Function	Field of use envisaged	Test substance	Test organism(s)	Test method	Test conditions	Test results: effects, mode of action, resistance	Reference*)
				respectively).		therefore considered as not reliable and results are not used in efficacy assessment.	
fungicide	PT-08	Boric acid	Several species *Gloeophylum abietineum* (Fr.) Karst 13851 highest boron tolerancy Other relevant species: *Gloeophyllum trabeum* (Fr.) Murr. 7520, *Serpula lacrymans* S.F. Gray 16508, *Coniophora olivacea* (Fr.) Karst, *Poria sp.* 2422, *Poria subcrassa* Rodway & Cleland 11040, *Trametes versicolor* (L.:Fr.) Pil. syn *Coriolus versicolor*.	Pinus radiata D Don sapwood and Eucalyptus regnans F. Muell heartwood treated by vacuum impregnation and diffusion. Blocks were air dried for 6 weeks (ageing). No leaching. Soil block test, mass loss in weight. Blocks were placed on a plastic mesh square, but not in contact with the feeder strips which were placed on the soil surface. Agar block test resulted in higher toxic threshold levels, results are considered not reliable because of larger concentration intervals. Results from agar block tests are not used for derivation of toxic threshold levels. Toxic threshold levels for pine and eucalyptus were similar for *Poria sp.* 2422, *Poria subcrassa* Rodway & Cleland 11040. The other relevant species were only tested on pine	Mean retentions in blocks of 0 and 0.5-2.0 kg/m^3 BAE for soil block test or 0 and 0.1-10.0 kg/m^3 BAE for agar block test. Blocks exposed for 12 weeks at 25°C.	Highest boron tolerancy for *Gloeophylum abietineum* (Fr.) Karst 13851 on pine (Pinus radiata) sapwood: Toxic threshold concentration determined as 0.4% w/w BAE (2.0 kg/m^3 BAE) in the soil block test. Conversion factor kg/m^3 → % w/w multiply by 0.2.	Cookson & Pham 1995
insecticide	PT-08	Sodium metaborate (assumed $NaBO_2$)	Egg larvae and larger larvae of *Lyctus brunneus* Stephens	Starch-free and starch-containing sapwood of Eucalyptus regnans or Eucalyptus obliqua treated by immersion in boiling solution. Blocks were air dried (period not stated). No ageing or leaching. Larval survival and mass loss in weight of wood.	Test concentrations 0.4-2.3 lb/ft^3 for larger larvae and 0.04-2.8 lb/ft^3 for beetle test (egg larvae). Duration of the test not stated, but at least 9 weeks. Large larvae hardly eat from the wood and pupate almost	Highest boron tolerancy for Lyctus brunneus on starch-free Eucalyptus obliqua: Toxic threshold concentrations for egg larvae determined as 0.30% w/w BAE (1.5 kg/m^3 BAE or 0.1 lb/ft^3 sodium metaborate) assuming wood density is 500 kg/m^3. Not effective against larger larvae	Cummins & Wilson 1936

Function	Field of use envisaged	Test substance	Test organism(s)	Test method	Test conditions	Test results: effects, mode of action, resistance	Reference*)
				Wood-boring in starch free wood is generally lower than in starch containing wood. Because of the reduced amount of toxic material passed through the digestive tract, toxic threshold levels for starch free wood is higher. Experiments with larger larvae were only carried out on Eucalyptus obliqua. Results from egg larvae on Eucalyptus obliqua and Eucalyptus regnans were similar.	immediately. Therefore tests were carried out with very small, small and medium sized larvae which have sufficient gluttony to ensure proper assessment of efficacy.	at highest level tested: 6.9% w/w BAE (35 kg/m^3 BAE, 2.3 lb/ft^3 sodium metaborate). Conversion factor lb/ft^3 → kg/m3 multiply by 15.99. Conversion factor kg/m^3 → % w/w multiply by 0.2. Conversion factor metaborate (MW 657996) → BAE multiply by 0.94.	
insecticide	PT-08	boric acid or borax or boric acid plus borax	Egg larvae of *Lyctus brunneus* Stephens	Starch containing yellow carrabeen (Sloanea woolsii). Wood treatment not stated. Visual damage to wood. Experimental conditions not stated.	Test concentrations 0.01-0.24 lb/ft^3 BAE for boric acid or 0.04-0.3 lb/ft^3 for borax. Duration of the test not stated.	Boron tolerancy for Lyctus brunneus on yellow carrabeen (Sloanea woolsii) For boric acid, toxic threshold concentration is 0.16% w/w BAE (0.80 kg/m^3 BAE, 0.05 lb/ft^3 BAE). For borax, toxic threshold concentration is 0.08% w/w (0.42 kg/m^3 BAE, 0.04 lb/ft^3 as borax). Toxicity of boric acid, borax or mixtures of borax and boric acid, is considered equal. Because of differences in concentration ranges, final endpoints are slightly different. Conversion factor lb/ft^3 → kg/m3 multiply by 15.99. Conversion factor kg/m^3 → % w/w multiply by 0.2. Conversion factor borax → BAE multiply by 0.65.	Cummins, 1939
insecticide	PT-08	Boric acid	Egg larvae of *Anobium punctatum*	Pinus radiata D. Don sapwood and Podocarpus dacrydoides sapwood;	Test concentrations 0.004-3.25 % (w/w) in wood. Duration of the test	Highest boron tolerancy for *Anobium punctatum* on pine (Pinus	Spiller 1948

Function	Field of use envisaged	Test substance	Test organism(s)	Test method	Test conditions	Test results: effects, mode of action, resistance	Reference*)
			de Geer	wood treatment not stated. Larval survival. Efficacy results for Pinus radiata D. Don sapwood and Podocarpus dacrydoides sapwood are similar.	not stated.	radiata) and kabikatea (Podocarpus Dacrydoides) sapwood: Toxic threshold concentrations determined as 0.022 – 0.043% (w/w) BAE (0.11 – 0.21 kg/m^3 BAE) assuming wood density is 500 kg/m^3. Conversion factor % w/w → kg/m^3 multiply by 5.	
insecticide	PT-08	Borax or DOT	Egg larvae and larger larvae of two species *Anobium punctatum* de Geer highest boron tolerancy Other relevant species: *Hylotrupes bajulus*	Corsican pine sapwood treated by vacuum impregnation. Details on wood treatment not stated. BS 3651 and BS 3652 newly hatched (egg larvae) or larger larvae introduced into holes. Larval survival and mass loss in weight of wood.	Borax test concentrations 0.068-3.4 kg/m3 or 0.013-0.70 % w/w (0.008-0.45 % w/w BAE) for egg larvae and larger larvae (1-3 mg). DOT test concentrations 0.077-7.7 kg/m3 or 0.016-1.6 % w/w (0.019-1.9% w/w BAE). for egg larvae and larger larvae (1.5-5.5 mg). Duration of the test 6-18 months.	Highest boron tolerancy for *Anobium punctatum* on pine sapwood. For borax the toxic threshold concentrations determined as 0.45% w/w BAE (2.2 kg/m^3 BAE, 3.4 kg/m^3 borax) for larger larvae. For DOT the toxic threshold concentrations determined as 1.9% w/w BAE (9.5 kg/m^3 BAE, 7.7 kg/m^3 DOT) for larger larvae. For DOT the toxic threshold concentrations determined as 0.09% w/w BAE (0.45 kg/m^3 BAE, 0.39 kg/m^3 DOT) for egg larvae. Toxicity of boric acid and DOT, is considered equal. Because the test conditions for DOT differ from test conditions for boric acid (length of larvae, test duration), final endpoints are different Conversion factor % w/w → kg/m^3 multiply by 5.	Taylor 1967
termiticide	PT-08	DOT	*Reticulitermes flavipes*	Slash pine (Pinus elliottii Engelm.	DOT loadings equivalent to 0.37-	Boron tolerancy for *Reticulitermes*	Mauldin and

Function	Field of use envisaged	Test substance	Test organism(s)	Test method	Test conditions	Test results: effects, mode of action, resistance	Reference*)
				variety elliottii) treated by vacuum/pressure impregnation. Air dried for 24 hrs. No ageing or leaching. Laboratory test with no choice (only treated wood) or choice (both treated and untreated wood available). Subterranean termite attack in a field test in Gulfport, MS, USA (non-leaching conditions and protected from rain). Termite mortality and mass loss of weight in wood.	2.9 kg/m^3 BAE or 0.10-0.54% (w/w) BAE (by analytical determination). Duration of the laboratory test 4 weeks at 25-28 °C. Duration of the field test 18 months.	*flavipes* on pine (Pinus elliottii). For DOT, toxic threshold concentrations determined as 0.30% BAE (1.5 kg/m^3 BAE) in the choice laboratory test. Field tests in USA are considered not relevant for EU. No conversion factors used, actual values from study report.	Kard, 1996
fungicide; insecticide	PT-08	Boric acid or borax or sodium borate (assumed to be borax)	Review article on decay fungi (e.g. *Coniophora cerebella* syn *Coniophora puteana*, *Lenzites trabea* syn *Gloeophyllum trabeum*, *Poria vaporaria* syn *Poria placenta*, *Polystictus versicolor* syn *Coriolus versicolor*, *Merulius lacrymans* syn *Serpula lacrymans*) and wood boring insects (egg larvae and larger larvae of *Anobium punctatum*, *Hylotrupes bajules*, *Lyctus brunneus*).	Not stated	Not stated	For boric acid highest toxic threshold levels for decay fungi were determined as 0.12%-0.40% w/w BAE (0.6-2.0 kg/m^3 BAE). For egg larvae, highest toxic threshold levels were 0.04%-0.12% w/w BAE (0.2-0.6 kg/m^3 BAE). For borax (or sodium borate) highest toxic threshold levels for decay fungi were determined as 0.065%-0.38% w/w BAE (0.32-1.9 kg/m^3 BAE, 0.5-2.9 kg/m^3 borax) Toxicity of boric acid and borax, is considered equal. Because the test conditions for borax differ from test conditions for boric acid, final endpoints are slightly different Conversion factor kg/m^3 → % w/w multiply by 0.2. Conversion factor % w/w → kg/m^3 multiply by 5.	Findlay, 1959

Function	Field of use envisaged	Test substance	Test organism(s)	Test method	Test conditions	Test results: effects, mode of action, resistance	Reference*)
						Conversion factor borax → BAE multiply by 0.65.	
fungicide; insecticide	PT-08	Boric acid or borax	Review article on decay fungi (e.g. *Coniophora cerebella* syn *Coniophora puteana*, *Lenzites trabea* syn *Gloeophyllum trabeum*, *Poria vaporaria* syn *Poria placenta*, ,*Merulius lacrymans* syn *Serpula lacrymans*) and wood boring insects (egg larvae and larger larvae of *Anobium punctatum*, *Hylotrupes bajules*, *Lyctus brunneus*).	Not stated	Not stated	For boric acid highest toxic threshold levels for decay fungi were determined as 0.072%-0.28 % w/w BAE (0.36-1.4 kg/m^3 BAE) if American test methods are omitted. Highest toxic threshold levels for egg larvae were 0.03%-0.12% w/w BAE (0.15-0.6 kg/m^3 BAE) after 12 weeks. Highest toxic threshold levels for larger larvae were 0.072%-1.5% w/w BAE (0.36-7.4 kg/m^3 BAE) after 16-24 weeks. For borax toxic highest threshold levels for decay fungi were determined as 0.065%-0.21% w/w BAE (0.32-1.0 kg/m^3 BAE, 0.5-1.6 kg/m^3 borax) if American test methods are omitted. Highest toxic threshold levels for egg larvae were 0.023%-0.084% w/w BAE (0.12-0.42 kg/m^3 BAE, 0.18-0.65 kg/m^3 borax) after 12 weeks. Highest toxic threshold levels for larger larvae were 0.091%-0.34% w/w BAE (0.46->1.7 kg/m^3 BAE, 0.7->2.6 kg/m^3 borax) after 24 weeks. Toxicity of boric acid and borax, is considered equal. Because the test conditions for borax differ from test conditions for boric acid, final endpoints are slightly different Conversion factor kg/m^3 → % w/w multiply by 0.2. Conversion factor % w/w → kg/m^3 multiply by 5. Conversion factor borax → BAE	Becker, 1959

Function	Field of use envisaged	Test substance	Test organism(s)	Test method	Test conditions	Test results: effects, mode of action, resistance	Reference*)
						multiply by 0.65.	
fungicide; insecticide	PT-08	Boric acid or borax or DOT (=TIMBOR = Polybor) or sodium metaborate	Review article on decay fungi (*Coniophora puteana, Gloeophyllum trabeum, Poria placenta, Coriolus versicolor, Serpula lacrymans*) and wood boring insects (egg larvae and larger larvae of *Anobium punctatum, Hylotrupes bajules, Lyctus brunneus*).	Not stated.	Not stated	Highest toxic threshold concentrations determined as 0.016%-0.42% w/w BAE (0.08-2.1 kg/m^3 BAE) for decay fungi (if ASTM values are deleted) and 0.008%-0.2% w/w BAE (0.04-1.0 kg/m^3 BAE) for egg larvae and 0.008%-1.8% w/w BAE (0.04-9.2 kg/m^3 BAE) for larger larvae assuming wood density is 500 kg/m^3. Conversion factor kg/m^3 → % w/w multiply by 0.2.	Bravery & Carey 1983

Section A6.1.1

Annex Point IIA6.1

Acute Toxicity

Section A6.1.1; Oral Route; Rat; LD_{50}

Official use only

6 REFERENCE

6.1	**Reference**	[redacted] Acute Oral Toxicity in Rats; Median Lethal Dosage of [redacted] 1988. [redacted]
6.2	**Data protection**	Yes
6.2.1	Data owner	[redacted]
6.2.2	Companies with letter of access	**Curent Access** [redacted]
6.2.3	Criteria for data protection	Data on new a.s. for first entry to Annex I/IA

7 GUIDELINES AND QUALITY ASSURANCE

7.1	**Guideline study**	Yes FIRFA (40 CFR) and meets OECD 410 guideline
7.2	**GLP**	Yes
7.3	**Deviations**	Yes. The report lacks detail. However, since the data is in line with other data on sodium borates, further testing is not warranted in the interests of animal welfare and protecting laboratory animals.

8 MATERIALS AND METHODS

8.1	**Test material**	As given in section 2
8.1.1	Lot/Batch number	#8E25H
8.1.2	Specification	As given in section 2
8.1.2.1	**Description**	White powder
8.1.2.2	**Purity**	>98%
8.1.2.3	**Stability**	Stable

Section A6.1.1 Acute Toxicity

Annex Point IIA6.1 **Section A6.1.1; Oral Route; Rat; LD_{50}**

8.2	**Test Animals**	Non-entry field
8.2.1	Species	Rat
8.2.2	Strain	Sprague Dawley
8.2.3	Source	Approved USDA supplier
8.2.4	Sex	Male and Female
8.2.5	Age/weight at study initiation	Males 262 –371g; Females 226 –275 g
8.2.6	Number of animals per group	5
8.2.7	Control animals	No
8.3	**Administration/ Exposure**	Oral
8.3.1	Post exposure period	14 days
		Oral
8.3.2	Type	Gavage
8.3.3	Concentration	Gavage 1.25; 2.0; 3.15; 5.0 g/kg bw
8.3.4	Vehicle	Distilled water
8.3.5	Concentration in vehicle	50% w/v
8.3.6	Total volume applied	
8.3.7	Controls	
8.4	**Examinations**	Clinical observations and Pathology
8.5	**Method of determination of LD_{50}**	Litchfield and Wilcoxon
8.6	**Further remarks**	

Section A6.1.1 Acute Toxicity

Annex Point IIA6.1 **Section A6.1.1; Oral Route; Rat; LD_{50}**

Section A6.1.1 **Acute Toxicity**

Annex Point IIA6.1 **Section A6.1.1; Oral Route; Rat; LD_{50}**

9 RESULTS AND DISCUSSION

9.1	**Clinical signs**	See Table A6_1-1.
9.2	**Pathology**	Autopsies on those animals that died indicated at the top dose (5.0 g/kg), darkened, reddened pale and/or mottled lungs; congested, mottled or pale kidneys, mottled and/or pale liver and spleens; pale intestines filled with clear yellow liquid; pale pancreas and green watery fluid in stomach and partially distended stomach. Similar, but less severe effects were observed at 3.15 and again less severe at 2.0 g/kg. No gross pathological changes were observed in the surviving animals
9.3	**Other**	
9.4	**LD_{50}**	LD_{50} males + females =2550 mg/kg bw

10 APPLICANT'S SUMMARY AND CONCLUSION

10.1	**Materials and methods**	LD_{50} study carried out to FIRFA (40 CFR) and meets OECD 410 guidelines.
10.2	**Results and discussion**	All of the animals died at the top dose of 5.0 g/kg; with 4/5 and 2/5 males dying at 3.15 and 2.0 g/kg, but no females dying at these doses. No gross pathological changes were observed in the surviving animals. Clinical signs included mild to extreme depression; faecal stains; loose mucoid faeces; urine stains; piloerection; dried brown stains around eyes; dirty hair coats; laboured breathing; comatose; hunched posture; body tremors; dried red material around muzzles or on head which became less severe with decreasing dose. Pathological changes in the animals that died included darkened, reddened pale and/or mottled lungs; congested, mottled or pale kidneys, mottled and/or pale liver and spleens; pale intestines filled with clear yellow liquid; pale pancreas and green watery fluid in stomach and partially distended stomach which reduced in severity with reducing dose
		LD_{50} 2550 g/kg bw
10.3	**Conclusion**	LD_{50} 2550 g/kg bw males and females
10.3.1	Reliability	*2*
10.3.2	Deficiencies	Although the report is lacking in detail the data is comparable with other data on sodium borates, and therefore further testing is not warranted in the interests of animal welfare and protecting laboratory animals.

Section A6.1.1 Acute Toxicity

Annex Point IIA6.1

Section A6.1.1; Oral Route; Rat; LD_{50}

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	22 February 2005
Materials and Methods	The applicant states that the study meets OECD guideline 410. Obviously, they mean OECD 401. Otherwise, the version of the applicant is acceptable.
Results and discussion	The applicant incorrectly reports that there are no deaths in the females of the 2.0 and 3.15 g/kg bw groups. Actually, in both groups 2 out of 5 females died at the first day after administration of the test substance.
Conclusion	The version of the applicant is adopted.
Reliability	2
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 A6_1-1. Table for Acute Toxicity

Dose g/kg	*Number of dead / number of investigated*	*Time of death (range)*	*Observations*
Males			
5.0	5/5	1-2 days	Mild to extreme depression; faecal stains; loose mucoid faeces; urine stains; piloerection; eye squinting; scruffy hair coats
3.15	4/4	1-3 days	Mild to extreme depression; faecal stains; loose mucoid faeces; urine stains; piloerection; dried brown stains around eyes; dirty hair coats; laboured breathing; comatose; hunched posture; body tremors; dried red material around muzzles or on head
2.0	2/5	1 day	Mild to severe depression; faecal stains; loose mucoid faeces; urine stains; piloerection; dirty hair coats; eye squinting
1.25	0		Mild depression; faecal stains; loose mucoid faeces
Females			Mild to extreme depression; faecal stains; loose mucoid faeces; urine stains; piloerection; eye squinting; scruffy hair coats
5.0	5/5	0 days	Mild to extreme depression; faecal stains; loose mucoid faeces; urine stains; piloerection; dried brown stains around eyes; dirty hair coats; laboured breathing; comatose; hunched posture; body tremors; dried red material around muzzles or on head
3.15	0		Mild to severe depression; faecal stains; loose mucoid faeces; urine stains; piloerection; dirty hair coats; eye squinting
2.0	0		Mild depression; faecal stains; loose mucoid faeces
1.25	0		
LD_{50} value Combined	2.55 g/kg bw (95% CL 2.1 - 3.1)		

Section A6.1.2 Acute Toxicity

Annex Point IIA6.1

Section A6.1.2; Dermal Route; Rat; LD_{50} Limit Test

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11 REFERENCE

11.1 Reference

[redacted] " Acute Dermal Toxicity in Rabbits of Disodium Octaborate Tetrahydrate", [redacted]

11.2 Data protection Yes

11.2.1 Data owner [redacted]

11.2.2 Companies with letter of access **Curent Access** [redacted]

11.2.3 Criteria for data protection *Data on new a.s. for first entry to Annex I/IA*

12 GUIDELINES AND QUALITY ASSURANCE

12.1 Guideline study Yes

FIFRA (40 CFR 158, 162); TSCA (40 CFR 798) and meets principles of OECD 402

12.2 GLP Yes

12.3 Deviations Yes

The protocol meets the requirements of OECD 402, but the report is lacking in detail. Since the data compatible with other data on sodium borates, and data is available to indicate the absorption through humans skin is negligible > 0.5% then further testing is not warranted in the interests of animal welfare and protecting laboratory animals.

13 MATERIALS AND METHODS

13.1 Test material As given in section 2

13.1.1 Lot/Batch number 8G1D

13.1.2 Specification As given in section 2

13.1.2.1 Description White powder

13.1.2.2 Purity >98%

Section A6.1.2 Acute Toxicity

Annex Point IIA6.1 **Section A6.1.2; Dermal Route; Rat; LD_{50} Limit Test**

13.1.2.3	**Stability**	Stable
13.2	**Test Animals**	Non-entry field
13.2.1	Species	Rabbit
13.2.2	Strain	New Zealand White
13.2.3	Source	Clerco Research Farm
13.2.4	Sex	Male and Female
13.2.5	Age/weight at study initiation	Males: 2720 -3379 grams; Females: 2699 –3057 grams
13.2.6	Number of animals per group	5 male; 5 female
13.2.7	Control animals	No
13.3	**Administration/ Exposure**	Dermal
13.3.1	Post exposure period	14 days
		Dermal
13.3.2	Area covered	Not specified but implies > 10 % of body surface The skin of all of the animals was abraded longitudinally every 2-3 cm , deep enough to penetrate the stratum corneum, but not cause bleeding.
13.3.3	Occlusion	Semi occlusive
13.3.4	Vehicle	Physiological saline
13.3.5	Concentration in vehicle	Substance moistened saline
13.3.6	Total volume applied	Dosage to 2 g/kg bw
13.3.7	Duration of exposure	24 h
13.3.8	Removal of test substance	Moist towel
13.3.9	Controls	None
13.4	**Examinations**	Clinical observations, necropsy, histopathology or other
13.5	**Method of determination of LD_{50}**	Not relevant – Limit test
13.6	**Further remarks**	Sample remained on binders indicating incomplete absorption of sample.

Section A6.1.2 Acute Toxicity

Annex Point IIA6.1

Section A6.1.2; Dermal Route; Rat; LD_{50} Limit Test

14 RESULTS AND DISCUSSION

14.1 Clinical signs	No clinical changes were observed
14.2 Pathology	No gross necropsy findings were observed. .
14.3 Other	
14.4 LD_{50}	LD_{50} > 2000 mg/kg bw No lethal effect at limit dose

15 APPLICANT'S SUMMARY AND CONCLUSION

15.1 Materials and methods	FIFRA (40 CFR 158, 162); TSCA (40 CFR 798) and meets principles of OECD 402 Limit test in which rabbits were treated with 2g/kg bw boric acid.
15.2 Results and discussion	LD_{50} > 2000 mg/kg bw indicating no acute dermal toxicity. No clinical or pathological findings were observed
15.3 Conclusion	LD_{50} > 2000 mg/kg bw
15.3.1 Reliability	2
15.3.2 Deficiencies	The protocol meets the requirements of OECD 402, but the report is lacking in detail. Since the data compatible with other data on sodium borates, and data is available to indicate the absorption through humans skin is negligible > 0.5% then further testing is not warranted in the interests of animal welfare and protecting laboratory animals.

Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	22 February 2005
Materials and Methods	The applicant states that the skin of the animals is abraded. However, this is not described in the study protocol. The description of the protocol suggests that the test material is applied under occlusion (sleeve of rubber dental dam).
Results and discussion	The version of the applicant is adopted.
Conclusion	The version of the applicant is adopted.
Reliability	2
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	

Section A6.1.3 Acute Toxicity

Annex Point IIA6.1 **Section A6.1.3; Inhalation Route; Rat; LC_{50} Limit Test**

Official use only

16 REFERENCE

16.1	**Reference**	[redacted] 1994, Acute inhalation toxicity limit test on disodium octaborate tetrahydrate, [redacted]
16.2	**Data protection**	Yes
16.2.1	Data owner	[redacted]
16.2.2	Companies with letter of access	**Curent Access** [redacted]
16.2.3	Criteria for data protection	Data on new a.s. for first entry to Annex I/IA

17 GUIDELINES AND QUALITY ASSURANCE

17.1	**Guideline study**	Yes OECD Guide-line 403 "Acute Inhalation Toxicity" (USEPA.FIFRA 40 CFR Part 160.
17.2	**GLP**	Yes
17.3	**Deviations**	Yes The report lacks detail. Since the data is in line with other data on sodium borates, further testing is not warrented in the interests of animal welfare and protecting laboratory animals.

18 MATERIALS AND METHODS

18.1	**Test material**	As given in section 2
18.1.1	Lot/Batch number	Lot #4H22
18.1.2	Specification	As given in section 2
18.1.2.1	**Description**	White powder
18.1.2.2	**Purity**	>98%
18.1.2.3	**Stability**	Stable

Section A6.1.3 Acute Toxicity

Annex Point IIA6.1

Section A6.1.3; Inhalation Route; Rat; LC_{50} Limit Test

18.2	**Test Animals**		
18.2.1	Species	Rat	
18.2.2	Strain	Sprague-Dawley	
18.2.3	Source	Hilltop Lab Animals, Scottdale, PA	
18.2.4	Sex		
18.2.5	Age/weight at study initiation	Young adults: Males 224-260 grams; Females 207 -234 grams	
18.2.6	Number of animals per group	5 male; 5 female	
18.2.7	Control animals	No	
18.3	**Administration/ Exposure**	Inhalation	
18.3.1	Postexposure period	14 days	
		Inhalation	
18.3.2	Concentrations	Nominal concentration	2000 mg/m³
		Analytical concentration	2010 ±140 mg/m³
18.3.3	Particle size	Not an aerosol study	
18.3.4	Type or preparation of particles	Sample was ground in a ball mill for 24 hours MMAD 2.8 µm ± GSD 2.15µm Top dose ~ 2 mg/l was the highest that was obtainable under the conditions of the test	
18.3.5	Type of exposure	Whole body	
18.3.6	Vehicle	Not relevant	
18.3.7	Concentration in vehicle	Not relevant	
18.3.8	Duration of exposure	4 h	
18.4	**Examinations**	Clinical observations, Pathology	
18.5	**Method of determination of LC_{50}**	Not relevant – Limit Test	
18.6	**Further remarks**		
18.6.1	Controls	None	

Section A6.1.3 Acute Toxicity

Annex Point IIA6.1

Section A6.1.3; Inhalation Route; Rat; LC_{50} Limit Test

		19 RESULTS AND DISCUSSION
19.1	**Clinical signs**	Animal observations were limited due to the accumulation of test material on the walls of the exposure chamber. During exposure, ocular discharge, hypoactivity and haunched posture were noted. All animals recovered after removal from chamber.
19.2	**Pathology**	No specific findings observed except red lung discolouration consistent with CO2 inhalation (caused by euthanasia technique). All tissue sand organs were normal.
19.3	**Other**	
19.4	**LC_{50}**	LC_{50} > 2.01.mg/L (2010 /m^3) No lethal effect at limit dose
		20 APPLICANT'S SUMMARY AND CONCLUSION
20.1	**Materials and methods**	Acute inhalation toxicity limit on boric acid. The Sample was ground in a ball mill for 24 hours to give a MMAD 2.8 µm ± GSD 2.15 µm Top dose ~ 2 mg/l was the highest that was obtainable under the conditions of the test
20.2	**Results and discussion**	LC_{50} > 2.01.mg/L (2.01g/m^3). Animal observations were limited due to the accumulation of test material on the walls of the exposure chamber.
20.3	**Conclusion**	LC_{50} > 2.01.mg/L (2.01g/m^3).
20.3.1	Reliability	1
20.3.2	Deficiencies	No

Section A6.1.3 Acute Toxicity

Annex Point IIA6.1

Section A6.1.3; Inhalation Route; Rat; LC_{50} Limit Test

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	22 February 2005
Materials and Methods	In the study report a nominal concentration of 9.06 mg/L is reported. Otherwise the version of the applicant is accepted.
Results and discussion	The version of the applicant is adopted.
Conclusion	The version of the applicant is adopted.
Reliability	2
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	

Section 6.1.4 Acute Eye Irritation

Annex Point IIA6.1.4

Section A6.1.4Rabbit Eye Irritation Study

Official use only

	1 REFERENCE	
1.1	**Reference**	[redacted] "Primary Eye Irritation in Rabbits of Disodium Octaborate Tetrahydrate", [redacted]
		Electronic File
1.2	**Data protection**	Yes
1.2.1	Data owner	[redacted]
1.2.2	Companies with letter of access	**Curent Access** [redacted]
1.2.3	Criteria for data protection	Data on new a.s. for first entry to Annex I/IA
	2 GUIDELINES AND QUALITY ASSURANCE	
2.1	**Guideline study**	Yes
		FIFRA (40 CFR 158, 162); TSCA (40 CFR 798). Although not carried out to an OECD protocol, the study has been carried out to an US EPA acceptable protocol and meets the requirements of OECD 405, although the report lacks detail. Since the data is in line with other data on sodium borates, further testing is not warranted in the interests of animal welfare and protecting laboratory animals.
2.2	**GLP**	Yes
2.3	**Deviations**	See above
	3 MATERIALS AND METHODS	
3.1	**Test material**	As given in section 2
3.1.1	Lot/Batch number	8G1D
3.1.2	Specification	As given in section 2
3.1.2.1	**Description**	White powder
3.1.2.2	**Purity**	>98%
3.1.2.3	**Stability**	Stable

Section 6.1.4 Acute Eye Irritation

Annex Point IIA6.1.4 Section A6.1.4Rabbit Eye Irritation Study

3.2	**Test Animals**	Non-entry field
3.2.1	Species	Rabbit
3.2.2	Strain	New Zealand White
3.2.3	Source	Clerco Research farm
3.2.4	Sex	Male and Female
3.2.5	Age/weight at study initiation	Not reported
3.2.6	Number of animals per group	3 male; 3 female
3.2.7	Control animals	No
3.3	**Administration/ Exposure**	
3.3.1	Preparation of test substance	*Test substance was used as delivered*
3.3.2	Amount of active substance instilled	0.1 ml volume – weight 0.053 g in accordance with the guidelines
3.3.3	Exposure period	24h followed by rinsing with physiological saline
3.3.4	Post exposure period	7 days
3.4	**Examinations**	
3.4.1	Ophthalmoscopic examination	No
3.4.1.1	**Scoring system**	Scoring in report according to Draize and US guidelines, but scoring reported here according to EU 67/548/EEC
3.4.1.2	**Examination time points**	60min, 24h, 48h, 72h, 4d, 7d. 10 d
3.4.2	Other investigations	
3.5	**Further remarks**	
		4 RESULTS AND DISCUSSION
4.1	**Clinical signs**	Table A6_1_4E-1.
4.2	**Average score**	Non-entry field
4.2.1	Cornea	0.00
4.2.2	Iris	0.11
4.2.3	Conjunctiva	Non-entry field
4.2.3.1	**Redness**	0.94
4.2.3.2	**Chemosis**	0.89

Section 6.1.4 Acute Eye Irritation

Annex Point IIA6.1.4

Section A6.1.4Rabbit Eye Irritation Study

4.3	**Reversibility**	Yes Chemosis and Redness reversed by ten days
4.4	**Other**	
4.5	**Overall result**	Not classifiable in the EU under Directive 67/548/EEC. In the US, The material is classified in Toxicity Category II (40 CFR 156, Proposed) by ocular administration (Corneal involvement or irritation clearing in 8-21 days). Non Irritant under US CPS (16 CFR 15000.42)
	5 APPLICANT'S SUMMARY AND CONCLUSION	
5.1	**Materials and methods**	Eye irritation study in New Zealand white rabbits to FIFRA (40 CFR 158, 162); TSCA (40 CFR 798). 0.1 ml, weight 0.053g substance was instilled in the eyes for 24 hours followed by rinsing with physiological saline
5.2	**Results and discussion**	Minor effects on the iris and effects on conjunctivae redness and Chemosis were reversed by day 10. Changes included blistered appearance to conjunctiva.
5.3	**Conclusion**	Not classifiable in the EU under directive 67/548/EEC.
5.3.1	Reliability	2
5.3.2	Deficiencies	Although not carried out to an OECD protocol, the study has been carried out to an US EPA acceptable protocol and meets the requirements of OECD 405, although the report lacks detail. Since the data is in line with another study on disodium octaborate tetrahydrate (see IUCLID database) and data on boric acid, further testing is not warranted in the interests of animal welfare and protecting laboratory animals.

Section 6.1.4 Acute Eye Irritation

Annex Point IIA6.1.4

Section A6.1.4Rabbit Eye Irritation Study

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	22 February 2005
Materials and Methods	In the study report it is described that 49 mg of DOT is instilled in the eyes of the animals.
Results and discussion	The description of the effects by the applicant is adopted.
Conclusion	The conclusion of the applicant is adopted
Reliability	2
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	

Section 6.1.4 **Acute Eye Irritation**

Annex Point IIA6.1.4 Section A6.1.4Rabbit Eye Irritation Study

Appendix

Table A6_1_4E-1. Results of eye irritation study

Use this table, if relevant effects occur.

	Cornea	Iris	Conjunctiva	
			redness	chemosis
score (average of animals investigated)	0 to 4	0 to 2	0 to 3	0 to4
60 min	0.00	1.00	1.17	2.00
24 h	0.00	0.33	1.00	1.00
48 h	0.00	0.00	1.00	1.00
72 h	0.00	0.00	0.83	0.67
Average 24h, 48h, 72h	0.00	0.11	0.94	0.89
Area effected				
Maximum average score (including area affected, max 110)				
Reversibility*		c	c	c
average time for reversion		By 48 h	By 10 days	By 10 days

Section A6.1.4
Annex Point IIA6.4

Acute Dermal Irritation
Section A6.1.4 : Rabbit Skin Irritation Study

Official use only

6 REFERENCE

6.1 Reference

[redacted] "Primary Skin Irritation in Rabbits of Disodium Octaborate Tetrahydrate", [redacted] 1989.

Electronic File

6.2 Data protection Yes

6.2.1 Data owner [redacted]

6.2.2 Companies with letter of access **Curent Access** [redacted]

6.2.3 Criteria for data protection Data on new a.s. for first entry to Annex I/IA

7 GUIDELINES AND QUALITY ASSURANCE

Section A6.1.4 Acute Dermal Irritation

Annex Point IIA6.4

Section A6.1.4 : Rabbit Skin Irritation Study

7.1	**Guideline study**	Yes FIFRA (40 CFR 158, 162) and Toxic Substances Control Act (40 CFR 798).
7.2	**GLP**	Yes.
7.3	**Deviations**	The protocol meets the requirements of OECD 404 although the report lacks detail. Since the data is in line with other data on sodium borates, further testing is not warranted in the interests of animal welfare and protecting laboratory animals
	8 MATERIALS AND METHODS	
8.1	**Test material**	As given in section 2
8.1.1	Lot/Batch number	8G1D
8.1.2	Specification	As given in section 2
8.1.2.1	**Description**	White powder
8.1.2.2	**Purity**	>98%
8.1.2.3	**Stability**	Stable
8.2	**Test Animals**	Non-entry field
8.2.1	Species	Rabbit
8.2.2	Strain	New Zealand White
8.2.3	Source	Clerco Research Farm
8.2.4	Sex	Male and Female
8.2.5	Age/weight at study initiation	Not reported
8.2.6	Number of animals per group	3 male; 3 female
8.2.7	Control animals	No
8.3	**Administration/ Exposure**	Dermal
8.3.1	Application	Non entry field
8.3.1.1	**Preparation of test substance**	0.5 grams of test substance was moistened physiological saline

Section A6.1.4 Acute Dermal Irritation

Annex Point IIA6.4

Section A6.1.4 : Rabbit Skin Irritation Study

8.3.1.2	**Test site and Preparation of Test Site**	Hair was clipped from the dorsal area of each rabbit and one area on each rabbit treated with substance
8.3.2	Occlusion	Occlusive
8.3.3	Vehicle	Physiological saline
8.3.4	Concentration in vehicle	
8.3.5	Total volume applied	0.5 gram test substance
8.3.6	Removal of test substance	Moistened towel
8.3.7	Duration of exposure	4 h
8.3.8	Post exposure period	72 h
8.3.9	Controls	None
8.4	**Examinations**	
8.4.1	Clinical signs	Ye
8.4.2	Dermal examination	Yes
8.4.2.1	**Scoring system**	Draize, 1959
8.4.2.2	**Examination time points**	1, 24, 48, and 72 hours
8.4.3	Other examinations	None
8.5	**Further remarks**	
		9 RESULTS AND DISCUSSION
9.1	**Average score**	See Table A6_1-4S-1.
9.1.1	Erythema	0.22
9.1.2	Edema	0
9.2	**Reversibility**	Effects reversed by 72 hours
9.3	**Other examinations**	
9.4	**Overall result**	Non Irritant

Section A6.1.4 Acute Dermal Irritation

Annex Point IIA6.4

Section A6.1.4 : Rabbit Skin Irritation Study

10 APPLICANT'S SUMMARY AND CONCLUSION

10.1 Materials and methods	FIFRA (40 CFR 158, 162) and Toxic Substances Control Act (40 CFR 798. Hair was clipped from the dorsal area of each rabbit and each rabbit treated with 0.5 grams substance under and occlusive dressing on one area.
10.2 Results and discussion	No irritancy was observed. The protocol meets the requirements of OECD 404 although the report lacks detail. Since the data is in line with other data on sodium borates, further testing is not warranted in the interests of animal welfare and protecting laboratory animals
10.3 Conclusion	Non-irritant
10.3.1 Reliability	*2*
10.3.2 Deficiencies	

Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	22 February 2005
Materials and Methods	The version of the applicant is accepted.
Results and discussion	The version of the applicant is adopted.
Conclusion	The version of the applicant is adopted
Reliability	2
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	

Section A6.1.4 Acute Dermal Irritation

Annex Point IIA6.4

Section A6.1.4 : Rabbit Skin Irritation Study

Table A6_1-4S-1. Table for skin irritation study

Site	time	Erythema	Edema
Intact	24 h	0	0
	48 h	0.5	0
	72 h	0.17	0
Average score	24h, 72h	0.22	0

Section A6.1.5 Skin sensitisation

Annex Point IIA6.1.5

Section A6.1.5 Buehler Test

Official use only

11 REFERENCE

11.1 Reference [redacted] 1994, Dermal sensitzation test - Beuhler method on disodium octaborate tetrahydrate, [redacted]

11.2 Data protection Yes

11.2.1 Data owner [redacted]

11.2.2 Companies with letter of access **Curent Access** [redacted]

11.2.3 Criteria for data protection Data on new a.s. for first entry to Annex I/IA

12 GUIDELINES AND QUALITY ASSURANCE

12.1 Guideline study Yes

OECD Guide-line 406 "Skin Sensitization" : 40CFR 158, Guideline #81-6

12.2 GLP Yes

12.3 Deviations No

13 MATERIALS AND METHODS

Section A6.1.5 Skin sensitisation

Annex Point IIA6.1.5 Section A6.1.5 Buehler Test

13.1	**Test material**	As given in section 2
13.1.1	Lot/Batch number	Lot #4H22
13.1.2	Specification	As given in section 2
13.1.2.1	**Description**	White powder
13.1.2.2	**Purity**	>98%
13.1.2.3	**Stability**	Stable
13.1.2.4	**Preparation of test substance for application**	*a) <u>for induction:</u> used as delivered moistened with distilled water (95%w/v)* *b) <u>for challenge:</u> used as delivered moistened with distilled water (95%w/v)*
13.1.2.5	**Pre-test performed on irritant effects**	Yes
13.2	**Test Animals**	Non-entry field
13.2.1	Species	Guinea pigs
13.2.2	Strain	Hartley albino
13.2.3	Source	Davidson's Mill Farms, South Brunswick, NJ
13.2.4	Sex	
13.2.5	Age/weight at study initiation	Young adults 282 -411 grams
13.2.6	Number of animals per group	Test Group: 20 animals Naive Control: 10 animals Positive Control: 20 animals Positive Naive Control: 10 animals
13.2.7	Control animals	Yes
13.3	**Administration/ Exposure**	State study type: Non-Adjuvant
13.3.1	Induction schedule	day 0 – day –7 – day 21 *Table A6_1_5-1.*
13.3.2	Way of Induction	Topical Occlusive

Section A6.1.5 Skin sensitisation

Annex Point IIA6.1.5 Section A6.1.5 Buehler Test

13.3.3	Concentrations used for induction	0.4 g 95% w/w/boric acid moistened with distilled water to enhance skin contact
13.3.4		
13.3.5	Challenge schedule	Day 28; Table A6_1_5-1.
13.3.6	Concentrations used for challenge	95% w/w/boric acid moistened with distilled water to enhance skin contact
13.3.7	Rechallenge	No
13.3.8	Scoring schedule	24h, 48h after challenge
13.3.9	Removal of the test substance	After 6 hours test substance wiped off with water
13.3.10	Positive control substance	Dinitrochlorobenzene
13.4	**Examinations**	Non-entry field
13.4.1	Pilot study	No
13.5	**Further remarks**	

14 RESULTS AND DISCUSSION

14.1	**Results of pilot studies**	No pilot study
14.2	**Results of test**	See Table A6_1_5-2
14.2.1	24h after challenge	0/20
14.2.2	48h after challenge	0/20
14.2.3	Other findings	
14.3	**Overall result**	Non -sensitiser

15 APPLICANT'S SUMMARY AND CONCLUSION

15.1	**Materials and methods**	OECD Guide-line 406 "Skin Sensitisation" method (Buehler test) using 95% w/w disodium octaborate decahydrate moistened with distilled water to enhance skin contact
15.2	**Results and discussion**	Very faint erythema (0.5) was noted at three test sites 24 hours after first induction dose. No other adverse effect observed
15.3	**Conclusion**	Non-sensitiser
15.3.1	Reliability	1
15.3.2	Deficiencies	No

Section A6.1.5 Skin sensitisation

Annex Point IIA6.1.5

Section A6.1.5 Buehler Test

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	22 February 2005
Materials and Methods	The version of the applicant is accepted.
Results and discussion	The version of the applicant is adopted.
Conclusion	The version of the applicant is adopted.
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	

Section A6.1.5 Skin sensitisation

Annex Point IIA6.1.5 Section A6.1.5 Buehler Test

Table A6_1_5-1. Detailed information including induction/challenge/scoring schedule for skin sensitisation test

Treatments	Buehler test	Observations/Remarks *give information on irritation effects*
	day of treatment	
Induction 1	day 0	Very faint erythema (0.5) was noted at three test sites 24 hours after first induction dose. No other adverse effect observed
Induction 2	7	No irritation observed
Induction 3	14	No irritation observed
challenge	28	No irritation observed
(rechallenge)		
scoring 1	29	No irritation observed
scoring 2	30	No irritation observed

Table A6_1_5-2. Result of skin sensitisation test

	Number of animals with signs of allergic reactions / number of animals in group		
	Negative control	**Test group**	**Positive control**
scored after 24h	***0 / 10***	***0 / 20***	***10/20***
scored after 48h	***0 / 10***	***0 / 20***	***7/20***

Section A6.2 Percutaneous absorption (in vivo test)

Annex Point IIA6.2

Section A6.2 Human In vivo

Official use only

16 REFERENCE

16.1 Reference

[redacted] (1996). In Vivo Percutaneous Absorption of Boric Acid, Borax and Octaborate Tetrahydrate (DOT) in Man. [redacted]

Also published as Wester RC, Hui X, Hartway T, Maibach HI, Bell K, Schell MJ, Northington DJ, Strong P and Culver, BD. In vivo percutaneous absorption of boric acid, Borax and disodium octaborate tetrahydrate in humans compared to in vitro absorption in human skin from infinite to finite doses. Toxicol Sciences 45 42-51 (1998)

16.2 Data protection Yes

16.2.1 Data owner [redacted]

16.2.2 Companies with letter of access **Curent Access** [redacted]

16.2.3 Criteria for data protection *Data on new a.s. for first entry to Annex I/IA*

17 GUIDELINES AND QUALITY ASSURANCE

17.1 Guideline study No

Human Study specifically designed and therefore no specific guidelines available, but designed to comply with US 40 CFR, 160

17.2 GLP Yes

17.3 Deviations Not relevant

(If yes, describe deviations from test guidelines or refer to respective field numbers where these are described, e.g. "see 3.x.y")

18 MATERIALS AND METHODS

Section A6.2 Percutaneous absorption (in vivo test)

Annex Point IIA6.2 Section A6.2 Human In vivo

18.1	**Test material**	As given in section 2
18.1.1	Lot/Batch number	
18.1.2	Specification	As given in section 2
18.1.2.1	**Description**	White powder
18.1.2.2	**Purity**	>99%
18.1.2.3	**Stability**	Stable
18.1.2.4	**Radiolabelling**	^{10}B
18.2	**Test Animals**	Non-entry field
18.2.1	Species	Humans
18.2.2	Strain	
18.2.3	Source	
18.2.4	Sex	Male & female
18.2.5	Age/weight at study initiation	Age 22 -50
18.2.6	Number of animals per group	8/groups
18.2.7	Control animals	Internal controls (i.e. baseline boron measured)
18.3	**Administration/ Exposure**	Dermal both intact and abraded skin
18.3.1	Preparation of test site	Skin was washed and a 30 cm x 30 cm area marked on back
18.3.2	Concentration of test substance	5% Boric acid ; 5% Borax or 10% DOT in distilled water
18.3.3	Specific activity of test substance	
18.3.4	Volume applied	3 ml/900 cm²
18.3.5	Size of test site	900 cm²

Section A6.2 Percutaneous absorption (in vivo test)

Annex Point IIA6.2

Section A6.2 Human In vivo

18.3.6	Exposure period	After 5 days during which urine samples were collected the test substance was applied topically; air-dried and a commercial white T-shirt worn for 24 hours during which time urine was collected. At 24 hours the T-shirt was removed and analysed. The exposed areas were analysed for transepidermal water loss (TEWL) and then washed carefully with soap and distilled deionised water and all washing analysed. On day 11 the TEWL was measured and the treatment site dosed with 1.8 ml of 2% SDS (sodium lauryl sulphate) to cause irritation. On day 12 the TEWL was measured and the test substance was applied again topically; air-dried and a commercial white T-shirt worn for 24 hours during which time urine was collected. At 24 hours the T-shirt was removed and analysed. The exposed areas were analysed for transepidermal water loss (TEWL) and then washed carefully with soap and distilled deionised water and all washing analysed.
18.3.7	Sampling time	See above – Sample time 24 hours
18.3.8	Samples	Urine sampled as well as T-shirts worn and skin washings samples – see above

19 RESULTS AND DISCUSSION

19.1	**Toxic effects, clinical signs**	No adverse effects
19.2	**Dermal irritation**	No skin Irriation observed
19.3	**Recovery of labelled compound**	BA -76.5%; Borax 72%; DOT 78.5% Since the skin was washed 10 times and less 1 % was found I the last wash, it is assumed that most of the substance unaccounted for was in lost to outside clothing (over the T-shirt) an bedding during the 24 hour dosing period

19.4 Percutaneous absorption

Substance	% Dose Absorbed (95% CI)	Flux $\mu g/cm^2/hr$	Permeability Kp cm/hr.
5 % Boric Acid	0.226 ± 0.125	0.009	1.8×10^{-7}
5 % Borax[1]	0.210 ± 0.194	0.009	1.8×10^{-7}
10% DOT[2]	0.122 ± 0.10	0.010	1.0×10^{-7}

[1] Disodium tetraborate decahydrate

[2] Disodium octaborate tetrahydrate

20 APPLICANT'S SUMMARY AND CONCLUSION

Section A6.2 Percutaneous absorption (in vivo test)

Annex Point IIA6.2

Section A6.2 Human In vivo

20.1 Materials and methods

This study was designed to address absorption of typical solutions used in wood preservation and other biocidal uses.

Human Volunteers (8 per group) Group I, group II, and group III received two separate topical application of B^{10}-enriched 5% Boric Acid, 5% Borax, and 10% DOT solutions on their back skin, respectively and the in vivo percutaneous absorption was determined for a 24-hour dosing period. One dose was applied on day 5 under normal skin conditions and the other on day 12 under irritated skin conditions created by applying 2% SLS solution. Twenty- four hours after each topical dose, residual chemical on the dosed skin site was removed by skin wash. Urine samples were collected every 24 hours for 17 days. Urine samples from day 1 to day 4 were used to establish base boron levels and isotope ratios in the urine. The samples from day 5 to day 11 and day 12 to the end were used to compare absorbed level under normal skin and irritated skin conditions. To evaluate the dosing site skin condition, TEWL measurement and skin visual scoring were taken each time before dosing (including SLS treatment) and washing. To control any boron intake some food/beverage restrictions were instituted and daily detailed records were required. Boron analysis was done using inductively coupled mass spectrometry

20.2 Results and discussion

Approximately one-half of the administered topical dose was recovered after 24 hours in the T-shirt covering the dosed skin area and the skin washes. Pre-treatment with the potential skin irritant 2~ sodium lauryl sulphate had no effect on boron skin absorption for all three different dosage forms. No skin irritation was noted for any of the dosage forms.

Substance	% Dose Absorbed (95% CI)	Flux $\mu g/cm^2/hr$	Permeability Kp cm/hr.
5 % Boric Acid	0.226 ± 0.125	0.009	1.8×10^{-7}
5 % Borax[1]	0.210 ± 0.194	0.009	1.8×10^{-7}
10% DOT[2]	0.122 ± 0.10	0.010	1.0×10^{-7}

[1] Disodium tetraborate decahydrate

[2] Disodium octaborate tetrahydrate

20.3 Conclusion

Low skin absorption. For risk assessment where an absorbed dose is used the mean plus the standard deviation is used as a conservative absorption figure Boric acid = 0.351% absorption; Borax = 0.404; DOT = 0.132

20.3.1 Reliability 1

20.3.2 Deficiencies No

Section A6.2 Percutaneous absorption (in vivo test)

Annex Point IIA6.2

Section A6.2 Human In vivo

Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	9 March 2005
Materials and Methods	The version of the applicant is accepted.
Results and discussion	In the studies total recovery of the applied dose ranged from 48.8-63.6%. Accordingly 36.4-51.2% of the applied dose is not accounted for. This may be due to loss to outside clothing and bedding, as suggested by the study authors. However, part of the lost dose may be located in the body or in the skin at the application site, which in that case should be considered as being absorbed. As such, the absorption estimates from this study are unreliable. On the other hand, toxicokinetic studies also indicate that borates have a low dermal absorption and low potential for accumulation in the body. In this respect the present data are in line with dermal absorption data from other studies. Therefore, based on this study and other data a dermal absorption borates of 0.5% can be assumed as a reasonable worst case estimate.
Conclusion	Reasonable worst case estimate for dermal absorption of borates is 0.5%.
Reliability	3
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	

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

Annex Point Section A6.2-A10

21 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).

$[B(OH)3] < 0{,}02M$

Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	9 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 disodium octaborate tetraborate 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 disodium octaborate tetraborate 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 disodium octaborate tetraborate 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

21.1 Reference

1. [redacted] 2001, A study on the identification and comparison of the dissociation products of [redacted] Aqueous Solution using Raman spectrometry. [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]

21.2 Data protection Yes on [redacted].

21.2.1 Data owner [redacted]

21.2.2 Companies with letter of access **Curent Access** [redacted]

21.2.3 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

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

Annex Point IIA7.6.2.1

23.1	**Test material**	Disodium Octaborate Tetrahydrate [redacted] Sodium Tetraborate Decahydrate (Borax, [redacted])
23.1.1	Lot/Batch number	144-99-303
23.1.2	Specification	[redacted]. B_2O_3: 66.2%-69.0% Equivalent $Na_2B_8O_{13}.4H_2O$: 98.0%-102.2% Na_2O: 14.0%-15.1% Borax, [redacted] B_2O_3: 36.9-38.2% Equivalent $Na_2B_4O_7.10H_2O$ 101.0%-104.6% Na_2O 16.4%-17.0%
23.1.3	Purity	[redacted].>98% Borax [redacted] >99%
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 0.02$mol.l^{-1}$ 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. 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*

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

Annex Point IIA7.6.2.1

23.4.1	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
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, 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)

$[B(OH)_3] < 0{,}02M$
$B(OH)_3 + H_2O \rightarrow [B(OH)_4]^+ + H^+$ pKa = 9,15

0,025M <= [B(OH)3] <= 0,4/0,6M

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

Annex Point IIA7.6.2.1

$[B_3O_3(OH)_4]^-$; $[B_3O_3(OH)_5]^{2-}$ 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 $[B_3O_3(OH)_5]^{2-}$

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

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 [redacted].

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

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

Annex Point IIA7.6.2.1

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