14.2	Medium, GCL of 0.3%

Post-implantation loss (%)	2.91	2.39	13.54	15.2	288.8	20.2	Medium, GCL of 0.3%
LOAEL for developmental effects					300	21	Medium, GCL of 0.3%

RAC's response

RAC thanks the Dossier Submitter for correcting the ED10s.

Date	Country	Organisation	Type of Organisation	Comment number
19.01.2022	Germany		MemberState	3

Comment received

Adverse effects on sexual function and fertility:
The classification of per(oxo)borate monohydrate (PBS-1) as Repr. 1B, H360F is based on a read across to boric acid and per(oxo)borate tetrahydrate (PBS-4). Boric acid is already classified as Repr.1B, H360F. Supporting information was provided by the results from a 28-day limit test conducted with PBS-4 showing reduced testes weight, testicular focal tubular atrophy and inhibition of spermiation.
As no data with PBS-1 are available to derive an ED10, it is agreed that read across data on boric acid correcting for the respective boron content (ED10 of 17.5 mg B/kg bw/d) can be used for PBS-1. Based on the estimated ED10 of 159 mg B/kg bw/d, PBS-1 is considered to belong to the medium potency group with a GCL of 0.3 % w/w.

Adverse effects on developmental toxicity
PBS-1 is already classified as Repr. 1B, H360D, based on one PNDT study of PBS-4 in rat showing developmental effects including skeletal, eye, CNS and cardiovascular malformations. In addition to that, RAC concluded that exposure to boric acid induced developmental toxicity in the absence of secondary or maternal toxicity. The available human data are limited but do not contradict the experimental studies performed in animals. Therefore, there is no evidence that the observed effects are not relevant for humans. Overall and in agreement with previous evaluations of RAC, the effects on developmental parameters after exposure to PBS-4, it is supported to retain the existing classification Repr.1B, H360D.
Due to the medium potency estimated for PBS-1 based on the LOAEL for developmental effects in the PNDT study with PBS-4 correcting for the percentage of boron, the use of a GCL of 0.3 % w/w as proposed by the DS is supported.

Dossier Submitter's Response

Thank you for your support.

RAC's response

RAC agrees.

OTHER HAZARDS AND ENDPOINTS – Acute Toxicity

Date	Country	Organisation	Type of Organisation	Comment number
20.01.2022	France		MemberState	4

Comment received

Acute toxicity:
Acute inhalation toxicity: We agree that the use of the thoracic fraction approach is not the most appropriate for classification, as the OECD guidelines for acute inhalation

toxicity recommend using aerosols with a mass median aerodynamic diameter (MMAD) ≤4 µm and a geometric standard deviation (GSD) in the range of 1.0 to 3.0, so particles can reach all regions of the respiratory tract. Moreover studies show that hydrogen peroxide released by hydrolysis contributes mainly of the acute toxicity of per(oxo)borates. Therefore, the acute toxicity of per(oxo)borates would not be due to the particle diameter size. FR agrees that the cut-off value of 50 µm for particle size should be removed. Given that hydrogen peroxide contribute mainly of the acute toxicity of per(oxo)borates, FR agrees with the reasoning to link hydrogen peroxide content and acute toxicity for the classification, as no study conducted on PBS-1 is available. Consequently, the proposed classification as Acute Tox.3, H331 and the ATE of 0.75 mg/L is supported. Acute oral study: FR agrees with the classification proposed as Acute Tox. 4, H302 and the ATE of 890 mg/kg bw/day.
Dossier Submitter's Response
Thank you for your support.
RAC's response
RAC has no further comments.

Date	Country	Organisation	Type of Organisation	Comment number
19.01.2022	Germany		MemberState	5
Comment received				
Acute toxicity – oral route: The proposed classification for PBS-1 as Acute Tox. category 4, H302, with removal of the asterisk (*) and setting of an ATE is supported. Two acute oral toxicity studies with PBS-1 according to US EPA-guideline were conducted in SD- and Wistar-rats, respectively, resulting in LD50 value > 300 but < 2000 mg/kg bw. Thus, the criterion for classification in Acute Tox. category 4 is fulfilled. The proposed inclusion of an ATE of 890 mg/kg bw based on the lowest LD50 value in female rats is supported. Acute toxicity – dermal route: One acute dermal toxicity study (OECD TG 402) was performed with PBS-1 showing a LD50 value above 2000 mg/kg bw. Therefore, no classification is warranted. Acute toxicity – inhalation route: Due to the lack of studies with PBS-1, read across was applied to PBS-4. The LC50 value for PBS-1 was 0.75 mg/l based on the calculated LC50 of PBS-4 (1.16 mg/l). As this value lies between 0.5 and 1.0, the criterion for classification of sodium peroxometaborate in category 3 is fulfilled. As the available study is considered reliable, its use to set an ATE for acute inhalation toxicity of PBS-1 is supported.				
Dossier Submitter's Response				
Thank you for your support. (We assume that you mean PBS-1 and not sodium peroxometaborate in the following sentence in your comment above: *As this value lies between 0.5 and 1.0, the criterion for classification of sodium peroxometaborate in category 3 is fulfilled*.)				
RAC's response				
RAC has no further comments.				

APPENDIX 1

Table 5: Proposed harmonised classification according to the CLP criteria

	Index No	International Chemical Identification	EC No.	CAS No.	Classification		Labelling			Specific Conc. Limits, M-factors	Notes
					Hazard Class and Category Code(s)	Hazard statement Code(s)	Pictogram, Signal Word Code(s)	Hazard statement Code(s)	Suppl. Hazard statement Code(s)		
Current Annex VI entries	005-019-00-8	perboric acid, sodium salt [1]; perboric acid, sodium salt, monohydrate [2]; perboric acid ($HBO(O_2)$), sodium salt, monohydrate [3]; sodium peroxoborate; [containing < 0.1 % (w/w) of particles with an aerodynamic diameter of below 50 µm]	234-390-0 [1] 234-390-0 [2] 231-556-4 [3]	11138-47-9 [1] 12040-72-1 [2] 10332-33-9 [3]	Ox. Sol. 3 Repr. 1B Acute Tox. 4 * STOT SE 3 Eye Dam. 1	H272 H360Df H302 H335 H318	GHS03 GHS05 GHS08 GHS07 Dgr	H272 H360Df H302 H335 H318		Repr. 1B; H360D: 6.5 % ≤ C < 9 % Repr. 1B; H360Df: C ≥ 9 % Eye Dam. 1; H318: C ≥ 22 % Eye Irrit. 2; H319: 14 % ≤ C < 22 %	
	005-019-01-5	perboric acid, sodium salt [1];	234-390-0 [1] 234-390-0 [2]	11138-47-9 [1] 12040-72-1 [2]	Ox. Sol. 3 Repr. 1B Acute Tox. 3 *	H272 H360Df H331 H302 H335	GHS03 GHS06 GHS05 GHS08 Dgr	H272 H360Df H331 H302 H335		Repr. 1B; H360D: 6.5 % ≤ C < 9 %	

		perboric acid, sodium salt, monohydrate [2]; perboric acid ($HBO(O_2)$), sodium salt, monohydrate [3]; sodium peroxoborate; [containing = 0.1 % (w/w) of particles with an aerodynamic diameter of below 50 µm]	231-556-4 [3]	10332-33-9 [3]	Acute Tox. 4 * STOT SE 3 Eye Dam. 1	H318		H318		Repr. 1B; H360Df: C ≥ 9 % Eye Dam. 1; H318: C ≥ 22 % Eye Irrit. 2; H319: 14 % ≤ C < 22 %	
	005-017-00-7	sodium perborate [1]; sodium peroxometaborate [2]; sodium peroxoborate; [containing < 0.1 % (w/w) of particles with an aerodynamic diameter of below 50 µm]	239-172-9 [1] 231-556-4 [2]	15120-21-5 [1] 7632-04-4 [2]	Ox. Sol. 2 Repr. 1B Acute Tox. 4 * STOT SE 3 Eye Dam. 1	H272 H360Df H302 H335 H318	GHS03 GHS05 GHS08 GHS07 Dgr	H272 H360Df H302 H335 H318		Repr. 1B; H360Df: C ≥ 9 % Repr. 1B; H360D: 6.5 % ≤ C < 9 % Eye Dam. 1; H318: C ≥ 22 % Eye Irrit. 2; H319: 14 % ≤ C < 22 %	
	005-017-01-4	sodium perborate [1]; sodium peroxometaborate [2];	239-172-9 [1] 231-556-4 [2]	15120-21-5 [1] 7632-04-4 [2]	Ox. Sol. 2 Repr. 1B Acute Tox. 3 * Acute Tox. 4 *	H272 H360Df H331 H302 H335 H318	GHS03 GHS06 GHS05 GHS08 Dgr	H272 H360Df H331 H302 H335 H318		Repr. 1B; H360Df: C ≥ 9 % Repr. 1B; H360D: 6.5 % ≤ C < 9 % Eye Dam. 1;	

		sodium peroxoborate; [containing ≥ 0.1 % (w/w) of particles with an aerodynamic diameter of below 50 µm]			STOT SE3 Eye Dam. 1					H318: C ≥ 22 % Eye Irrit. 2; H319: 14 % ≤ C < 22 %	
Dossier submitters proposal	**Merge:** 005-019-00-8 005-019-01-5 005-017-00-7 005-017-01-4	**<u>Retain</u>:** perboric acid, sodium salt [1] perboric acid, sodium salt, monohydrate [2] perboric acid ($HBO(O_2)$), sodium salt, monohydrate; sodium peroxoborate [3] sodium perborate [4] **Remove:** sodium peroxometaborate [containing < 0.1 % (w/w) of particles with an aerodynamic diameter of below 50 µm] [containing = 0.1 % (w/w) of	**<u>Retain:</u>** 234-390-0 [1] 234-390-0 [2] 239-172-9 [4] **Remove:** 231-556-4 [3]	**<u>Retain:</u>** 11138-47-9 [1] 12040-72-1 [2] 10332-33-9 [3] 15120-21-5 [4] **<u>Remove:</u>** 7632-04-4	**<u>Modify:</u>** Repr. 1B Acute Tox. 3 Acute Tox. 4	**<u>Modify:</u>** H360FD H331 H302	**<u>Retain:</u>** GHS06 GHS08 Dgr	**<u>Modify:</u>** H360FD H331 H302		**Remove:** Repr. 1B; H360D: 6.5 % ≤ C < 9 % Repr. 1B; H360Df: C ≥ 9 % **Add:** Inhalation: ATE = 0.75 mg/L (dusts and mists) Oral: ATE = 890 mg/kg bw/day	

		particles with an aerodynamic diameter of below 50 µm] containing ≥ 0.1 % (w/w) of particles with an aerodynamic diameter of below 50 µm									
Resulting Annex VI entry if agreed by RAC and COM	TBD	perboric acid, sodium salt [1] perboric acid, sodium salt, monohydrate [2] perboric acid ($HBO(O_2)$), sodium salt, monohydrate; sodium peroxoborate [3] sodium perborate [4]	234-390-0 [1] 234-390-0 [2] 239-172-9 [4]	11138-47-9 [1] 12040-72-1 [2] 10332-33-9 [3] 15120-21-5 [4]	Ox. Sol. 3 Repr. 1B Acute Tox. 3 Acute Tox. 4 STOT SE 3 Eye Dam. 1	H272 H360FD H331 H302 H335 H318	GHS03 GHS06 GHS05 GHS08 Dgr	H272 H360FD H331 H302 H335 H318		Inhalation: ATE = 0.75 mg/L (dusts and mists) Oral: ATE = 890 mg/kg bw/day Eye Dam. 1; H318: C ≥ 22 % Eye Irrit. 2; H319: 14 % ≤ C < 22 % §	#