CLH report

Proposal for Harmonised Classification and Labelling

**Based on Regulation (EC) No 1272/2008 (CLP Regulation),
Annex VI, Part 2**

International Chemical Identification:

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]

EC Numbers: 233-139-2 [1]; 234-343-4 [1]; 215-125-8 [2]; 235-541-3 [3]; 215-540-4 [4;6;7]; 237-560-2 [5]

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]

Index Numbers: 005-007-00-2 [1]; 005-008-00-8 [2]; 005-011-00-4 [3;4;5]; 005-011-01-1 [6]; 005-011-02-9 [7]

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0. BACKGROUND INFORMATION

The present proposal for harmonised classification and labelling concerns several existing entries in Annex VI of the Regulation (EC) No 1272/2008 (CLP Regulation). The borates covered in the proposal are harmonised as toxic to reproduction for both developmental and fertility effects, i.e. Repr. 1B (H360FD). They also have various specific concentration limits (SCLs) (table 0 below) which were set based on the developmental effects of the boron moiety (B) using an approach proposed by BauA (1998). Later this approach have been challenged and the committee for risk assessment (RAC) have removed SCLs set by the approach for a number of substances (see for example RAC opinions on NMP[1] and N,N-dimethylacetamide (DMAC)[2]).

The classification of mixtures containing substances classified for reproductive toxicity and of substances containing impurities, additives or constituents classified for reproductive toxicity is based on the concentration of the reproductive toxic component(s). Table 3.7.2 of Annex I to CLP contains generic concentration limits (GCLs) above which classification for reproductive toxicity is required. The GCL is 0.3% (w/w) for reproductive toxicants in Category 1A and 1B.

The RAC concluded in March 2014 on the classification of two octaborates[3,4] as Repr. 1B (H360FD) with a GCL of 0.3% w/w. A proposal for a revised harmonised classification of boric acid submitted in September 2013 did not include a suggestion to revise the SCL and it was therefore not addressed by the RAC. However, in the opinion for boric acid[5] the RAC notes that a GCL of 0.3% would apply if the concentration limit had been addressed. Hence, the objective of the present CLH proposal is to harmonise the seven borates with a GCL of 0.3% w/w. The reason for combining the borates in one CLH-report is that the data and argumentation is the same for all the substances.

Experimental data and information on the borates included in the present CLH proposal originate from the publically disseminated REACH Registration Dossiers (ECHA 2018a;b;c) and the Assessment Reports under the Biocide Products Regulation, BPR (ECHA 2011a;b;c;d;e). Two of the borates covered by the proposal i.e. tetraboron disodium heptaoxide, hydrate and orthoboric acid, sodium salt have not been registered under REACH nor have they been evaluated under BPR, but they have been notified by 55 and 584 notifiers[6], respectively.

[1] https://www.echa.europa.eu/documents/10162/355b86c1-5a0f-f104-0931-8ffdce4e1cbd

[2] https://www.echa.europa.eu/documents/10162/a435d3fc-a05f-b558-3f51-9aff166f2de0

[3] https://www.echa.europa.eu/documents/10162/7d740d8c-5cd5-872b-5da2-e549983a9ff9

[4] https://www.echa.europa.eu/documents/10162/658b802c-1ca3-663e-4bd4-437369d715de

[5] https://www.echa.europa.eu/documents/10162/4db9bc68-844e-c557-8914-ab491743d471

[6] C&L inventory accessed Nov 1, 2018

Table 0: Borates covered by the present CLH proposal

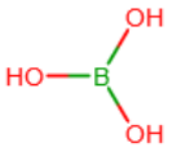
Entry in CLP (Index number)	**Chemical name(s)**	**CAS**	**EC**	**Existing specific concentration limit (SCL) (% w/w)**	**Proposed generic concentration limit (GCL) (% w/w)**
005-007-00-2	boric acid	10043-35-3 11113-50-1	233-139-2 234-343-4	5,5	0,3
005-008-00-8	diboron trioxide	1303-86-2	215-125-8	3,1	0,3
005-011-00-4	disodium tetraborate, anhydrous; boric acid, disodium salt	1330-43-4	215-540-4	4,5	0,3
	tetraboron disodium heptaoxide, hydrate	12267-73-1	235-541-3	4,5	0,3
	orthoboric acid, sodium salt	13840-56-7	237-560-2	4,5	0,3
005-011-01-1	disodium tetraborate decahydrate; borax decahydrate	1303-96-4	215-540-4	8,5	0,3
005-011-02-9	disodium tetraborate pentahydrate; borax pentahydrate	12179-04-3	215-540-4	6,5	0,3

1. IDENTITY OF THE SUBSTANCES

1.1 Names and other identifiers of the substances

1.1.1 Annex VI Index No. 005-007-00-2

Table 1: Substance identity and information related to molecular and structural formula of boric acid (CAS No: 10043-35-3; 11113-50-1)

Name(s) in the IUPAC nomenclature or other international chemical name(s)	Boric acid
Other names (usual name, trade name, abbreviation)	Optibor orthoboric acid
ISO common name (if available and appropriate)	Not available
EC number (if available and appropriate)	233-139-2; 234-343-4
EC name (if available and appropriate)	Boric acid
CAS number (if available)	10043-35-3; 11113-50-1
Other identity code (if available)	Not available
Molecular formula	H3BO3
Structural formula	
SMILES notation (if available)	B(O)(O)O; OB(O)O
Molecular weight or molecular weight range	61.831 g/mol
Information on optical activity and typical ratio of (stereo) isomers (if applicable and appropriate)	Not applicable
Description of the manufacturing process and identity of the source (for UVCB substances only)	Not applicable
Degree of purity (%) (if relevant for the entry in Annex VI)	Not relevant

1.1.2 Annex VI Index No. 005-008-00-8

Table 2: Substance identity and information related to molecular and structural formula of diboron trioxide (CAS No: 1303-86-2)

Name(s) in the IUPAC nomenclature or other international chemical name(s)	Diboron trioxide
Other names (usual name, trade name, abbreviation)	Anhydrous boric acid boric oxide borium oxide Boroglas Boron oxide Boropowder
ISO common name (if available and appropriate)	Not available
EC number (if available and appropriate)	215-125-8
EC name (if available and appropriate)	Diboron trioxide
CAS number (if available)	1303-86-2
Other identity code (if available)	Not available
Molecular formula	B2O3
Structural formula	
SMILES notation (if available)	O=BOB=O
Molecular weight or molecular weight range	69.6182 g/mol
Information on optical activity and typical ratio of (stereo) isomers (if applicable and appropriate)	Not applicable
Description of the manufacturing process and identity of the source (for UVCB substances only)	Not applicable
Degree of purity (%) (if relevant for the entry in Annex VI)	Not relevant

1.1.3 Annex VI Index No. 005-011-00-4

Table 3: Substance identity and information related to molecular and structural formula of tetraboron disodium heptaoxide, hydrate (CAS No: 12267-73-1)

Name(s) in the IUPAC nomenclature or other international chemical name(s)	Tetraboron disodium heptaoxide, hydrate
Other names (usual name, trade name, abbreviation)	-
ISO common name (if available and appropriate)	Not available
EC number (if available and appropriate)	235-541-3
EC name (if available and appropriate)	Tetraboron disodium heptaoxide, hydrate
CAS number (if available)	12267-73-1
Other identity code (if available)	Not available
Molecular formula	Na2B4O7·xH2O
Structural formula	*
SMILES notation (if available)	[Na+].[Na+].O.O=BOB([O-])OB([O-])OB=O
Molecular weight or molecular weight range	219.24 g/mol
Information on optical activity and typical ratio of (stereo) isomers (if applicable and appropriate)	Not applicable
Description of the manufacturing process and identity of the source (for UVCB substances only)	Not applicable
Degree of purity (%) (if relevant for the entry in Annex VI)	Not relevant

*no definite structural formula is available for describing the complexity of the structure of these substances, including metastable structures, hydrated and hydroxylated forms.

Table 4: Substance identity and information related to molecular and structural formula of disodium tetraborate, anhydrous (CAS No: 1330-43-4)

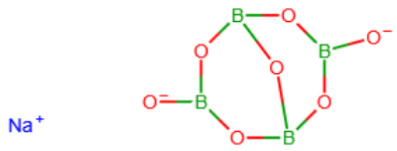
Name(s) in the IUPAC nomenclature or other international chemical name(s)	Tetraboron disodium heptaoxide, anhydrous
Other names (usual name, trade name, abbreviation)	Borax Borax anhydrous Borax Dehybor Dehybor Etibor-48 PYROBOR Dehydrated borax sodium borate anhydrous
ISO common name (if available and appropriate)	Not available
EC number (if available and appropriate)	215-540-4
EC name (if available and appropriate)	Tetraboron disodium heptaoxide, anhydrous
CAS number (if available)	1330-43-4
Other identity code (if available)	Not available
Molecular formula	Na2B4O7
Structural formula	
SMILES notation (if available)	[B]1(O[B]2O[B](O[B](O1)O2)[O-])[O-].[Na+].[Na+]
Molecular weight or molecular weight range	202.22 g/mol
Information on optical activity and typical ratio of (stereo) isomers (if applicable and appropriate)	Not applicable
Description of the manufacturing process and identity of the source (for UVCB substances only)	Not applicable
Degree of purity (%) (if relevant for the entry in Annex VI)	Not relevant

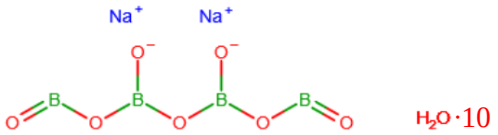
Table 5: Substance identity and information related to molecular and structural formula of orthoboric acid sodium salt (CAS No:13840-56-7)

Name(s) in the IUPAC nomenclature or other international chemical name(s)	Orthoboric acid, sodium salt
Other names (usual name, trade name, abbreviation)	-
ISO common name (if available and appropriate)	Not available
EC number (if available and appropriate)	237-560-2
EC name (if available and appropriate)	Orthoboric acid, sodium salt
CAS number (if available)	13840-56-7
Other identity code (if available)	Not available
Molecular formula	$BH_3O_3 \cdot xNa$
Structural formula	*
SMILES notation (if available)	[Na+].B([O-])([O-])[O-]
Molecular weight or molecular weight range	127.8 g/mol
Information on optical activity and typical ratio of (stereo) isomers (if applicable and appropriate)	Not applicable
Description of the manufacturing process and identity of the source (for UVCB substances only)	Not applicable
Degree of purity (%) (if relevant for the entry in Annex VI)	Not relevant

* no definite structural formula is available for describing the complexity of the structure of these substances, including metastable structures, hydrated and hydroxylated forms

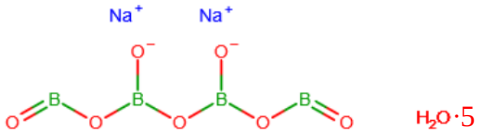
1.1.4 Annex VI Index No. 005-011-01-1

Table 6: Substance identity and information related to molecular and structural formula of disodium tetraborate decahydrate (CAS No: 1330-43-3; 1303-96-4)

Name(s) in the IUPAC nomenclature or other international chemical name(s)	Disodium tetraborate decahydrate
Other names (usual name, trade name, abbreviation)	Borax Borax 10 mol Borax 10-Hydrate borax decahydrate DECAHYDRATE BORAX
ISO common name (if available and appropriate)	Not available
EC number (if available and appropriate)	215-540-4
EC name (if available and appropriate)	Disodium tetraborate decahydrate
CAS number (if available)	1303-96-4
Other identity code (if available)	Not available
Molecular formula	Na2B4O7·10H2O
Structural formula	
SMILES notation (if available)	[Na+].[Na+].[O-]B1OB2OB([O-])OB(O1)O2.O.O.O.O.O.O.O.O.O.O
Molecular weight or molecular weight range	381.38 g/mol
Information on optical activity and typical ratio of (stereo) isomers (if applicable and appropriate)	Not applicable
Description of the manufacturing process and identity of the source (for UVCB substances only)	Not applicable
Degree of purity (%) (if relevant for the entry in Annex VI)	Not relevant

1.1.5 Annex VI Index No. 005-011-02-9

Table 7: Substance identity and information related to molecular and structural formula of disodium tetraborate pentahydrate (CAS No: 1330-43-3; 12179-04-3)

Name(s) in the IUPAC nomenclature or other international chemical name(s)	Disodium tetraborate pentahydrate
Other names (usual name, trade name, abbreviation)	Borax Borax 5 mol borax pentahydrate Etibor-68 Neobor V-BOR Refined Pentahydrate Borax
ISO common name (if available and appropriate)	Not available
EC number (if available and appropriate)	215-540-4
EC name (if available and appropriate)	Disodium tetraborate pentahydrate
CAS number (if available)	12179-04-3
Other identity code (if available)	Not available
Molecular formula	Na2B4O7·5H2O
Structural formula	
SMILES notation (if available)	B(=O)OB([O-])OB([O-])OB=O.O.O.O.O.O.[Na+].[Na+]
Molecular weight or molecular weight range	291.35 g/mol
Information on optical activity and typical ratio of (stereo) isomers (if applicable and appropriate)	Not applicable
Description of the manufacturing process and identity of the source (for UVCB substances only)	Not applicable
Degree of purity (%) (if relevant for the entry in Annex VI)	Not relevant

1.2 Composition of the substances

The constituents of the borates included in the present CLH-proposal are given below (Tables 8-14). There are no impurities or additives that affect the classification of the substances.

1.2.1 Annex VI Index No. 005-007-00-2

Table 8: Constituents (non-confidential information) of boric acid (CAS No: 10043-35-3; 11113-50-1)

Constituent (Name and numerical identifier)	Concentration range (% w/w minimum and maximum in multi-constituent substances)	Current CLH in Annex VI Table 3.1 (CLP)	Current self-classification and labelling (CLP)
Boric acid	≥ 80% - ≤ 100%	Repr. 1B, H360FD	Repr. 1B, H360FD Repr. 1A, H360 STOT SE 1, H370 STOT RE 1, H372 Skin Irrit. 2, H315 STOT SE 3, H335

1.2.2 Annex VI Index No. 005-008-00-8

Table 9: Constituents (non-confidential information) of diboron trioxide (CAS No: 1303-86-2)

Constituent (Name and numerical identifier)	Concentration range (% w/w minimum and maximum in multi-constituent substances)	Current CLH in Annex VI Table 3.1 (CLP)	Current self-classification and labelling (CLP)
Diboron trioxide	≥ 80% - ≤ 100%	Repr. 1B, H360FD	Repr. 1B, H360FD Acute Tox. 4, H302 Repr. 1A, H360 STOT RE 1, H372 Eye Irrit. 2, H319 STOT SE 3, H336

1.2.3 Annex VI Index No. 005-011-00-4

Table 10: Constituents (non-confidential information) of disodium tetraborate heptaoxide, hydrate (CAS No: 12267-73-1)

Constituent (Name and numerical identifier)	Concentration range (% w/w minimum and maximum in multi-constituent substances)	Current CLH in Annex VI Table 3.1 (CLP)	Current self-classification and labelling (CLP)
Disodium tetraborate heptaoxide, hydrate	≥ 80% - ≤ 100%	Repr. 1B, H360FD	Repr. 1B, H360DF Eye Irrit. 2, H319 Repr. 1B, H360

Table 11: Constituents (non-confidential information) of disodium tetraborate, anhydrous (CAS No: 1330-43-4)

Constituent (Name and numerical identifier)	Concentration range (% w/w minimum and maximum in multi-constituent substances)	Current CLH in Annex VI Table 3.1 (CLP)	Current self-classification and labelling (CLP)
Disodium tetraborate,	≥ 80% - ≤ 100%	Repr. 1B, H360FD	Repr. 1B, H360DF

Constituent (Name and numerical identifier)	Concentration range (% w/w minimum and maximum in multi-constituent substances)	Current CLH in Annex VI Table 3.1 (CLP)	Current self-classification and labelling (CLP)
anhydrous			Eye Irrit. 2, H319 Repr. 2, H360 Repr. 1A, H360 Acute Tox. 4, H302 Eye Dam. 1, H318 Repr. 1B, H360

Table 12: Constituents (non-confidential information) of orthoboric acid, sodium salt (CAS No: 13840-56-7)

Constituent (Name and numerical identifier)	Concentration range (% w/w minimum and maximum in multi-constituent substances)	Current CLH in Annex VI Table 3.1 (CLP)	Current self-classification and labelling (CLP)
Orthoboric acid, sodium salt	≥ 80% - ≤ 100%	Repr. 1B, H360FD	Repr. 1B, H360DF Repr. 1B, H360

1.2.4 Annex VI Index No. 005-011-01-1

Table 13: Constituents (non-confidential information) of disodium tetraborate decahydrate (CAS No: 1303-96-4)

Constituent (Name and numerical identifier)	Concentration range (% w/w minimum and maximum in multi-constituent substances)	Current CLH in Annex VI Table 3.1 (CLP)	Current self-classification and labelling (CLP)
Disodium tetraborate decahydrate	≥ 80% - ≤ 100%	Repr. 1B, H360FD	Repr. 1B, H360DF Eye Irrit. 2, H319 Repr. 2, H360 Repr. 1A, H360 Acute Tox. 4, H302 Eye Dam. 1, H318 Repr. 1B, H360 Aquatic Chronic 3, H412 STOT SE 3, H335

1.2.5 Annex VI Index No. 005-011-02-9

Table 14: Constituents (non-confidential information) of disodium tetraborate pentahydrate (CAS No: 12179-04-3)

Constituent (Name and numerical identifier)	Concentration range (% w/w minimum and maximum in multi-constituent substances)	Current CLH in Annex VI Table 3.1 (CLP)	Current self-classification and labelling (CLP)
Disodium tetraborate pentahydrate	≥ 80% - ≤ 100%	Repr. 1B, H360FD	Repr. 1B, H360DF Eye Irrit. 2, H319 Repr. 2, H360 Repr. 1A, H360 Acute Tox. 4, H302 Eye Dam. 1, H318 Repr. 1B, H360

2 PROPOSED HARMONISED CLASSIFICATION AND LABELLING

2.1 Proposed harmonised classification and labelling according to the CLP criteria

2.1.1 Annex VI Index No. 005-007-00-2

Table 15: Boric acid

	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 entry	005-007-00-2	boric acid [1] boric acid [2]	233-139-2 [1] 234-343-4 [2]	10043-35-3 [1] 11113-50-1 [2]	Repr. 1B	H360FD	GHS08 Dgr	H360FD		Repr. 1B; H360FD: C ≥ 5,5%	
Dossier submitters proposal	005-007-00-2	boric acid [1] boric acid [2]	233-139-2 [1] 234-343-4 [2]	10043-35-3 [1] 11113-50-1 [2]	**Retain:** Repr. 1B	**Retain:** H360FD	**Retain:** GHS08 Dgr	**Retain:** H360FD		**Remove:** Repr. 1B; H360FD: C ≥ 5,5%	
Resulting Annex VI entry if agreed by RAC and COM	005-007-00-2	boric acid [1] boric acid [2]	233-139-2 [1] 234-343-4 [2]	10043-35-3 [1] 11113-50-1 [2]	Repr. 1B	H360FD	GHS08 Dgr	H360FD		*	

*The generic concentration limit of 0,3% will apply

2.1.2 Annex VI Index No. 005-008-00-8

Table 16: Diboron trioxide

	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 entry	005-008-00-8	diboron trioxide	215-125-8	1303-86-2	Repr. 1B	H360FD	GHS08 Dgr	H360FD		Repr. 1B; H360FD: ≥ 3,1%	
Dossier submitters proposal	005-008-00-8	diboron trioxide	215-125-8	1303-86-2	**Retain:** Repr. 1B	**Retain:** H360FD	**Retain:** GHS08 Dgr	**Retain:** H360FD		**Remove:** Repr. 1B; H360FD: ≥ 3,1%	
Resulting Annex VI entry if agreed by RAC and COM	005-008-00-8	diboron trioxide	215-125-8	1303-86-2	Repr. 1B	H360FD	GHS08 Dgr	H360FD		*	

*The generic concentration limit of 0,3% will apply

2.1.3 Annex VI Index No. 005-011-00-4

Table 17: Tetraboron disodium heptaoxide, hydrate; disodium tetraborate, anhydrous; orthoboric acid, sodium salt

	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 entry	005-011-00-4	tetraboron disodium heptaoxide, hydrate [1] disodium tetraborate, anhydrous [2] orthoboric acid, sodium salt [3]	235-541-3 [1] 215-540-4 [2] 237-560-2 [3]	12267-73-1 [1] 1330-43-4 [2] 13840-56-7 [3]	Repr. 1B	H360FD	GHS08 Dgr	H360FD		Repr. 1B; H360FD: ≥ 4,5%	
Dossier submitters proposal	005-011-00-4	tetraboron disodium heptaoxide, hydrate [1] disodium tetraborate, anhydrous [2] orthoboric acid, sodium salt [3]	235-541-3 [1] 215-540-4 [2] 237-560-2 [3]	12267-73-1 [1] 1330-43-4 [2] 13840-56-7 [3]	**Retain:** Repr. 1B	**Retain:** H360FD	**Retain:** GHS08 Dgr	**Retain:** H360FD		**Remove:** Repr. 1B; H360FD: ≥ 4,5%	
Resulting Annex VI entry if agreed by RAC and COM	005-011-00-4	tetraboron disodium heptaoxide, hydrate [1] disodium tetraborate, anhydrous [2] orthoboric acid, sodium salt [3]	235-541-3 [1] 215-540-4 [2] 237-560-2 [3]	12267-73-1 [1] 1330-43-4 [2] 13840-56-7 [3]	Repr. 1B	H360FD	GHS08 Dgr	H360FD		*	

*The generic concentration limit of 0,3% will apply

2.1.4 Annex VI Index No. 005-011-01-1

Table 18: Disodium tetraborate decahydrate

	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 entry	005-011-01-1	disodium tetraborate decahydrate	215-540-4	1303-96-4	Repr. 1B	H360FD	GHS08 Dgr	H360FD		Repr. 1B; H360FD: ≥ 8,5%	
Dossier submitters proposal	005-011-01-1	disodium tetraborate decahydrate	215-540-4	1303-96-4	**Retain:** Repr. 1B	**Retain:** H360FD	**Retain:** GHS08 Dgr	**Retain:** H360FD		**Remove:** Repr. 1B; H360FD: ≥ 8,5%	
Resulting Annex VI entry if agreed by RAC and COM	005-011-01-1	disodium tetraborate decahydrate	215-540-4	1303-96-4	Repr. 1B	H360FD	GHS08 Dgr	H360FD		*	

*The generic concentration limit of 0,3% will apply

2.1.5 Annex VI Index No. 005-011-02-9

Table 19: Disodium tetraborate pentahydrate

	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 entry	005-011-02-9	disodium tetraborate pentahydrate	215-540-4	12179-04-3	Repr. 1B	H360FD	GHS08 Dgr	H360FD		Repr. 1B; H360FD: ≥ 6,5%	
Dossier submitters proposal	005-011-02-9	disodium tetraborate pentahydrate	215-540-4	12179-04-3	**Retain:** Repr. 1B	**Retain:** H360FD	**Retain:** GHS08 Dgr	**Retain:** H360FD		**Remove:** Repr. 1B; H360FD: ≥ 6,5%	
Resulting Annex VI entry if agreed by RAC and COM	005-011-02-9	disodium tetraborate pentahydrate	215-540-4	12179-04-3	Repr. 1B	H360FD	GHS08 Dgr	H360FD		*	

*The generic concentration limit of 0,3% will apply

Table 20: Reason for not proposing harmonised classification and status under public consultation – applies for all substances covered by the proposal.

Hazard class	Reason for no classification	Within the scope of public consultation
Explosives	Hazard class not assessed in this dossier	No
Flammable gases (including chemically unstable gases)	Hazard class not assessed in this dossier	No
Oxidising gases	Hazard class not assessed in this dossier	No
Gases under pressure	Hazard class not assessed in this dossier	No
Flammable liquids	Hazard class not assessed in this dossier	No
Flammable solids	Hazard class not assessed in this dossier	No
Self-reactive substances	Hazard class not assessed in this dossier	No
Pyrophoric liquids	Hazard class not assessed in this dossier	No
Pyrophoric solids	Hazard class not assessed in this dossier	No
Self-heating substances	Hazard class not assessed in this dossier	No
Substances which in contact with water emit flammable gases	Hazard class not assessed in this dossier	No
Oxidising liquids	Hazard class not assessed in this dossier	No
Oxidising solids	Hazard class not assessed in this dossier	No
Organic peroxides	Hazard class not assessed in this dossier	No
Corrosive to metals	Hazard class not assessed in this dossier	No
Acute toxicity via oral route	Hazard class not assessed in this dossier	No
Acute toxicity via dermal route	Hazard class not assessed in this dossier	No
Acute toxicity via inhalation route	Hazard class not assessed in this dossier	No
Skin corrosion/irritation	Hazard class not assessed in this dossier	No
Serious eye damage/eye irritation	Hazard class not assessed in this dossier	No
Respiratory sensitisation	Hazard class not assessed in this dossier	No
Skin sensitisation	Hazard class not assessed in this dossier	No
Germ cell mutagenicity	Hazard class not assessed in this dossier	No
Carcinogenicity	Hazard class not assessed in this dossier	No
Reproductive toxicity	Existing classification as Repr. 1B (H360FD) retained. Existing SCLs removed and replaced with GCLs.	Yes
Specific target organ toxicity-single exposure	Hazard class not assessed in this dossier	No
Specific target organ toxicity-repeated exposure	Hazard class not assessed in this dossier	No
Aspiration hazard	Hazard class not assessed in this dossier	No
Hazardous to the aquatic environment	Hazard class not assessed in this dossier	No
Hazardous to the ozone layer	Hazard class not assessed in this dossier	No

3 HISTORY OF THE PREVIOUS CLASSIFICATION AND LABELLING

The borates covered by the present CLH-proposal have harmonised classifications as Repr. 1B, H360DF, with various specific concentration limits (SCL). The SCLs were set based on an approach proposed by BAuA (1998) in which the molecular weight of the different borates was used to recalculate the contribution of their boron contents to the overall hazard. Existing SCLs for the borates were derived 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).

The RAC concluded in March 2014 on the classification of the borates disodium octaborate, anhydrous[7] and disodium octaborate tetrahydrate[8] (EC No. 234-541-0, Index No. 005-020-00-3), using new recommendations on how to determine the concentration limits for reproductive toxicity (first included in version 4.0 of in the CLP Guidance, November 2013). According to the guidance, the SCL should be based on the most sensitive reproductive effect. For borates, it was found to be the increased incidence of short rib XIII in a developmental toxicity study in rats. The fetal incidence of this malformation was 1.2 and 1.5% at the lowest observed adverse effect level, LOAEL (13.3 mg B/kg bw/day) and the highest dose (25 mg B/kg bw/day) respectively. As the incidences were low, it was not possible to derive an ED10 (the dose that corresponds to a 10% increase in incidence compared to controls). Hence, the LOAEL was used instead. Correcting for the percentage of boron (w/w), the LOAEL of 13.3 mg B/kg bw/day corresponds to a LOAEL of 51.5 mg/kg bw/day disodium octaborate, anhydrous and 63.3 mg/kg bw/day disodium octaborate tetrahydrate. Both substances were found to belong to the medium potency group (4 mg/kg bw/day < ED10 (LOAEL) < 400 mg/kg bw/day). For medium potency substances, the GCL applies. As disodium octaborate, anhydrous and disodium octaborate tetrahydrate are classified in category 1B, the GCL is 0.3% w/w.

A proposal for a revised harmonised classification of boric acid submitted in September 2013 did not include a revision of the SCL and the concentration limit was therefore not addressed in detail by the RAC. However, in the opinion for boric acid[9] the RAC notes that the SCL of 5.5% was derived by using the “German method” and that the GCL of 0.3% would apply for boric acid if the CLP guidance available at the time (version 4.0 - November 2013) had been used.

4 JUSTIFICATION THAT ACTION IS NEEDED AT COMMUNITY LEVEL

Justification that action is needed at Community level: Change in existing entry due to new evaluation of existing data.

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. Revising the SCL for the borates will ensure that all borates are assessed similarly and according to the new guidance. It will result in a level playing field in between the borates as well as in relation to other classified substances.

[7] https://www.echa.europa.eu/documents/10162/7d740d8c-5cd5-872b-5da2-e549983a9ff9

[8] https://www.echa.europa.eu/documents/10162/658b802c-1ca3-663e-4bd4-437369d715de

[9] https://www.echa.europa.eu/documents/10162/4db9bc68-844e-c557-8914-ab491743d471

5 IDENTIFIED USES

Boron is a widely occurring element found mainly in minerals in sediments and sedimentary rock. It is found in the environment primarily combined with oxygen in borates, and never as a free element. Boron appears to be a micronutrient in animals and humans (Nielsen 2002; Pizzorno 2015), and the World Health Organization has classified boron as being “probably essential” for humans.

Borates are versatile substances used as both industrial chemicals and biocides. According to the REACH registration dossiers, borates are manufactured and used in several industries in Europe, including the glass, ceramics, detergents and insulation fiberglass industries and are used to produce other borate compounds. Boric acid and sodium tetraborates are also used in a range of consumer products including cosmetic and personal care products. Boric acid, diboron trioxide, disodium tetraborate decahydrate, disodium tetraborate pentahydrate and disodium tetraborate, anhydrous have been evaluated as active substances under the biocide product regulation (BPR), and were all approved in 2011 for use in wood preservatives.

Boric acid has recently been evaluated and approved for use in additives in plastic food contact materials (EFSA, 2018). Boric acid is also used as an antimicrobial preservative and as a buffering agent to control the pH. Additionally, it can have the function as tonicity-adjusting agent (EMA, 2017).

6 DATA SOURCES

Experimental data and information on the borates included in the present CLH-report originates from the publically disseminated REACH Registration Dossiers (ECHA 2018a;b;c) and Assessment Reports under the Biocide Product Regulation (BPR) (ECHA, 2011a;b;c;d;e). Two of the borates covered by the proposal (tetraboron disodium heptaoxide, hydrate and orthoboric acid, sodium salt) have not been registered under REACH nor have they been evaluated under BPR, and therefore lack such data. Relevant studies available in the scientific literature have also been included.

7 PHYSICOCHEMICAL PROPERTIES

The information on physicochemical properties originates from the publically disseminated REACH Registration Dossiers. The values are taken from the key study or, in the absence of a key study the study with the highest reliability score. Physicochemical properties are available for five of the seven substances included in the proposal (Tables 21-25). Tetraboron disodium heptaoxide, hydrate (CAS No: 12267-73-1) and orthoboric acid sodium salt (CAS No: 13840-56-7) covered by Annex VI Index No. 005-011-00-4 are not registered within REACH nor have been evaluated under BPR, and therefore lack data. Similar to the Annex XV dossier for disodium tetraborates (ECHA, 2010a), the physicochemical properties for tetraboron disodium heptaoxide, hydrate are considered herein to be described by the physicochemical properties for the pentahydrate and the decahydrate forms of disodium tetraborate.

7.1.1 Annex VI Index No. 005-007-00-2

Table 21: Summary of physicochemical properties for boric acid (CAS No: 10043-35-3; 11113-50-1)

Property	Value	Reference [1]	Comment (e.g. measured or estimated)
Physical state at 20°C and 101,3 kPa	Solid	Study report 2003	Observed
Melting/freezing point	> 1 000 °C	Study report 2003	Measured
Boiling point	Data waived	-	-
Relative density	1.49	Study report 2003	Measured
Vapour pressure	0 Pa	Study report 1998	Measured
Surface tension	Data waived	-	-
Water solubility	49.2 g/L at pH 3.7 and 20 °C	Study report 2003	Measured
Partition coefficient n-octanol/water	-1.09 at 22 °C	Study report 2003	Measured
Flash point	Data waived	-	-
Flammability	No ignition on contact with air	Study report 2010	Observed
Explosive properties	Data waived	-	-
Self-ignition temperature	No ignition on contact with air	Study report 2010	Observed
Oxidising properties	Data waived	-	-
Granulometry	74.395 µm	Study report 2010	Measured
Stability in organic solvents and identity of relevant degradation products	Data waived	-	-
Dissociation constant	8.94 at 20 °C	Study report 2010	Measured
Viscosity	Data waived	-	-

[1] As cited in the publically disseminated REACH registration dossier

7.1.2 Annex VI Index No. 005-008-00-8

Table 22: Summary of physicochemical properties for diboron trioxide (CAS No: 1303-86-2)

Property	Value	Reference[1]	Comment (e.g. measured or estimated)
Physical state at 20°C and 101,3 kPa	Solid	Study report 2010	Observed
Melting/freezing point	> 633 K	Study report 2003	Measured
Boiling point	Not determined	-	-
Relative density	1 838 kg/m³ at 21.5 °C	Study report 2003	Measured
Vapour pressure	Data waived	-	-
Surface tension	Data waived	-	-
Water solubility	22 g/L at pH 3.7 and 20	Secondary literature	Not specified

Property	Value	Reference[1]	Comment (e.g. measured or estimated)
	°C	source	
Partition coefficient n-octanol/water	Data waived	-	-
Flash point	Data waived	-	-
Flammability	No ignition on contact with air	Study report 2010	Observed
Explosive properties	Data waived	-	-
Self-ignition temperature	No ignition on contact with air	Study report 2010	Observed
Oxidising properties	Data waived	Study report 2010	-
Granulometry	262.074 µm	Study report 2010	Measured
Stability in organic solvents and identity of relevant degradation products	Data waived	-	-
Dissociation constant	8.94 at 20 °C	Study report 2010	Read across from boric acid
Viscosity	61 GPa at 260 ºC; 3.9 kPa at 500 ºC	Secondary literature source	Not specified

[1] As cited in the publically disseminated REACH registration dossier

7.1.3 Annex VI Index No. 005-011-00-4

Table 23: Summary of physicochemical properties for disodium tetraborate, anhydrous (CAS No: 1330-43-4)

Property	Value	Reference[1]	Comment (e.g. measured or estimated)
Physical state at 20°C and 101,3 kPa	Solid	Study report 2003	Observed
Melting/freezing point	> 1 000 °C	Study report 2003	Measured
Boiling point	1 575 °C	Secondary literature source	Not specified
Relative density	2.35 at 26 ºC	Study report 2005	Measured
Vapour pressure	0.213 kPa at 20 °C	Study report 1998	Measured
Surface tension	71.0 ± 0.4 mN/m at 23 °C and a concentration of 0.3 g/L	Other company data, 1963	Measured
Water solubility	49.74 g/L at pH 3.7 and 20 °C	Study report 2003	Measured
Partition coefficient n-octanol/water	-1.53 at 22 °C	Study report 2003	Measured
Flash point	Data waived	-	-
Flammability	No ignition on contact with air	Study report 2010	Observed
Explosive properties	Data waived	-	-
Self-ignition temperature	No ignition on contact	Study report 2010	Observed

Property	Value	Reference[1]	Comment (e.g. measured or estimated)
	with air		
Oxidising properties	Data waived	Study report 2010	-
Granulometry	29.131 µm	Study report 2010	Measured
Stability in organic solvents and identity of relevant degradation products	Data waived	-	-
Dissociation constant	9 at 25 °C	Study report 2010	Measured
Viscosity	Data waived	-	-

[1] As cited in the publically disseminated REACH registration dossier

7.1.4 Annex VI Index No. 005-011-01-1

Table 24: Summary of physicochemical properties for disodium tetraborate decahydrate (CAS No: 1303-96-4)

Property	Value	Reference[1]	Comment (e.g. measured or estimated)
Physical state at 20°C and 101,3 kPa	Solid	Study report 2003	Observed
Melting/freezing point	> 1 000 °C	Study report 2003	Measured
Boiling point	1 575 °C	Secondary literature source	Not specified
Relative density	1.72 at 23 ºC	Study report 2005	Measured
Vapour pressure	0.213 kPa at 20 °C	Study report 1998	Measured
Surface tension	71.0 ± 0.4 mN/m at 23 °C and a concentration of 0.3 g/L	Other company data, 1963	Measured
Water solubility	49.74 g/L at pH 3.7 and 20 °C	Study report 2003	Measured
Partition coefficient n-octanol/water	-1.53 at 22 °C	Study report 2003	Measured
Flash point	Data waived	-	-
Flammability	No ignition on contact with air	Study report 2010	Observed
Explosive properties	Data waived	-	-
Self-ignition temperature	No ignition on contact with air	Study report 2010	Observed
Oxidising properties	Data waived	Study report 2010	-
Granulometry	88 µm	Study report 2010	Measured
Stability in organic solvents and identity of relevant degradation products	Data waived	-	-
Dissociation constant	9 at 25 °C	Study report 2010	Measured
Viscosity	Data waived	-	-

[1] As cited in the publically disseminated REACH registration dossier

7.1.5 Annex VI Index No. 005-011-02-9

Table 25: Summary of physicochemical properties for disodium tetrabotrate pentahydrate (CAS No: 12179-04-3)

Property	Value	Reference[1]	Comment (e.g. measured or estimated)
Physical state at 20°C and 101,3 kPa	Solid	Study report 2003	Observed
Melting/freezing point	> 1 000 °C	Study report 2003	Measured
Boiling point	1 575 °C	Secondary literature source	Not specified
Relative density	2.35 at 26 ºC (disodium tetraborate, anhydrous) 1.72 at 23 ºC (disodium tetraborate decahydrate)	Study report 2005	Measured
Vapour pressure	0.213 kPa at 20 °C	Study report 1998	Measured
Surface tension	71.0 ± 0.4 mN/m at 23 °C and a concentration of 0.3 g/L	Other company data, 1963	Measured
Water solubility	49.74 g/L at pH 3.7 and 20 °C	Study report 2003	Measured
Partition coefficient n-octanol/water	-1.53 at 22 °C	Study report 2003	Measured
Flash point	Data waived	-	-
Flammability	No ignition on contact with air	Study report 2010	Observed
Explosive properties	Data waived	-	-
Self-ignition temperature	No ignition on contact with air	Study report 2010	Observed
Oxidising properties	Data waived	Study report 2010	-
Granulometry	95.71 µm	Study report 2010	Measured
Stability in organic solvents and identity of relevant degradation products	Data waived	-	-
Dissociation constant	9 at 25 °C	Study report 2010	Measured
Viscosity	Data waived	-	-

[1] As cited in the publically disseminated REACH registration dossier

8 EVALUATION OF PHYSICAL HAZARDS

Not evaluated in this dossier.

9 TOXICOKINETICS (ABSORPTION, METABOLISM, DISTRIBUTION AND ELIMINATION)

When exposed via the oral or inhalational route borates are easily taken up (up to 100%) into the blood stream and distributed throughout the tissues and organs of the body. By dermal exposure, an uptake of 0.5% over intact skin is considered as a maximum uptake. Boric acid is not metabolized

in the body but is excreted as such mainly via the urine, with an elimination half-life of less than 24 hours in humans.

In aqueous solutions at physiological and acidic pH, low concentrations of simple borates such as boric acid $B(OH)_3$, diboron trioxide (B_2O_3), tetraboron disodium heptaoxide, hydrate ($Na_2B_4O_7 \cdot H_2O$) disodium tetraborate, anhydrous ($Na_2B_4O_7$), orthoboric acid sodium salt (Na_3BO_3), disodium tetraborate decahydrate ($Na_2B_4O_7 \cdot 10H_2O$) and disodium tetraborate pentahydrate ($Na_2B_4O_7 \cdot 5H_2O$) will predominantly exist as undissociated boric acid. Above pH 10 the metaborate anion $B(OH)_4$ becomes the main species in solution. The toxicokinetics and toxicological effects of systemic boric acid, diboron trioxide, tetraboron disodium heptaoxide hydrate, disodium tetraborate anhydrous, orthoboric acid sodium salt, disodium tetraborate decahydrate and disodium tetraborate pentahydrate will therefore be expected to be similar on a boron equivalents basis.

As stated in the CLH-reports of disodium octaborate, anhydrate and disodium octaborate tetrahydrate (2013), read-across from boric acid to other borates and between borates has long been accepted in a regulatory context. Experts from the CL Working Group, the TC-C&L and the ATP Committee agreed that borates have similar properties and therefore that read-across between substances can be applied (boric acid, diboron trioxide, disodium tetraborate anhydrous, disodium tetraborate decahydrate and disodium tetraborate) and was indeed applied when setting the existing SCLs. Moreover, in a report on boron, drawn up in 1998 as part of the International Programme on Chemical Safety established jointly by the World Health Organisation, the International Labour Organisation and the United Nations Environment Programme, the experts stated that the chemical and toxicological properties of boric acid, disodium tetraborate pentahydrate, disodium tetraborate decahydrate, and other borates are expected to be similar on a mol boron/litre equivalent basis when dissolved in water or biological fluids at the same pH and low concentration. They add that diboron trioxide will exhibit properties identical to those of boric acid, as it is an anhydride that will hydrolyse to give boric acid. The RAC opinion on new scientific evidence on the use of boric acid and borates in photographic applications by consumers (ECHA, 2010b) also used read-across between the different borates as the DNEL was expressed as mg B/kg bw/day. Judgment of the European Court of Justice on borates concludes that read-across may indeed be used for the assessment of borates (Case C-15/10: Judgment of the Court (Fourth Chamber) of 21 July 2011 - Etimine SA v Secretary of State for Work and Pensions)[10].

Read-across between borates is also used by the registrants to fulfil the data requirements in the REACH registrations of borates included in the present proposal (see Table I and II, Annex I).

9.1 Short summary and overall relevance of the provided toxicokinetic information on the proposed classification(s)

It is well established that borates have similar toxicokinetics and toxicological effects and that low concentrations of simple borates will mainly exist as undissociated boric acid in aqueous solutions at physiological and acidic pH. The existing SCLs for boric acid, diboron trioxide and the sodium borates were indeed derived on a boron-equivalent basis and it can therefore be assumed that a similar read-across may be used in the derivation of new concentration limits for the substances.

[10] http://eur-lex.europa.eu/legal-content/EN/TXT/HTML/?isOldUri=true&uri=CELEX:62010CJ0015

10 EVALUATION OF HEALTH HAZARDS

10.1 Acute toxicity

Not evaluated in this dossier.

10.2 Skin corrosion/irritation

Not evaluated in this dossier.

10.3 Serious eye damage/eye irritation

Not evaluated in this dossier.

10.4 Respiratory sensitisation

Not evaluated in this dossier.

10.5 Skin sensitisation

Not evaluated in this dossier.

10.6 Germ cell mutagenicity

Not evaluated in this dossier.

10.7 Carcinogenicity

Not evaluated in this dossier.

10.8 Reproductive toxicity

All relevant scientific data related to the reproductive toxicity of boron published before March 2014 has been thoroughly reviewed by the RAC in the discussions forming the opinions on harmonised classifications of boric acid (2014), disodium octaborate anhydrate (2014) and disodium octaborate tetrahydrate (2014).

This CLH-report proposes no change to the existing harmonised classifications; however, a withdrawal of the specific concentration limits is suggested. Therefore, only the reproductive toxicity studies that were previously pointed out as key studies for harmonised classification and derivation of concentration limits for borates by the RAC (RAC opinions on boric acid, disodium octaborate, anhydrous and disodium octaborate tetrahydrate, 2014) and relevant studies published thereafter are given and discussed below.

For completeness, an overview of all studies on reproductive toxicity that are included in the publically disseminated REACH Registration Dossiers[11] and/or in the Assessment Reports under BPR are given in Annex I, Table I (animal data) and Table II (human data).

[11] Accessed 2018-10-15

10.8.1 Adverse effects on sexual function and fertility

To our knowledge, no new animal studies on effects of boron on sexual function and fertility has been published since 2014. The studies given in Table 26 were appointed key studies by the RAC in their 2014 opinions on boric acid, disodium octaborate anhydrate and disodium octaborate tetrahydrate. One human study on the effects of boron on male fertility has been published since March 2014. It is given in Table 27.

Table 26: Summary table of key animal studies on adverse effects on sexual function and fertility

<table>
<tr><th>Method, guideline, deviations if any, species, strain, sex, no/group</th><th>Test substance, dose levels duration of exposure</th><th>Results</th><th>Reference</th></tr>
<tr><td>2-year feeding study
Rat
Sprauge-Dawley
M/F
35(M)+35(F) per dose
70(M)+70(F) controls</td><td>Boric acid, 0; 670 (117); 2000 (350); 6690 (1170) ppm boric acid equivalent to 0, 33 (5.9), 100 (17.5), 334 (58.5) mg boric acid (B)/kg bw /day.</td><td>Testes atrophy at 24 months:
<table><tr><td>Dose (B) mg/kg bw/day</td><td>0 (0)</td><td>33 (5.9)</td><td>100 (17.5)</td><td>334 (58.5)</td></tr><tr><td>N of animals</td><td>3/10</td><td>1/10</td><td>4/10</td><td>10/10</td></tr></table>
NOAEL is 2000 ppm equivalent to 100 (17.5) boric acid (B)/kg bw/day.
LOAEL is 6690 ppm, equivalent to 334 (58.5) mg boric acid (B)/kg bw/day</td><td>Study report, 1966
Study report, 1967
Weir and Fisher, 1972
Weir, 1996a[1]</td></tr>
<tr><td>2-year feeding study
Rat
Sprauge-Dawley
M/F
35(M)+35(F) per dose
70(M)+70(F) controls</td><td>Disodium tetraborate decahydrate, 0, 1030, 3080, 10300 ppm equivalent to 0, 52 (5.9), 155 (17.5), 516 (58.5) mg disodium tetraborate decahydrate (B)/kg bw/day.</td><td>Testes atrophy at 24 months:
<table><tr><td>Dose (B) mg/kg bw/day</td><td>0 (0)</td><td>52 (5.9)</td><td>155 (17.5)</td><td>516 (58.5)</td></tr><tr><td>N of animals</td><td>3/10</td><td>1/10</td><td>4/10</td><td>10/10</td></tr></table>
NOAEL is 3080 ppm, equivalent to 155 (17.5) mg disodium tetraborate decahydrate (B)/kg bw/day.
LOAEL is 10300 ppm, equivalent to 516 (58.5) mg disodium tetraborate decahydrate (B)/kg bw/day.</td><td>Study report, 1966
Study report, 1967
Weir and Fisher, 1972
Weir, 1996b[1]</td></tr>
</table>

[1] As cited in the RAC opinions on disodium octaborate anhydrate and disodium octaborate tetrahydrate, 2014

Table 27: Summary table of human information on effects on sexual function and fertility, published since March, 2014

Type of data/report	Test substance,	Relevant information about the study (as applicable)	Observations	Reference
Publication	Boron, occupational and environmental exposure	Low exposure group: DBE = 15.07 mg B/day, (74.03 ng B/g blood) Medium exposure group: DBE = 19.85 mg B/day, (126.6 ng B/g blood) High exposure group: DBE = 26.84 mg B/day, (269.2 ng B/g blood) Extreme exposure group: DBE = 47.17 mg B/day, (570.6 ng B/g blood, 571 ppb)	The study did not observe statistical significant differences in sperm quality parameters (concentration, morphology, motility) or reproductive hormone levels (LSH, FH and testosterone) between exposure groups.	Duydu *et al*., 2018a

10.8.2 Short summary and overall relevance of the provided information on adverse effects on sexual function and fertility

10.8.2.1 Animal information

The animal data on effects on fertility of the borates included in the present proposal has previously been assessed by the RAC (RAC opinion on boric acid; disodium octaborate anhydrate and disodium octaborate tetrahydrate, 2014). The RAC concluded that studies of reproductive toxicity and repeated dose toxicity studies in mice, rats and dogs clearly indicate that boron impairs fertility through an effect on the testes. The effects observed in the different species are similar in nature. Based on data from the 2-year feeding study with boric acid in rats, the NOAEL for fertility is therefore 100 mg/kg bw/day, equal to 17.5 mg B/kg bw/day. The LOAEL is 334 mg/kg bw/day, equal to 58.5 mg B/kg bw/day. This conclusion is supported by the similar study with disodium tetraborate decahydrate. There were no indications that the impaired fertility is secondary to other toxic effects.

10.8.2.2 Human information

The human data published until March 2014 on the potential effects of boron exposure on fertility is discussed in the RAC opinions on boric acid, disodium octaborate anhydrate and disodium octaborate tetrahydrate. The data consists of epidemiological studies of males exposed to boron via the environment and/or their occupation. RAC concluded that the human studies showed no clear evidence of adverse effects on male fertility by boron. The boron exposures in the human studies were well below the LOAELs for fertility reported from studies in mice and rats. The RAC pointed out that the epidemiological studies had several limitations in study design, and therefore should be regarded as additional information.

Recently, Duydu *et al.* (2018a) published a study investigating the effects of boron on semen parameters and reproductive hormone levels (FSH, LH and testosterone) in environmentally and occupationally exposed workers in Turkey (Bandirma and Bigadic regions). The workers (n =122) where divided into three exposure groups based on their mean daily boron exposure (DBE). In the

highest exposure group (n=98) the DBE was 47.17 mg B/day, corresponding to 570.6 ng B/g blood (571 ppb, with highest individual value 1100 ppb). No difference related to semen parameters, FSH, LH and testosterone levels was detected between the exposure groups. For comparison, animal studies has revealed that boric acid treatment results in increased serum FSH and LH levels and decreased serum testosterone levels (Ku *et al*., 1993; Fail *et al*., 1998). The LOAELs in the animal studies correspond to serum boron concentrations of 10 000 to 17 000 ppb (Ku *et al*., 1993).

The available human data collectively shows no effects on fertility parameters, semen parameters, FSH, LH or testosterone levels at boron exposure levels that were well below the LOAELs from corresponding animal studies. Since the available human data does not contradict the animal data, there is no evidence that the effects observed in animals are not relevant to humans.

10.8.3 Comparison with the CLP criteria

The borates covered by the present proposal have harmonised classifications as Repr. 1B, H360DF. No change to the classifications is proposed.

Concentration limits:

According to the current CLP guidance (v.5 July 2017), concentration limits for adverse effects on sexual function and fertility should be based on the lowest ED10. The RAC has previously concluded that the most sensitive effect on sexual function and fertility is testicular atrophy in a toxicity study in rats with boric acid (RAC opinions on boric acid, disodium octaborate anhydrate and disodium octaborate tetrahydrate, 2014). There is no reason to reconsider this conclusion based on the human information published since 2014. The incidence of testicular atrophy at 24 months was 10%, 40% and 100% at doses corresponding to 5.9, 17.5 and 58.5 mg/kg bw/day boron. The incidence in control animals was 30% (Study report, 1966a). The same incidences were observed with disodium tetraborate decahydrate (Study report, 1966b). Hence, the ED10 corresponds to 17.5 mg B/kg bw/day (100 mg boric acid/kg bw/day). According to section 3.7.2.6.3 of the CLP Guidance, a substance with a 4 mg/kg bw/day < ED10 < 400 mg/kg bw/day belongs to the medium potency 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 for boric acid. Since boric acid has a harmonised classification for reproductive toxicity in category 1B (H360FD), the GCL of 0.3% would apply (Table 3.14 of the CLP guidance). Concentration limits were derived in a similar way for diboron trioxide and the sodium borates by correcting for the percentage of boron (calculations are available in Table 30). All borates included in the present proposal fall within the range of the medium potency group for effects on fertility, which means that the GCL of 0.3% should apply. Similar to boric acid, the modifying factors described above does not apply for the borates.

10.8.4 Adverse effects on development

To our knowledge, no new animal studies on the effects of boron on development has been published since March 2014. The studies given in Table 28 were appointed key studies by the RAC in the 2014 opinions on harmonised classifications of boric acid, disodium octaborate anhydrate and disodium octaborate tetrahydrate. Two epidemiological studies regarding developmental effects by boron exposure has been published since 2014. These are given in Table 29.

Table 28: Summary table of key animal studies on adverse effects on development

<table>
<tr><th>Method, guideline, deviations if any, species, strain, sex, no/group</th><th>Test substance, dose levels duration of exposure</th><th>Results</th><th>Reference</th></tr>
<tr><td>Prenatal developmental toxicity study
OECD TG 414
Rat
Sprague-Dawley
F
28-32 per dose
GD 0-20</td><td>Boric acid
Doses: 0, 250, 500, 750,1000, 2000 ppm), equivalent to 19 (3.3), 36 (6.3), 55(9.6), 76 (13.3) and 143 (25) mg boric acid (mg B)/kg bw/day</td><td><u>Dams:</u> no toxicity. NOAEL is 2000 ppm, equivalent to 25 mg B/kg bw/day.
<u>Fetuses:</u> at 750 ppm boric acid, corresponding to 13.3 mg B/kg bw/day: reduction in the mean fetal bodyweight per litter; short 13th rib; wavy rib.
<table>
<tr><th>Dose (mg boron/kg bw/day)</th><th>Mean fetal bw/litter, gd 20 (% of control weight)</th><th>Short 13th rib, gd 20 (%, fetuses/ litter)</th><th>Wavy rib, gd 20 (%, fetuses/ litter)</th></tr>
<tr><td>0</td><td>100</td><td>0.7</td><td>0</td></tr>
<tr><td>3.3</td><td>99</td><td>0.6</td><td>0.3</td></tr>
<tr><td>6.3</td><td>98</td><td>0.6</td><td>0</td></tr>
<tr><td>9.6</td><td>97</td><td>0.7</td><td>0.8</td></tr>
<tr><td>13.3</td><td>96*</td><td>1.2*</td><td>2.1*</td></tr>
<tr><td>25.0</td><td>88*</td><td>1.5*</td><td>9.9*</td></tr>
</table>
* $p < 0.05$, pair-wise comparison to concurrent control group.
NOAEL is 750 ppm, equivalent to 9.6 mg B/kg bw/day.
LOAEL is 1000 ppm, equivalent to 13.3 mg B/kg bw/day.</td><td>Study report, 1994
Price, 1996[1]</td></tr>
</table>

[1] As cited in the RAC opinions on disodium octaborate anhydrate and disodium octaborate tetrahydrate, 2014

Table 29: Summary table of human information on effects on development, published since March, 2014

Type of data/report	Test substance,	Relevant information about the study (as applicable)	Observations	Reference
Publication	Boron, environmental exposure	Prospective study. Mother:child cohort in Northen Argentina. n: 194. 1-3 samples of serum, whole blood and urine was taken during pregnancy. Infant weight , length and head circumference was measured at birth.	Serum B > 80 µg/l were found to be inversely associated with birth length (B-0.69 cm, 95% CI:-1.4, p=0.043 per 100 µg/L serum B). No statistical significant associations between boron exposure and birth weight or head circumference were found.	Igra *et al.*, 2016
Publication	Boron,	Retrospective study	No boron-mediated differences	Duydu *et al.*, 2018b

Type of data/report	Test substance,	Relevant information about the study (as applicable)	Observations	Reference
	environmental exposure	Females residing in Marmara, Turkey. n: 190 Pregnancy outcomes (sex ratio, preterm birth, birth weights, congenital anomalies, abortions, miscarriage, stillbirth, early neonatal death, neonatal death and infant death) determined based on questionnaire. Boron blood levels at time of pregnancy were estimated from levels at time of study.	on pregnancy outcomes was detected between exposure groups (low exposure n=143; medium exposure n=29 and high exposure n=27) Estimated blood boron levels ranged from 151.81 to 957.66 (mean 274.58) ng/g in the high exposure group.	

10.8.5 Short summary and overall relevance of the provided information on adverse effects on development

10.8.5.1 Animal information

The existing animal data for effects on development of the borates included in the present proposal has previously been assessed by the RAC (RAC opinions on boric acid, disodium octaborate anhydrate and disodium octaborate tetrahydrate, 2014). The conclusion of the RAC was that developmental toxicity (malformations) was clearly observed in studies in rats and rabbits, the rat being the most sensitive species, with an overall NOAEL of 9.6 mg B/kg bw/day. The LOAEL corresponds to 13.3 mg B/kg bw/day. Malformations consisted primarily of anomalies of the eyes, the central nervous system, the cardiovascular system, and the axial skeleton (Price *et al*., 1996). The most common malformations were enlargement of lateral ventricles in the brain and agenesis or shortening of rib XIII. There were no indications that the developmental effects were secondary to other toxic effects. In addition, the RAC stated that the teratogenicity was possibly caused by an altered hox gene expression, caused by inhibition of histone deacetylases, a mechanism that is likely to be relevant also for humans.

10.8.5.2 Human information

Epidemiological studies on possible adverse pregnancy outcomes in female workers, or females environmentally exposed to boron via food or drinking water were not available in 2014, and such data was therefore not discussed in the 2014 RAC opinions on boric acid, disodium octaborate anhydrate and disodium octaborate tetrahydrate.

In 2016, an epidemiological study investigating boron-mediated developmental effects in pregnant women from exposure via drinking water was published (Igra *et al*., 2016). The study was performed in a mother-child cohort in northern Argentina (n = 194). 1–3 samples of serum, whole blood and urine were collected per woman during pregnancy and analysed for boron. The samples were also analysed for lithium, cesium and arsenic, which was also present in the drinking water. Infant weight, length and head circumference were measured at birth. The serum boron

concentrations during pregnancy was 0.73–605 μg/L (median 133 μg/L). The study found that serum boron concentrations above 80 μg/L were inversely associated with birth length (0.69 cm shorter, p=0.043), per 100 μg/L increase in serum boron). The study authors report that the impact of boron was stronger when the exposure was restricted to the third trimester, when the serum boron concentrations were the highest (0.73–447 μg/L). An increase in serum boron of 100 μg/L in the third trimester corresponded to 0.9 cm shorter and 120 g lighter new-borns (p = 0.001 and 0.021, respectively).

The information contained in the publication suggests that the women's serum boron levels are in the same range as boron levels in whole blood. A serum concentration of 80 μg B/L (above which effects on birth size were detected) would then correspond to around 75 ng B/g blood, assuming a blood density of 1060 kg/m^3. This concentration is below the level of 1270 ng B/g blood that corresponds to the NOAEL for developmental effects in rats (Price *et al*., 1997).

The study has a high participation rate (88%) and a prospective design but a small sample size and a lack of samples in both early and late pregnancy for all the participating women. Although the authors adjusted for potential confounding by lithium exposure in the model, they state that they cannot rule out that the observed diminished birth length is a result of combined exposure to both boron and lithium. Lithium was found to be associated with decreased birth length but not birth weight in a previous study by the same authors (Harari *et al*., 2015).

Recently, a retrospective epidemiological study on the effect of boron on human development was published (Duydu *et al*., 2018b). The study investigates pregnancy outcomes in 199 females (giving birth to 326 children; 162 girls and 164 boys) residing in boron-rich areas in Turkey (Bandirma and Bigadic) and thus being environmentally exposed to the substance. Pregnancy outcomes (including items sex ratio, preterm birth, birth weights, congenital anomalies, abortions, miscarriage, stillbirth, early neonatal death, neonatal death and infant death) were determined based on a questionnaire survey. The daily boron exposure at the time of pregnancy was estimated from boron levels in food and water at the time of the study using the "double plate method" or by blood samples, by assuming that the environmental exposure had been chronic and constant over time. Individual blood boron levels were used to classify females into three exposure groups (low, medium, and high). There was no effects from boron exposure on pregnancy outcomes, including birth weight, in any group.

The blood boron concentrations of the participating women in the highest exposure group (mean 274.6 ng B/g blood, highest value 957.7 ng B/g blood) are clearly below those corresponding to the NOAEL for developmental effects in rats, i.e. 9.6 mg B/kg bw/day, corresponding to 1270 ng B/g blood (Price *et al*., 1997).

The human information on developmental effects should be seen as additional information. The prospective study detected a dose dependent influence on birth size at boron exposure levels that were below the NOAEL for developmental effects in animal studies. However, it is possible that the results were influenced by co-exposure to lithium. The retrospective study reports no adverse effects on development at exposure levels that were well below the NOAELs for developmental effects in animal studies. There are some methodological limitations, mainly associated with the retrospective design and the small sample size. Overall, the available human data does not contradict the animal data and gives no evidence that the effects observed in animals are not relevant to humans.

10.8.6 Comparison with the CLP criteria

The borates covered by the present proposal have harmonised classifications as Repr. 1B, H360DF. No change to the classifications is proposed.

Concentration limits

According to the current CLP guidance (v.5 July 2017), concentration limits for adverse effects on development should be based on the lowest ED10. The RAC has previously concluded that the most sensitive effect on development by borates is the increased incidence of short rib XIII, considered a malformation (RAC opinions on boric acid, disodium octaborate anhydrate and disodium octaborate tetrahydrate, 2014). The human information which has been published since 2014 gives no reason to challenge this conclusion. The fetal incidence of the short XIII malformation was 1.2 and 1.5% at the LOAEL (13.3 [76] mg B [boric acid]/kg bw/day) and the highest dose (25 [143] mg B [boric acid]/kg bw/day), respectively. As the incidences are low, it is not possible to derive an ED10. In this instance, the LOAEL should be used for setting the SCL according to the guidance. Boric acid belongs to the medium potency groups (4 mg/kg bw/day < ED10 (LOAEL) < 400 mg/kg bw/day). 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. As boric acid has a harmonised classification for reproductive toxicity in category 1B (H360FD) according to the CLP guidance, the GCL of 0.3% would apply (Table 3.14 of the CLP guidance). Concentration limits were derived for diboron trioxide and the sodium borates from the same LOAEL and by correcting for the percentage of boron (calculations are available in Table 30). All the borates included in the present classification proposal fall within the range of the medium potency group for adverse effects on development, which means that the GCL of 0.3% should apply. Similar to boric acid, the modifying factors described above does not apply for the borates.

Table 30: Derivation of ED10 values and concentration limits for borate compounds based on boron contents

Substance	**Formula**	**EC**	**CAS**	**Molecular weight (g/mol)**	**Conversion factor for equivalent dose of boron**[1]	**ED10 for fertility corrected for boron-content** (mg/kg bw/day)	**LOAEL for development corrected for boron-content** (mg/kg bw/day)	**Proposed generic concentration limit (GCL, % w/w), fertility**	**Proposed generic concentration limit (GCL, % w/w), development**
Boric acid	H_3BO_3	233-139-2; 234-343-4	10043-35-3; 11113-50-1	61.83	0.17	17.5/0.17 = 103	13.3/0.17 = 78	0.3	0.3
Diboron trioxide	B_2O_3	215-125-8	1303-86-2	69.62	0.31	17.5/0.31 = 56	13.3/0.31 = 43	0.3	0.3
Tetraboron disodium heptaoxide, hydrate	$Na_2B_4O_7 \cdot H_2O$	215-540-4	12267-73-1	219.24	0.20	17.5/0.20 = 88	13.3/0.20 = 67	0.3	0.3
Disodium tetraborate anhydrous	$Na_2B_4O_7$	235-541-3	1330-43-4	201.22	0.21	17.5/0.21 = 83	13.3/0.21 = 63	0.3	0.3
Orthoboric acid, sodium salt	Na_3BO_3	237-560-2	13840-56-7	127.80	0.08	17.5/0.08 = 219	13.3/0.08 = 166	0.3	0.3
Disodium tetraborate decahydrate	$Na_2B_4O_7 \cdot 10H_2O$	215-540-4	1303-96-4	381.38	0.11	17.5/0.11 = 159	13.3/0.11 = 121	0.3	0.3
Disodium tetraborate pentahydrate	$Na_2B_4O_7 \cdot 5H_2O$	215-540-4	12179-04-3	291.35	0.15	17.5/0.15 = 117	13.3/0.15 = 89	0.3	0.3

[1] Molecular weight of boron equals 10.8 g/mol

10.8.7 Adverse effects on or via lactation

In the absence of relevant data, there are no indications that boron exposure through lactation has adverse effects. It should however be noted that numerous studies have shown that borates are absorbed from the gastrointestinal tract, as indicated by increased levels of boron in the blood, tissues or urine or by systemic toxic effects in exposed individuals or laboratory animals. In addition, boron compounds have been found in human breast milk (BfR, 2005), with reported (background) concentrations of approximately 4 µg B/L (Hunt *et al*., 2005, as reported in WHO, 2009) and in an experiment where 1–13 g of boric acid was given to lactating women 10–285 mg/l was found in milk (Moseman, 1994). The dossier submitter proposes no classification for adverse effects on or via lactation due to lack of data.

10.8.8 Conclusion on classification and labelling for reproductive toxicity

The borates covered by the present proposal have harmonised classifications as Repr. 1B, H360FD. Withdrawal of the specific concentration limits is warranted and therefore the GCL:s of 0.3% applies for both developmental effects and effects on sexual function and fertility.

10.9 Specific target organ toxicity-single exposure

Not evaluated in this dossier.

10.10 Specific target organ toxicity-repeated exposure

Not evaluated in this dossier.

10.11 Aspiration hazard

Not evaluated in this dossier.

11 EVALUATION OF ENVIRONMENTAL HAZARDS

Not evaluated in this dossier.

12 EVALUATION OF ADDITIONAL HAZARDS

Not evaluated in this dossier.

13 ADDITIONAL LABELLING

Not relevant.

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15 ANNEXES

15.1 Annex I

Table I: Overview of experimental animal studies for boric acid; diboron trioxide; disodium tetraborate, anhydrous; disodium tetraborate decahydrate and disodium tetraborate pentahydrate on reproductive toxicity available in the publically disseminated REACH Registration Dossiers or in the Assessment Reports under BPR. Tetraboron disodium heptaoxide, hydrate and orthoboric acid, sodium salt are not registered nor evaluated as active substances under the biocide regulation and therefore lack data.

Test substance	Type of study	Species/ Strain/ Breed	NOAEL	Reliability score	Reference[1]	In the registration dossier /CAR of substance (CAS)
Fertility/sexual function						
Boric acid	Three generation reproductive toxicity	Sprague-Dawley rat	17.5 mg B/kg bw/day	2	Study report, 1966; Weir and Fisher, 1972 Weir, 1966	• Boric acid (10043-35-3, 11113-50-1) • Diboron trioxide (1303-86-2) • Disodium tetraborate, anhydrous (1330-43-4) • Disodium tetraborate decahydrate (1303-96-4) • Disodium tetraborate pentahydrate (12179-04-3)
Sodium tetraborate decahydrate	Three generation reproductive toxicity	Sprague-Dawley rat	17.5 mg B/kg bw/day	2	Study report, 1966; Weir and Fisher, 1972 Weir, 1966	• Boric acid (10043-35-3, 11113-50-1) • Diboron trioxide (1303-86-2) • Disodium tetraborate, anhydrous (1330-43-4) • Disodium tetraborate decahydrate (1303-96-4) • Disodium tetraborate pentahydrate (12179-04-3)
Boric acid	Two generation reproductive toxicity	Swiss CD-1 mice	27 mg B/kg bw/day (LOAEL)	2	Fail *et al*., 1998; 1991	• Boric acid (10043-35-3, 11113-50-1) • Diboron trioxide (1303-86-2) • Disodium tetraborate, anhydrous (1330-43-4) • Disodium tetraborate decahydrate (1303-96-4) • Disodium tetraborate pentahydrate (12179-04-3)
Boric acid	Fertility, other	Rat, strain not specified	35 mg B/kg bw/day	3	Caujolle *et al*., 1962	• Boric acid (10043-35-3, 11113-50-1) • Diboron trioxide (1303-86-2) • Disodium tetraborate, anhydrous (1330-43-4) • Disodium tetraborate decahydrate (1303-96-4) • Disodium tetraborate pentahydrate (12179-04-3)
Boric acid	Fertility, other	Wistar rat	8.75 mg B/kg bw/day	2	Yoshizaki *et al*., 1999	• Boric acid (10043-35-3, 11113-50-1) • Diboron trioxide (1303-86-2)

Test substance	Type of study	Species/ Strain/ Breed	NOAEL	Reliability score	Reference[1]	In the registration dossier /CAR of substance (CAS)
						• Disodium tetraborate, anhydrous (1330-43-4) • Disodium tetraborate decahydrate (1303-96-4) • Disodium tetraborate pentahydrate (12179-04-3)
Sodium tetraborate decahydrate	Fertility, other	Sprague-Dawley rat	50 mg B/kg bw	2	Lee *et al*., 1978	• Boric acid (10043-35-3, 11113-50-1) • Diboron trioxide (1303-86-2) • Disodium tetraborate, anhydrous (1330-43-4) • Disodium tetraborate decahydrate (1303-96-4) • Disodium tetraborate pentahydrate (12179-04-3)
Boric acid	Fertility, other	CD-1 rat	21 mg B/kg bw/day	3	Harris *et al*., 1992	• Boric acid (10043-35-3, 11113-50-1) • Diboron trioxide (1303-86-2) • Disodium tetraborate, anhydrous (1330-43-4) • Disodium tetraborate decahydrate (1303-96-4) • Disodium tetraborate pentahydrate (12179-04-3)
Boric acid	Fertility, other	In vitro, rat	-	2	Study report, 2013	• Boric acid (10043-35-3, 11113-50-1) • Diboron trioxide (1303-86-2)
Development						
Boric acid	BMD – study development	In silico	10.3 mg B/kg bw/day ($BMDL_{0.5}$)	2	Allen *et al*., 1996	• Boric acid (10043-35-3, 11113-50-1) • Diboron trioxide (1303-86-2) • Disodium tetraborate, anhydrous (1330-43-4) • Disodium tetraborate decahydrate (1303-96-4) • Disodium tetraborate pentahydrate (12179-04-3)
Boric acid	Prenatal development toxicity study, OECD 414	Sprague-Dawley rat	9.6 mg B/kg bw/day	1	Study report, 1994 Price CJ *et al*., 1994	• Boric acid (10043-35-3, 11113-50-1) • Diboron trioxide (1303-86-2) • Disodium tetraborate, anhydrous (1330-43-4) • Disodium tetraborate decahydrate (1303-96-4) • Disodium tetraborate pentahydrate (12179-04-3)

Test substance	Type of study	Species/ Strain/ Breed	NOAEL	Reliability score	Reference[1]	In the registration dossier /CAR of substance (CAS)
Boric acid	Prenatal development toxicity study, OECD 414	New Zealand White rabbit	21.8 mg B/kg bw/day	1	Publication, 1991 Price CJ *et al*., 1991	• Boric acid (10043-35-3, 11113-50-1) • Diboron trioxide (1303-86-2) • Disodium tetraborate, anhydrous (1330-43-4) • Disodium tetraborate decahydrate (1303-96-4) • Disodium tetraborate pentahydrate (12179-04-3)
Boric acid	Developmental toxicity	Sprague-Dawley rat	0.1% boric acid (LOAEL)	2	Publication, 1990	• Boric acid (10043-35-3, 11113-50-1) • Diboron trioxide (1303-86-2) • Disodium tetraborate, anhydrous (1330-43-4) • Disodium tetraborate decahydrate (1303-96-4) • Disodium tetraborate pentahydrate (12179-04-3)
Boric acid	Developmental toxicity	Swiss albino CD-1 mice	43 mg B/kg bw/day	2	Publication, 1989; Heindel *et al*., 1992	• Boric acid (10043-35-3, 11113-50-1) • Diboron trioxide (1303-86-2) • Disodium tetraborate, anhydrous (1330-43-4) • Disodium tetraborate decahydrate (1303-96-4) • Disodium tetraborate pentahydrate (12179-04-3)
Boric acid	Developmental toxicity	Sprague-Dawley rat	250 mg boric acid/kg bw/day	4	Harrouk *et al*., 2005	• Boric acid (10043-35-3, 11113-50-1) • Diboron trioxide (1303-86-2) • Disodium tetraborate, anhydrous (1330-43-4) • Disodium tetraborate decahydrate (1303-96-4) • Disodium tetraborate pentahydrate (12179-04-3)
Boric acid	Developmental toxicity – MoA study	CD-1 mice	-	2	Di Renzo *et al*., 2007	• Boric acid (10043-35-3, 11113-50-1) • Diboron trioxide (1303-86-2) • Disodium tetraborate, anhydrous (1330-43-4) • Disodium tetraborate decahydrate (1303-96-4) • Disodium tetraborate pentahydrate (12179-04-3)
Boric acid	Developmental toxicity –	Sprague-Dawley rat	-	2	Wéry *et al*., 2003	• Boric acid (10043-35-3, 11113-50-1)

Test substance	Type of study	Species/ Strain/ Breed	NOAEL	Reliability score	Reference[1]	In the registration dossier /CAR of substance (CAS)
	MoA study					• Diboron trioxide (1303-86-2)
Boric acid	Developmental toxicity	Sprague-Dawley rat (embryos)	-	2	Narotsky *et al*., 2004	• Boric acid (10043-35-3, 11113-50-1) • Diboron trioxide (1303-86-2)
Boric acid	Developmental toxicity	Frog	-	2	Fort *et al*.,1998; 1999a; 1999b; 2000; 2002	• Boric acid (10043-35-3, 11113-50-1) • Diboron trioxide (1303-86-2)
Boric acid	Developmental toxicity	Sprague-Dawley rat; CD-1 mice	-	2	Lanoue *et al*., 1998; 1999	• Boric acid (10043-35-3, 11113-50-1) • Diboron trioxide (1303-86-2)
Boric acid	Developmental toxicity	Trout; Zebrafish	-	2	Eckhert, 1998; Eckhert and Rowe, 1999; Rowe *et al*., 1998	• Boric acid (10043-35-3, 11113-50-1) • Diboron trioxide (1303-86-2)
Boric acid	Developmental toxicity, in vitro	Embryonic stem cells, fibroblasts	-	1	Study report, 2013	• Boric acid (10043-35-3, 11113-50-1) • Diboron trioxide (1303-86-2)
Repeated dose toxicity studies reporting effects on fertility parameters						
Boric acid	2-years feeding study	Sprague-Dawley rat	17.5 mg B/kg bw/day	2	Study report, 1966; Study report 1967; Weir and Fisher, 1972	• Boric acid (10043-35-3, 11113-50-1) • Diboron trioxide (1303-86-2) • Disodium tetraborate, anhydrous (1330-43-4) • Disodium tetraborate decahydrate (1303-96-4) • Disodium tetraborate pentahydrate (12179-04-3)
Sodium tetraborate decahydrate	2-years feeding study	Sprague-Dawley rat	17.5 mg B/kg bw/day	2	Study report, 1966; Study report 1967; Weir and Fisher, 1972	• Boric acid (10043-35-3, 11113-50-1) • Diboron trioxide (1303-86-2) • Disodium tetraborate, anhydrous (1330-43-4) • Disodium tetraborate decahydrate (1303-96-4) • Disodium tetraborate pentahydrate (12179-04-3)
Boric acid	Chronic toxicity, oral	Beagle dog	41 mg B/kg bw/day (LOAEL)	3	Study report 1967; Weir and Fisher, 1972	• Boric acid (10043-35-3, 11113-50-1) • Diboron trioxide (1303-86-2) • Disodium tetraborate, anhydrous (1330-43-4) • Disodium tetraborate decahydrate (1303-96-4) • Disodium tetraborate

Test substance	Type of study	Species/ Strain/ Breed	NOAEL	Reliability score	Reference[1]	In the registration dossier /CAR of substance (CAS)
						pentahydrate (12179-04-3)
Boric acid	Short-term repeated dose toxicity: oral	Fisher 344 rats	61 mg B/kg bw/day (LOAEL)	2	Treinen and Chapin, 1991	• Boric acid (10043-35-3, 11113-50-1) • Diboron trioxide (1303-86-2) • Disodium tetraborate, anhydrous (1330-43-4) • Disodium tetraborate decahydrate (1303-96-4) • Disodium tetraborate pentahydrate (12179-04-3)
Boric acid	Short-term repeated dose toxicity: oral	Rat	140 mg B/kg bw/day (LOAEL)	3	Bouissou and Castagnol, 1965	• Boric acid (10043-35-3, 11113-50-1) • Diboron trioxide (1303-86-2) • Disodium tetraborate, anhydrous (1330-43-4) • Disodium tetraborate decahydrate (1303-96-4) • Disodium tetraborate pentahydrate (12179-04-3)
Boric acid	Short-term repeated dose toxicity: oral	Long-Evans rat	47.4 mg B/kg bw/day (LOAEL)	3	Seal and Weeth, 1980	• Boric acid (10043-35-3, 11113-50-1) • Diboron trioxide (1303-86-2) • Disodium tetraborate, anhydrous (1330-43-4) • Disodium tetraborate decahydrate (1303-96-4) • Disodium tetraborate pentahydrate (12179-04-3)
Boric acid	Short-term repeated dose toxicity: oral	Sprague-Dawley rat	100 mg boric acid/kg bw/day (LOAEL)	2	Kocatürk *et al*. 2005	• Boric acid (10043-35-3, 11113-50-1) • Diboron trioxide (1303-86-2) • Disodium tetraborate, anhydrous (1330-43-4) • Disodium tetraborate decahydrate (1303-96-4) • Disodium tetraborate pentahydrate (12179-04-3)
Boric acid	Short-term repeated dose toxicity: oral	B6C3F1 mouse	142 mg B/kg bw/day (LOAEL)	2	Publication, 1987	• Boric acid (10043-35-3, 11113-50-1) • Diboron trioxide (1303-86-2) • Disodium tetraborate, anhydrous (1330-43-4) • Disodium tetraborate decahydrate (1303-96-4) • Disodium tetraborate pentahydrate (12179-04-3)
Disodium	Short-term	Long-	47.4 mg	3	Seal and	• Boric acid (10043-35-3,

Test substance	Type of study	Species/ Strain/ Breed	NOAEL	Reliability score	Reference[1]	In the registration dossier /CAR of substance (CAS)
tetraborate decahydrate	repeated dose toxicity: oral	Evans rat	B/kg bw/day (LOAEL)		Weeth, 1980	11113-50-1) • Diboron trioxide (1303-86-2) • Disodium tetraborate, anhydrous (1330-43-4) • Disodium tetraborate decahydrate (1303-96-4) • Disodium tetraborate pentahydrate (12179-04-3)
Boric acid	Sub-chronic toxicity: oral	Fisher 344 rat	26 mg B/kg bw/day	2	Ku *et al*. 1993	• Boric acid (10043-35-3, 11113-50-1) • Diboron trioxide (1303-86-2) • Disodium tetraborate, anhydrous (1330-43-4) • Disodium tetraborate decahydrate (1303-96-4) • Disodium tetraborate pentahydrate (12179-04-3)
Boric acid	Sub-chronic toxicity: oral	Sprague-Dawley rat	26 mg B/kg bw/day	2	Study report, 1962; Weir and Fisher, 1972	• Boric acid (10043-35-3, 11113-50-1) • Diboron trioxide (1303-86-2) • Disodium tetraborate, anhydrous (1330-43-4) • Disodium tetraborate decahydrate (1303-96-4) • Disodium tetraborate pentahydrate (12179-04-3)
Boric acid	Sub-chronic toxicity: oral	Beagle dog	4.4 mg B/kg bw/day	3	Study report, 1963; Weir and Fisher, 1972 Paynter, 1963	• Boric acid (10043-35-3, 11113-50-1) • Diboron trioxide (1303-86-2) • Disodium tetraborate, anhydrous (1330-43-4) • Disodium tetraborate decahydrate (1303-96-4) • Disodium tetraborate pentahydrate (12179-04-3)
Boric acid	Sub-chronic toxicity: oral	Rat	0.3 mg B/L	3	Krasovskii *et al*. 1976	• Boric acid (10043-35-3, 11113-50-1) • Diboron trioxide (1303-86-2) • Disodium tetraborate, anhydrous (1330-43-4) • Disodium tetraborate decahydrate (1303-96-4) • Disodium tetraborate pentahydrate (12179-04-3)

[1] As cited in the publically disseminated REACH registration dossiers and/or biocide assessment reports

Table II: Overview of human epidemiology studies for boric acid; diboron trioxide; disodium tetraborate, anhydrous; disodium tetraborate decahydrate and disodium tetraborate pentahydrate with endpoint toxicity to reproduction/fertility, which are included in the publically disseminated REACH Registration Dossiers or in the Assessment Reports under BPR. Tetraboron disodium heptaoxide, hydrate and orthoboric acid, sodium salt are not registered nor evaluated as active substances under the biocide regulation and therefore lack data.

Type of study	**Reference[1]**	**In the registration dossier / CAR of substance (CAS)**
Worker reproductive toxicity study	Duydu *et al*., 2011	• Boric acid (10043-35-3, 11113-50-1) • Diboron trioxide (1303-86-2) • Disodium tetraborate, anhydrous (1330-43-4) • Disodium tetraborate decahydrate (1303-96-4) • Disodium tetraborate pentahydrate (12179-04-3)
Worker reproductive toxcity study	Scialli *et al*., 2010	• Boric acid (10043-35-3, 11113-50-1) • Diboron trioxide (1303-86-2) • Disodium tetraborate, anhydrous (1330-43-4) • Disodium tetraborate decahydrate (1303-96-4) • Disodium tetraborate pentahydrate (12179-04-3)
Worker reproductive toxcity study	Robbins *et al*., 2010	• Boric acid (10043-35-3, 11113-50-1) • Diboron trioxide (1303-86-2) • Disodium tetraborate, anhydrous (1330-43-4) • Disodium tetraborate decahydrate (1303-96-4) • Disodium tetraborate pentahydrate (12179-04-3)
Cohort study (retrospective)	Study report, 1992 Whorton *et al*., 1994a;b	• Boric acid (10043-35-3, 11113-50-1) • Diboron trioxide (1303-86-2) • Disodium tetraborate, anhydrous (1330-43-4) • Disodium tetraborate decahydrate (1303-96-4) • Disodium tetraborate pentahydrate (12179-04-3)
Cohort study (retrospective)	Sayli *et al*., 1998	• Boric acid (10043-35-3, 11113-50-1) • Diboron trioxide (1303-86-2) • Disodium tetraborate, anhydrous (1330-43-4) • Disodium tetraborate decahydrate (1303-96-4) • Disodium tetraborate pentahydrate (12179-04-3)
Epidemiology study	Sayli, 1998	• Boric acid (10043-35-3, 11113-50-1) • Diboron trioxide (1303-86-2) • Disodium tetraborate, anhydrous (1330-43-4) • Disodium tetraborate decahydrate (1303-96-4) • Disodium tetraborate pentahydrate (12179-04-3)
Epidemiology study	Sayli, 2001	• Boric acid (10043-35-3, 11113-50-1) • Diboron trioxide (1303-86-2) • Disodium tetraborate, anhydrous (1330-43-4) • Disodium tetraborate decahydrate (1303-96-4) • Disodium tetraborate pentahydrate (12179-04-3)
Epidemiology study	Sayli *et al*., 2004	• Boric acid (10043-35-3, 11113-50-1) • Diboron trioxide (1303-86-2) • Disodium tetraborate, anhydrous (1330-43-4) • Disodium tetraborate decahydrate (1303-96-4) • Disodium tetraborate pentahydrate (12179-04-3)
Epidemiology study	Sayli, 2003	• Boric acid (10043-35-3, 11113-50-1)

Type of study	Reference[1]	In the registration dossier / CAR of substance (CAS)
		• Diboron trioxide (1303-86-2) • Disodium tetraborate, anhydrous (1330-43-4) • Disodium tetraborate decahydrate (1303-96-4) • Disodium tetraborate pentahydrate (12179-04-3)
Epidemiology study	Col *et al*., 2000	• Boric acid (10043-35-3, 11113-50-1) • Diboron trioxide (1303-86-2) • Disodium tetraborate, anhydrous (1330-43-4) • Disodium tetraborate decahydrate (1303-96-4) • Disodium tetraborate pentahydrate (12179-04-3)
Epidemiology study	Yazbeck *et al*., 2005	• Boric acid (10043-35-3, 11113-50-1) • Diboron trioxide (1303-86-2) • Disodium tetraborate, anhydrous (1330-43-4) • Disodium tetraborate decahydrate (1303-96-4) • Disodium tetraborate pentahydrate (12179-04-3)
Occupational exposure study	Robbins *et al*., 2008	• Boric acid (10043-35-3, 11113-50-1) • Diboron trioxide (1303-86-2) • Disodium tetraborate, anhydrous (1330-43-4) • Disodium tetraborate decahydrate (1303-96-4) • Disodium tetraborate pentahydrate (12179-04-3)
Epidemiology study	Chang *et al*., 2006	• Boric acid (10043-35-3, 11113-50-1) • Diboron trioxide (1303-86-2) • Disodium tetraborate, anhydrous (1330-43-4) • Disodium tetraborate decahydrate (1303-96-4) • Disodium tetraborate pentahydrate (12179-04-3)
Retrospective case control study	Acs *et al*. 2006	• Boric acid (10043-35-3, 11113-50-1) • Diboron trioxide (1303-86-2) • Disodium tetraborate, anhydrous (1330-43-4) • Disodium tetraborate decahydrate (1303-96-4) • Disodium tetraborate pentahydrate (12179-04-3)
Retrospective cohort study	Tuccar *et al*., 1998	• Boric acid (10043-35-3, 11113-50-1) • Diboron trioxide (1303-86-2) • Disodium tetraborate, anhydrous (1330-43-4) • Disodium tetraborate decahydrate (1303-96-4) • Disodium tetraborate pentahydrate (12179-04-3)

[1] As cited in the publically disseminated REACH registration dossiers and/or biocide assessment reports