$[B_4O_5(OH)_4]^-$; $[B_5O_6(OH)_4]^{2-}$ predominant

The nucleation process can be described as the interaction of boric acid with the borate anion shown in the following equation for the example of $[B_3O_3(OH)_5]^{2-}$

$$B(OH)_3 + 2\ [B(OH)_4]^- \leftrightarrow [B_3O_3(OH)_5]^{2-} + 3\ H_2O$$

It has been shown for solutions of boric acid and sodium borates below pH 8 and at a solution concentration of below 0.1M, the borate is present as undissociated boric acid, whereas above pH 10 the metaborate ion becomes the main species(Ingr, 1963; Kirk-Othmer, 1992). The metaborate ion will also be present in aqueous solutions at environmental temperature and pH mainly as weakly dissociated boric acid (pKa value at room temperature 9.25, Holleman, 1995).

Therefore, regardless of whether the boron source is boric acid or one of the other borates (such as boric oxide or a sodium borate), monomeric species are predominant in most biological fluids as well as under environmental conditions (Maeda, 1979). This was verified in an independent study aimed at identifying the species present in systems under typical biologically active conditions, i.e. pH 6.5-pH7.5 and <0.02M. Raman spectroscopy confirmed the presence of undissociated boric $B(OH)_3$ as the species present (Doc IIIA 7.1.1.1 Hydrolysis Boric Acid.doc) (de Vette et al., 2001)

Boric Oxide

$B_2O_3 + 3H_2O = 2(H_3BO_3)$

Disodium Octaborate Tetrahydrate

$Na_2B_8O_{13}.4H_2O + H_2O = Na_2O + 4(B_2O_3).4H_2O = 2NaOH + 8(H_3BO_3)$

Disodium Tetraborates

$Na_2B_4O_7\ xH_2O$ (x = 0, 5 or 10) $= 2Na_2O + B_2O_3\ x\ H_2O = 4NaOH + 2\ (H_3BO_3)$

At environmental pHs undissociated boric acid will be present in aqueous environment.

Specific Toxicological Considerations

The borates will only be bioavailable when they are in solution and therefore will be available as undissociated boric acid. As a solid they will not be bioavailable. The dissolution rates at physiological levels and environmental levels will be very fast. For boric acid, boric oxide, Disodium octaborate tetrahydrate and disodium tetraborate decahydrate, even at high concentrations such as 2% the dissolution rate is less than 15 mins at neutral pH, while the dissolution of disodium tetraborate pentahydrate and disodium tetraborate anhydrous appears to be slower. At lower concentrations the dissolution rates will be much quicker (at 0.5% more than 10 times faster based on the data for disodium tetraborate pentahydrate). Moreover, at pH 2, to represent the gastric environment, dissolution rates will be more than 11 times faster (by analogy with the data for boric oxide and disodium tetraborate anhydrous) and therefore be instantaneous. (Rickards and Arian, 2004). Data is not currently available on the dissolution rates at physiological and toxicological levels, but it is likely to be very fast at lower concentrations, based on the data at 2%.

In the blood, boron occurs at relatively low concentrations. Background levels of blood boron in humans from exposure in diet and drinking water is in the low parts per billion (ppb) range. Toxic levels of blood boron in animal studies is in the parts per million (ppm) range. Any borate absorbed into the blood will exist at very low concentrations (many orders less than 2%), and, at low concentrations and physiological pH, any borate in blood will rapidly dissociate to boric acid.

At the levels of substance introduced in toxicological studies the rates of dissolution may vary with tetraborate anhydrous and disodium tetraborate pentahydrate being slower. The main concerns could be local irritation at the site of contact. However, local irritation is not observed acute studies.

In long-term oral studies of boric acid and disodium tetraborate decahydrate, the test substance was administered in the diet (over a period of roughly 8 hours when rodents eat) and therefore the test material was given over an extended period of time, not as a bolus. Any differences in the dissolution rates of borates should make no difference in their systemic toxicity, which is the primary concern. No evidence of local GI tract irritation has been seen in any study carried out.

For dermal studies, absorption is very low (>0.4%) in human studies and there is no evidence to indicate that any borate is absorbed significantly more than another borate.

Absorption by inhalation is expected to be 100%. Since respirable particles are very small, they are likely to be dissolved very quickly on the lung surfaces. The data from acute inhalation limit studies indicates some minor effects of dust exposure, but there does not appear to be a significant difference in effects between the borates tested.

In genotoxicity *in vitro* studies the borates will not be bioavailable unless dissolved in the test media. Once absorbed in the cells they will exist as undissociated boric acid. In *in vivo* studies, bioavailability will also be dependent on dissolution and the same arguments apply as for long-term toxicity.

The equivalence between the borates is indicated by studies in dogs and rats where both boric acid and disodium tetraborate decahydrate were tested. The results indicate that the effects seen are equivalent on boron basis indicating that the bioavailability of the two borates is similar.

Section A6.2-A10 **Doc III A Read Across to Boric Acid**

Annex Point Section A6.2-A10

Comparison of Toxicology of Boric Acid and Borax (Disodium Tetraborate Decahydrate)

Dose in diet	**Dose**	**Symptoms**
*****2 Year Dog Studies** Doc IIIA A_6_4.1 Subchronic 2 year Dogs Boric acid.doc & Doc IIIA A_6_4.1 Subchronic 2 year Dogs Tetraborates BA Entry.doc		
0.2 % BA	**10.9 mg B/kg (8.8)	No symptoms
0.309 % Borax	**9.6 mg B/kg (8.8)	No symptoms
0.67 % BA	**40.8 mg B/kg (39)	3/8 diarrhoea on 2-4 occasions. Soft stools in all dogs on 2 –5 occasions. 1/8 exema after 19 weeks ↓ Testicular weight; 2 dogs azospermic; 2
1.03 % Borax	**38.1 mg B/kg (39)	6/8 diarrhoea 1-6 occasions. Instances of soft stools in all dogs up to 26 weeks. ↓ Testicular weight; generalised spermatic arrest; atrophy of the seminiferous
2 Year Rat Studies Doc IIIA A_6_5 Chronic rat Boric acid.doc & Doc IIIA A_6_5 Chronic Rat Tetraborates BA Entry.doc		
0.2 % BA	17.5 mg B/kg	No effects
0.308% Borax	17.5 mg B/kg	No effects
0.67 % BA	58.5 mg B/kg	Clinical signs of Coarse hair coats, hunched position, swollen pads and inflamed bleeding eyes ↓ Body weight gain

		Complete sterility ↓ Body weight gain in females ↓ Reduced food intake
1.03 % Borax	58.5 mg B/kg	Clinical signs of Coarse hair coats, hunched position, swollen pads and inflamed bleeding eyes ↓ Body weight gain ↓ Red cell volume and haemoglobin Testicular degeneration Testicular atrophy No viable sperm in atrophied testis Complete sterility ↓ Reduced food intake

* There are a number of flaws in these studies that make them unsuitable for evaluation for risk assessment see Doc III Dog 90 day studies

** Dose estimated form actual dietary intake. Dose in Brackets based on standard assumptions regarding body weight and food consumption and as reported in the study reports

*** There are a number of flaws in these studies that make them unsuitable for evaluation for risk assessment see Doc IIIA Dog 2 year studies

References

1. Farmer, 1982 Structural Chemistry in the Borate Industry., Chem and Ind.,
2. Ingri, N Sven. Kem. Tidskr. 75(4), 199 (1963)
3. Kirk – Othmer Encyclopedia of Chemical Technology, V4, 1992, pp 378-380
4. Holleman, 1995. Lehrbuch der anorganischen Chemie. 101st ed de Gruyter, Berlin, copyright
5. De Vette, [redacted] 2001 Hydrolysis as a function of pH and identification of breakdown products. [redacted]
6. Maeda M, Raman Spectra of polyborate ions in aqueous solution. J Inorg. Nucl. Chem., Vol 41, pp 1217-1220 (1979)
7. [redacted] 2004 Rate of Dissolution Study of [redacted], [redacted]

Section A6.2-A10 Doc III A Read Across to Boric Acid

Annex Point Section A6.2-A10

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	25 March 2005
Materials and Methods	Not applicable.
Results and discussion	In aqueous solutions at physiological and acidic pH, simple borates such as disodium tetraborate decahydrate ($Na_2B_4O_7 \bullet 10H_2O$; borax), disodium tetraborate pentahydrate ($Na_2B_4O_7 \bullet 5H_2O$; borax pentahydrate), boric oxide (B_2O_3) and disodium octaborate tetrahydrate ($Na_2B_8O_{13} \bullet 4H_2O$) will exist as undissociated boric acid. Therefore, the toxicokinetics and toxicological effects of boric acid, disodium tetraborate decahydrate, boric oxide (B2O3) and disodium octaborate tetrahydrate are likely to be similar on a boron equivalents basis. Therefore, it is justified to draw conclusions on boric oxide on the basis of data on studies on toxicokinetics and toxicity of other simple borates such as boric acid and the disodium tetraborates.
Conclusion	It is justified to draw conclusions on boric oxide on the basis of data on studies on toxicokinetics and toxicity of other simple borates such as boric acid and the disodium tetraborates. The effects assessment of borates, as described above by the applicant, is not adopted. For a detailed evaluation of the toxicokinetics and toxicology of borates see DOC II A of the boric oxide evaluation.
Reliability	
Acceptability	
Remarks	
	COMMENTS FROM ... *(specify)*
Date	*Give date of comments submitted*
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Section A7.1.1.1.1 Hydrolysis as a function of pH and identification of breakdown products

Annex Point IIA7.6.2.1

Official use only

21.4 Reference	1. [redacted] 2001, A study on the identification and comparison of the dissociation products [redacted] 2. Farmer, J. 1982. Structural Chemistry in the Borate Industry. Chem. and Ind., 6 March 1982 3. Holleman, 1995. Lehrbuch der anorganischen Chemie. 101st ed de Gruyter, Berlin 4. Kemp P H, 1956 "The Chemistry of Borates Part 1", Borax 5. Maeda, M. 1979. Raman spectra of polyborate ions in aqueous solution. J.Inorg. Nucl. Chem., Vol 41, pp 1217-1220 (1979) 6. [redacted] (2004). Boric Acid (CAS No. 10043-35-3): Statement on Hydrolysis as a function of pH and identification of breakdown products [redacted]
21.5 Data protection	Yes on [redacted].
21.5.1 Data owner	[redacted]
21.5.2 Companies with letter of access	**Curent Access** [redacted]
21.5.3 Criteria for data protection	Data on new a.s. for first entry to Annex I

22 GUIDELINES AND QUALITY ASSURANCE

22.1 Guideline study	No.
22.2 GLP	Yes
22.3 Deviations	No

23 MATERIALS AND METHODS

23.1	**Test material**	
23.1.1	Lot/Batch number	
23.1.2	Specification	Disodium Octaborate Tetrahydrate [redacted] Sodium Tetraborate Decahydrate (Borax, [redacted])
23.1.3	Purity	144-99-303
23.1.4	Further relevant properties	none
23.2	**Reference substance**	Yes Orthoboric acid (Boric Acid, [redacted]
23.2.1	Initial concentration of reference substance	0.02 mol.l^{-1}
23.3	**Test solution**	Solutions of [redacted] (Disodium octaborate tetrahydrate) tech., Borax [redacted] and Boric Acid [redacted], with a final solution concentration of 0.02mol.l^{-1} were prepared by dissolving 0.5181g, 0.9578g and 0.6206g of the test substances in 500ml ultrapure water respectively. From these test solutions, five portions of 100ml of each substance solution were made. One portion of each test substance was not buffered, whereas the other portions were acidified or made alkaline to pH 6.0, 7.0, 8.0 and 9.0 with the aid of 2M HCl and 2M NaOH respectively. The Raman spectra of these solutions were recorded. **Note:** the final solution volumes and concentrations of the buffered solutions were similar to those of the non-buffered, since only a few drops of HCl or NaOH were required to change the pH.
23.4	**Testing procedure**	*Non-entry field*
23.4.1	Test system	The principle of the test is based upon the article of Maeda(1). Test solutions of the substances [redacted] *(*Disodium octaborate tetrahydrate*)* tech.; Borax [redacted]) and of Boric Acid, [redacted] are prepared under non-buffered conditions and at pH 6.0, 7.0, 8.0 and 9.0. The Raman spectrum of each solution was measured and the spectrum of the test substance compared to Raman spectra of boric acid reported in the literature (Maeda, 1979) and that of Boric Acid, [redacted], under the same circumstances. Comparison of the unique Raman bands of the products used show whether the dissociation products of [redacted] and Borax, [redacted] are comparable to those of Boric Acid, [redacted].
23.4.2	Temperature	Room temperature
23.4.3	pH	See Tables

Section A7.1.1.1.1 Hydrolysis as a function of pH and identification of breakdown products

Annex Point IIA7.6.2.1

23.4.4	Duration of the test	Because we are dealing with an inorganic system, no decomposition products are formed. The system equilibrates rapidly, therefore, test duration is not relevant in the circumstances.
23.4.5	Number of replicates	Non reported
23.4.6	Sampling	Stable system, therefore sampling interval and storage not relevant
23.4.7	Analytical methods	Raman Spectrometry
23.5	**Preliminary test**	No

24 RESULTS

Section A7.1.1.1.1 Hydrolysis as a function of pH and identification of breakdown products

Annex Point IIA7.6.2.1

24.1 Concentration and hydrolysis values	*See table A7_1_1_1_1-4*
24.2 Hydrolysis rate constant (k_h)	Not determined. Inorganic material speciation under consideration.
24.3 Dissipation time	Not relevant – Inorganic Material
24.4 Concentration – time data	Concentration is constant in all cases (0.02M).
24.5 Specification of the transformation products	There are no transformation products (inorganic material). Reference Farmer, 1982

25 APPLICANT'S SUMMARY AND CONCLUSION

25.1 Materials and methods	The objective of the study was to identify and compare the dissociation products of [redacted], and Borax, [redacted], in aqueous solution with those of Boric acid, [redacted], using Raman spectrometry. The Raman spectra of dilute solutions of [redacted] and Borax [redacted] were measured and compared to Boric Acid, [redacted] as well as data on boric acid from open literature Maeda, 1979). The measurements were carried out under non-buffered conditions and at pH6, 7, 8 and 9. The test was performed in compliance with the OECD principles of Good Laboratory Practice.
25.2 Results and discussion	Solutions containing suitable low concentrations of all three boron salts were examined so as to simulate those occurring under aqueous environmental conditions. In the spectra from all three substances, a major band was found at 872 cm^{-1}, which corresponds to that reported by Maeda’ 1979 for dissociated and undissociated boric acid. A few characteristic bands of boric acid that were reported in the literature were less clearly seen or were absent in the spectra due to the low concentrations of the test and reference substances. The concentrations used in this study were 75 times lower than those reported by Maeda , 1979. Most of the simple inorganic borates (for example, boric acid, boric oxide, sodium metaborates, tetraborates and octaborates) are highly water-soluble. The mode of dissolution of metal borates as well as of boric acid is complex and depends very much on the conditions (pH, temperature, and concentration). Depending on the boron concentration monomeric and, with increasing concentration of boron, polymeric species will be found (Farmer, 1982) $[B(OH)_3] < 0{,}02M$ $B(OH)_3 + H_2O \dashrightarrow [B(OH)_4]^+ + H^+$ pKa = 9,15

0,025M <= [B(OH)3] <= 0,4/0,6M
$[B_3O_3(OH)_4]^-$; $[B_3O_3(OH)_5]^{2-}$ predominant

$[B(OH)_3]$ > 0,6M
$[B_4O_5(OH)_4]$-; $[B_5O_6(OH)_4]^{2-}$ predominant

The nucleation process can be described as the interaction of boric acid with the borate anion shown in the following equation for the example of $[B_3O_3(OH)_5]^{2-}$

$B(OH)_3 + 2\,[B(OH)_4]^- \longleftrightarrow [B_3O_3(OH)_5]^{2-} + 3\,H_2O$

Therefore, regardless of whether the boron source is boric acid or one of the other borates (such as boric oxide or a sodium borate), monomeric species are predominant in most biological fluids as well as under environmental conditions. Below pH 7 boric acid and borates exist as undissociated boric acid, whereas above pH 10 the metaborate ion becomes the main species. The metaborate ion will also be present in aqueous solutions at environmental temperature and pH mainly as weakly dissociated boric acid (pKa value at room temperature 9.25, Holleman, 1995). As a result, the toxicology and the ecotoxicology of all these simple borates are likely to be similar on an equivalent boric acid basis or boron basis.

Since disodium octaborate tetrahydrate is a solidsolution of boric acid and disodium tetraborate decahydrate (borax), disodium octaborate tetrahydrate in dilute aqueous solution dissociates to predominantly free boric acid plus some monoborate anions (Kemp, 1956), therefore it can be considered to exist as undissociated boric acid under physiological conditions.

The dissolution to undissociated boric acid by all the borates was confirmed in the study by de Vette et al, which identified and compared the dissociation products of sodium borates (disodium tetraborate decahydrate and disodium octaborate tetrahydrate) and boric acid in dilute aqueous solutions. The data showed through Raman spectra that the predominant species present was undissociated boric acid.

25.2.1 k_H	Not determined
25.2.2 DT_{50}	Not determined
25.2.3 r^2	Not determined
25.3 Conclusion	Conclusions are based on the fact that this is the speciation of an inorganic material. The band at 872 cm^{-1} which appeared in every spectrum, corresponds to the literature. A relationship between intensity of the peaks and pH was found and is also reported by Maeda 1979,. It is therefore concluded that all bands correspond to bands of dissociation products of Boric Acid

manufacturing Grade.

The most recent internationally accepted test guideline for a hydrolysis test is the OECD 111 guideline. Buffers with different pH values (pH 4, 7 and 9) containing the test substance is incubated at an elevated temperature for at least one week in the preliminary test. The concentration of the test substance is measured. If hydrolyzed a Tier 1 study will follow. Persistent (i.e. not biodegradable) breakdown products should also be considered

Boric acid is an inorganic compound and does not have any chemical bonds prone to hydrolysis. However, polymeric borate species occurs in significant amounts at certain pH values, temperatures and at concentrations above 0.1 molar. The most important polyborate species are tri-, tetra- and pentaborate anions. Boric acid and tetrahydroxyborate are the dominant species at low pH values and at pH values >9, respectively. These and other borate species are at equilibrium with each other; the concentration of the individual species dependent on the conditions.

Hydrolysis of boric acid is therefore not a relevant ‘degradation’ mechanism and this study by [redacted] is adequate to cover the endpoint ([redacted] 2004).

25.3.1	Reliability	1
25.3.2	Deficiencies	None

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	26-04-2005
Materials and Methods	Applicant's version is acceptable
Results and discussion	Applicant's version is adopted
Conclusion	The proportion of boric acid in dilute solutions with a neutral pH is > 99 %. The relative concentration of the tetrahydrate anion, $[B(OH)4]^{-}$, becomes dominant at pH > 9. Boric acid is an inorganic compound and does not have any chemical bonds prone to hydrolysis. Hydrolysis is thus not a relevant pathway at environmental pH.
Reliability	1
Acceptability	acceptable
Remarks	
	COMMENTS FROM ...
Date	*Give date of comments submitted*
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Table A7_1_1_1_1-1: Type and composition of buffer solutions (specify kind of water if necessary)

Test Substance*	**Natural pH**	**Buffered pH's**			
[redacted].	8.62	6.03	6.99	8.03	9.00
Borax [redacted]	9.18	5.99	6.99	8.03	9.02
Boric Acid [redacted]	5.10	6.02	6.99	7.99	9.00

* Solutions of [redacted]., Borax [redacted] and Boric Acid [redacted], with a final solution concentration of 0.02mol.l^{-1} were prepared by dissolving 0.5181g, 0.9578g and 0.6206g of the test substances in 500ml ultrapure water respectively. From these test solutions, five portions of 100ml of each substance solution were made. One portion of each test substance was not buffered, whereas the other portions were acidified or made alkaline to pH 6.0, 7.0, 8.0 and 9.0 with the aid of 2M HCl and 2M NaOH respectively.

Results of the comparison of the bands found **for** [redacted]. In non-buffered solution and at pH 6.0, pH 7.0 and pH 8.0 and the bands found for the polyborate solutions in the literature (1)

Raman shift (Rel. cm^{-1})	Non- buffered pH 8.62	pH 6.03	pH 6.99	pH 8.03	pH 9.00
385	-	-	-	-	-
430	-	-	-	-	-
447	-	-	-	-	-
458	-	-	-	-	-
490	+	+	+/-	+/-	+/-
524/525	+	-	-	+/-	+/-
565	+	+	+	+	+/-
609	-	-	-	+/-	-
745	+/-	-	-	+/-	-
872	+	+	+	+	+
917	-	-	-	-	-
940	-	-	-	-	-
995	-	-	-	-	-

(1) *Maeda, M. Raman spectra of polyborate ions in aqueous solution. J.Inorg. Nucl. Chem., Vol 41, pp 1217-1220 (1979)*

\+ = band in accordance with (1)

+/- = intensity of band on detection level

\- = band not found in spectrum

Results of the comparison of the bands found **Borax**[redacted]. In non-buffered solution and at pH 6.0, pH 7.0 and pH 8.0 and the bands found for the polyborate solutions in the literature (1)

Raman shift (Rel. cm^{-1})	Non- buffered pH 8.62	pH 6.03	pH 6.99	pH 8.03	pH 9.00
385	-	-	-	-	-
430	-	-	-	-	-
447	-	-	-	-	-
458	-	-	-	-	-
490	-	-	-	-	-
524/525	+	-	-	-	-
565	+/-	+	-	-	+/-
609	+/-	-	+/-	-	-
745	+	-	-	+/-	+
872	+	+	+	+	+
917	-	-	-	-	-
940	-	-	-	-	-
995	-	-	-	-	-

(1) Maeda, M. Raman spectra of polyborate ions in aqueous solution. J.Inorg. Nucl. Chem., Vol 41, pp 1217-1220 (1979)

+ = band in accordance with (1)

+/- = intensity of band on detection level

- = band not found in spectrum

Results of the comparison of the bands found **Boric Acid,** [redacted]. In non-buffered solution and at pH 6.0, pH 7.0 and pH 8.0 and the bands found for the polyborate solutions in the literature (1)

Raman shift (Rel. cm^{-1})	Non- buffered pH 8.62	pH 6.03	pH 6.99	pH 8.03	pH 9.00
385	-	-	-	-	-
430	-	-	-	-	-
447	-	-	-	-	-
458	-	-	-	-	-
490	+/-	+/-	+	+	+
524/525	+/-	-	-	-	-
565	+/-	+/-	-	-	-
609	-	-	-	-	+/-
745	-	-	-	-	+/-
872	+	+	+	+	+
917	-	-	-	-	-
940	-	-	-	-	-
995	-	-	-	-	-

(1) *Maeda, M. Raman spectra of polyborate ions in aqueous solution. J.Inorg. Nucl. Chem., Vol 41, pp 1217-1220 (1979)*

+ = band in accordance with (1)

+/- = intensity of band on detection level

- = band not found in spectrum

In all spectra a band is observed at 872cm^{-1}. the spectra of Borax, [redacted], contain a band at 745cm^{-1} in the natural pH and at pH 9.0. Boric acid, [redacted], has a vibration at 490cm^{-1} at pH 7.0, pH 8.0 and pH 9.0 apart from the band at 872 cm^{-1} in all samples. The Raman spectra of [redacted]. show a band at 565cm^{-1} (non-buffered, pH 6.0, pH7.0 and pH 8.0), a band at 524/525 cm^{-1} (pH = natural) and at 490cm^{-1} (pH= natural and pH=6.0).

Table A7_1_1_1_1-2: Description of test solution

Criteria	**Details**
Purity of water	Ultrapure water, per description by [redacted], where the study was conducted.
Preparation of test medium	Solutions of [redacted]., Borax [redacted] and Boric Acid [redacted], with a final solution concentration of 0.02$mol.l^{-1}$ were prepared by dissolving 0.5181g, 0.9578g and 0.6206g of the test substances in 500ml ultrapure water respectively. From these test solutions, five portions of 100ml of each substance solution were made. One portion of each test substance was not buffered, whereas the other portions were acidified or made alkaline to pH 6.0, 7.0, 8.0 and 9.0 with the aid of 2M HCl and 2M NaOH respectively. *Describe preparation in detail*
Test concentrations (mg a.i./L)	0.02M
Temperature (°C)	Ambient
Controls	Boric Acid
Identity and concentration of co-solvent	No co-solvent
Replicates	None

Table A7_1_1_1_1-3: Description of test system

Glassware	Standard chemical laboratory-ware
Other equipment	Raman spectrometer
Method of sterilization	Not necessary – inorganic speciation under investigation.

16 APPLICANT'S SUMMARY AND CONCLUSION

Since all the borates will exist as undissociated boric acid under physiological and environmental conditions, the toxicology and the ecotoxicology of all these simple borates is similar on an equivalent boric acid basis or boron basis. Therefore the data for boric acid and disodium tetraborate decahydrate can be read across to the other borates for both toxicological and ecotoxicological effects

Conversion factors are given below. These conversion factors are important as some studies express dose in terms of B, whereas other studies express the dose in units of boric acid or disodium tetraborate decahydrate. The B equivalents used are a generic designation rather than a designation of the element boron. For comparative purposes, dose levels of borates are expressed in terms B in most toxicology studies

Conversion factors to Boron Equivalents

		Conversion Factor for Equivalent dose of B
Boric acid	H_3BO_3	0.175
Boric oxide	B_2O_3	0.311
Disodium tetraborate decahydrate (Borax)	$Na_2B_4O_7 \bullet 10H_2O$	0.113
Disodium tetraborate pentahydrate	$Na_2B_4O_7 \bullet 5H_2O$	0.148
Disodium tetraborate anhydrous	$Na_2B_4O_7$	0.215
Disodium octaborate tetrahydrate	$Na_2B_8O_{13} \bullet 4H_2O$	0.210

The simple inorganic borates (for example, boric acid, boric oxide, sodium tetraborates and octaborates) are highly water-soluble. The mode of dissolution of metal borates as well as of boric acid is complex and depends on the conditions (pH, temperature, and concentration). Boric acid is a weak acid and is considered a Lewis acid. As such it is an electron acceptor, rather than a proton donor, so will accept hydroxide. Depending on the boron concentration monomeric and, with increasing concentration of boron, polymeric species will be found (Farmer, 1982).

[B(OH)3] < 0,02M
B(OH)3 + H2O --> [B(OH)4]+ + H+ pKa = 9,15

0,025M <= [B(OH)3] <= 0,4/0,6M
[B3O3(OH)4]-; [B3O3(OH)5]2- predominant

[B(OH)3] > 0,6M
[B4O5(OH)4]-; [B5O6(OH)4]2- predominant

The nucleation process can be described as the interaction of boric acid with the borate anion shown in the following equation for the example of [B3O3(OH)5]2-

B(OH)3 + 2 [B(OH)4]- <---> [B3O3(OH)5]2- + 3 H2O

It has been shown for solutions of boric acid and sodium borates below pH 8 and at a solution concentration of below 0.1M, the borate is present as undissociated boric acid, whereas above pH 10 the metaborate ion becomes the main species(Ingr, 1963; Kirk-Othmer, 1992). The metaborate ion will also be present in aqueous solutions at environmental temperature and pH mainly as weakly dissociated boric acid (pKa value at room temperature 9.25, Holleman, 1995).

Therefore, regardless of whether the boron source is boric acid or one of the other borates (such as boric oxide or a sodium borate), monomeric species are predominant in most biological fluids as well as under environmental conditions (Maeda, 1979). This was verified in an independent study aimed at identifying the species present in systems under typical biologically active conditions, i.e. pH 6.5-pH7.5 and <0.02M. Raman spectroscopy confirmed the presence of undissociated boric $B(OH)_3$ as the species present (Doc IIIA 7.1.1.1 Hydrolysis Boric Acid.doc) (de Vette et al., 2001)

Boric Oxide

B2O3 + 3H2O = 2(H3BO3)

Disodium Octaborate Tetrahydrate

Na2B8O13.4H2O + H2O = Na2O + 4(B2O3).4H2O = 2NaOH + 8(H3BO3)

Disodium Tetraborates

Na2B4O7 xH2O (x = 0, 5 or 10) = 2Na2O + B2O3 x H2O = 4NaOH + 2 (H3BO3)

At environmental pHs undissociated boric acid will be present in aqueous environment.

References

8. Farmer, 1982 Structural Chemistry in the Borate Industry., Chem and Ind.,
9. Ingri, N Sven. Kem. Tidskr. 75(4), 199 (1963)
10. Kirk – Othmer Encyclopedia of Chemical Technology, V4, 1992, pp 378-380
11. Holleman, 1995. Lehrbuch der anorganischen Chemie. 101st ed de Gruyter, Berlin, copyright
12. De Vette, [redacted] 2001 Hydrolysis as a function of pH and identification of breakdown products. [redacted]

Section A7.2-A7.5 **Doc III A Read Across to Boric Acid**

Annex Point Section A7.2-A10

[redacted]

13. Maeda M, Raman Spectra of polyborate ions in aqueous solution. J Inorg. Nucl. Chem., Vol 41, pp 1217-1220 (1979)

14. [redacted] 2004 Rate of Dissolution Study of [redacted]

Section A7.2-A7.5 Doc III A Read Across to Boric Acid

Annex Point Section A7.2-A10

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	25 March 2005
Materials and Methods	Not applicable.
Results and discussion	In aqueous solutions at physiological and acidic pH, simple borates such as disodium tetraborate decahydrate ($Na_2B_4O_7 \bullet 10H_2O$; borax), disodium tetraborate pentahydrate ($Na_2B_4O_7 \bullet 5H_2O$; borax pentahydrate), boric oxide (B_2O_3) and disodium octaborate tetrahydrate ($Na_2B_8O_{13} \bullet 4H_2O$) will exist as undissociated boric acid. Therefore, the toxicokinetics and toxicological effects of boric acid, disodium tetraborate decahydrate, boric oxide (B2O3) and disodium octaborate tetrahydrate are likely to be similar on a boron equivalents basis. Therefore, it is justified to draw conclusions on boric oxide on the basis of data on studies on toxicokinetics and toxicity of other simple borates such as boric acid and the disodium tetraborates.
Conclusion	It is justified to draw conclusions on boric oxide on the basis of data on studies on toxicokinetics and toxicity of other simple borates such as boric acid and the disodium tetraborates. The effects assessment of borates, as described above by the applicant, is not adopted.
Reliability	
Acceptability	
Remarks	
	COMMENTS FROM ... *(specify)*
Date	*Give date of comments submitted*
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Section A8
Annex Point IIA8

26 MEASURES TO BE ADOPTED TO PROTECT MAN, ANIMALS AND THE ENVIRONMENT

Section B8

Subsection		Official use only
8.1 Handling and Storage	No special handling precautions are required, but dry indoor storage is recommended. Good housekeeping procedures should be followed to minimise dust generation and accumulation. No specific firefighting measures are required since boric acid in not flammable, combustible or explosive. The product is itself a flame retardant.	X
8.2 Combustion Products	Fused borate glass and water	
8.3 Emergency measures in case of accident	**Inhalation:** If symptoms such as nose or throat irritation are observed, remove to fresh air. **In case of contact with Eyes:** Rinse immediately with plenty of clean water or sterile saline solution for at least 15 minutes. If appropriate, remove contact lenses after 5 minutes rinsing. If symptoms persist, seek medical attention. **Skin Contact:** No treatment necessary because non-irritating. **Ingestion:** Swallowing small quantities (one teaspoon) will cause no harm to healthy adults. If larger amounts are swallowed, give two glasses of water to drink and seek medical attention. Avoid creation of dust. Use vacuum cleaners wherever possible.	
8.4 Decontamination	a) **Air:** Borates are non-volatile. As a dust borates rapidly settle from the atmosphere. b) **Water:** Borates are naturally occurring minerals and are present in surface and underground waters. Borates are rapidly dissolved in water and will disperse with dilution. Removal at low concentrations is unnecessary. Where water containing high levels of borates can be captured precipitation with lime can be used to reduce boron levels to the 100ppm range. Treatments with boron specific ion exchange resins and activated carbon are also possible. c) **Soil:** Borates are naturally found in rocks and soil and are an essential micronutrient for all plant growth. Contaminated soil can be leached with water or acid to reduce boron levels.	
8.5 Waste Management	Small quantities can usually be disposed to landfill sites. No special disposal treatment is required, but local authorities should be consulted about any specific local requirements. Tonnage quantities of products are not considered appropriate for landfills. Such products should, if possible, be used for an appropriate application.	

8.6 Unintended side effects	Borates are essential micronutrients for all plant life but at high levels they are phytotoxic.

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	27-May-08
Materials and methods	Section 8.1 Information on container material is given in Doc IIIA3.17
Conclusion	Adapted in doc IIC and Doc I
Reliability	-
Acceptability	acceptable
Remarks	-
	COMMENTS FROM OTHER MEMBER STATE *(specify)*
Date	*Give date of comments submitted*
Evaluation of applicant's justification	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Remarks	