



**Human and Environmental Risk Assessment
on ingredients of Household Cleaning Products**

Substance: Boric Acid

(CAS No 10043-35-3)

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1 EXECUTIVE SUMMARY

Boric acid and borax are used in small quantities for the stabilisation of enzymes in liquid detergents used in both liquid laundry and liquid dishwashing products. The amount of boric acid used in this application was 6,400 tonnes in 2004. This represents approximately 1% of the European market for borates. The major uses of borates include the manufacture of glass (insulation, textile and specialty), ceramics, as a raw material for the manufacture of perborate bleach used in powdered detergents, agriculture, as an essential micronutrient and as a flame retardant in plastics. Borates have been safely used in household cleaning products for nearly a century.

Borates are naturally present and widely distributed in the environment and are essential for the healthy development of all higher plants. They are essential to fish and frogs and there is some evidence to suggest that they are essential to humans. Borates appear to have beneficial uses in animal husbandry.

Boric acid and borax are white crystalline products that readily dissolve in water to form undissociated boric acid and borate anion at high pH. The solubility of borates means that they are widely dispersed and do not bio-accumulate in the environment or in humans.

Boric acid and borax are of low acute toxicity and do not have any genotoxic or carcinogenic potential. The toxicological endpoints of concern arise from feeding studies in laboratory animals and relate to effects on fertility as well as developmental effects at high doses. Possible effects on fertility are indicated by reversible histological effects on the testis, with irreversible effects and a reduction in fertility occurring at much higher doses. Effects on developmental toxicity relate to minor effects on foetal body weight and minor skeletal variations, which, with one exception, had reversed by postnatal day 21. All other effects occurred at maternally toxic doses. Developmental or fertility effects have never been demonstrated in human beings even among population groups with high exposure to borates.

The highest exposure of the general population to borates is through a healthy diet of fresh fruit, vegetables and nuts. Dermal exposure to borates through their use in liquid household cleaning products is low due to the lack of absorption of borates through skin.

The additional contribution to borates from household cleaning products is approximately 2000-6000 times less than normal dietary intake from which it can be concluded that borates pose no risk to human health.

The environmental risks of borates were evaluated by considering exposures resulting from wastewater entering rivers or being used for irrigation and from sewage sludge being applied to agricultural soil. No significant risks were identified.

The amount of borates entering the aquatic environment would be significantly less than associated with historical and current uses of perborate-based cleaning products. The concentrations of borates entering the terrestrial environment would be less than results from agricultural application of borates as plant micro-nutrients. Use of wastewaters for irrigation is presently subject to limitations based on total salinity and from use of perborates; the use of boric acid and borax in liquid detergent applications would not result in unacceptable concentrations.

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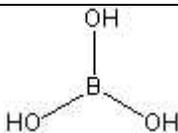
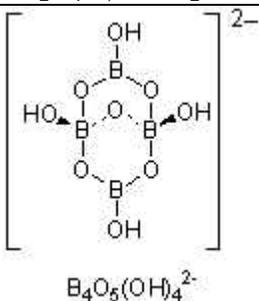
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3 SUBSTANCE CHARACTERISATION

3.1 CAS NO AND GROUPING INFORMATION

Boric acid (H_3BO_3) and borax ($Na_2B_4O_7 \cdot 10H_2O$) are used as enzyme stabilisers in liquid fabric detergents. Boric acid (Orthoboric acid) exists in nature as the mineral sassolite. It is a white crystalline material; its solubility in water increases rapidly with temperature and is a weak acid. Borax decahydrate (disodium tetraborate decahydrate) exists in nature as the mineral tincal. Borax is readily soluble in water and the pH of a borax solution increases slightly with increasing concentration and drops slightly with increasing temperature. Substance identification is contained in Table 1.

Table 1: Substance Identification

	Boric Acid	Borax
CAS No	10043-35-3	1303-96-4
EINECS No	233-139-2	215-540-4 ¹
IUPAC Name	ortho-boric acid: boric acid	Disodium tetraborate decahydrate
Synonyms	ortho boric acid, boracic acid and boric acid	Borax; Sodium tetraborate dehydrate; Borax decahydrate; sodium biborate decahydrate; sodium pyroborate decahydrate; Boron sodium oxide ($B_4Na_2O_7$), decahydrate; Boric acid ($H_2B_4O_7$), disodium salt decahydrate
Molecular Formula	H_3BO_3	$Na_2B_4O_7 \cdot 10H_2O$
Structural Formula		
Molecular Weight	61.83	381.37

¹ Listed in EINECS (European Inventory of Existing Commercial Chemical Substance) under the anhydrous form of sodium tetraborate.

3.2 CHEMICAL STRUCTURE AND COMPOSITION

3.2.1 MOLECULAR DESCRIPTION/MACRO-MOLECULAR DESCRIPTION (PHYSICAL STATE/PARTICLE SIZE)

Boric acid crystallises as white waxy plates (triclinic system). At the molecular level, boric acid consists of triangular $B(OH)_3$ molecules as depicted in the structural formula diagram above. In the solid state these molecules assemble into planar sheets held together by hydrogen bonding. The stacking pattern of these molecular layers is completely disordered, indicating that rather weak van der Waals forces are operating. The layers are 3.18Å apart. This arrangement accounts for the slippery feel of boric acid, and the cleavage planes observed in boric acid crystals. The acidic behaviour is due to the molecule being a base acceptor, rather than a proton donor. Commercial boric acid products exist as granules or finer powders and are stable under normal conditions. Particle sizes in commercial products tend to be in the range of $d_{50} = 50\mu m - 250\mu m$.

Borax decahydrate is a white, free-flowing crystalline material, in the monoclinic system. In the crystal, the polyborate ion has the structure depicted in the structural formula above. The sodium ions exist in two crystallographically unique positions, each being octahedrally coordinated by water molecules. These octahedra share edges to form chains that cross-link the polyborate ions to form parallel sheets. A network of hydrogen bonds integrates these sheets. There are eight moles of the water of crystallisation, and two moles of water exist as hydroxyl groups. Commercial borax decahydrate products exist as crystalline granular or powder materials; particle sizes typically no greater than $2000\mu m$, with a $d_{50} = 50\mu m - 250\mu m$.

Boric acid, borax decahydrate, and related borates are moderately soluble in water (see Table 2 below). The chemical species present in solution depend on concentration and pH. At concentrations below 0.025 M, essentially only mononuclear species $B(OH)_3$ and $B(OH)_4^-$ are present (Cotton and Wilkinson, 1988). The relative proportion of $B(OH)_3$ and $B(OH)_4^-$ is controlled by pH, reflecting the pK_a of 9.2. Polyborate structures, such as in borax decahydrate, depolymerise rapidly in solution. Therefore, at physiologically relevant concentrations, only the boric acid and borate ion are present (Power and Woods, 1997). In dilute aqueous solutions and physiological conditions the predominant species present is undissociated boric acid (de Vette et al. 2001).

3.2.2 PHYSICO-CHEMICAL DATA

Table 2: Physico-chemical data for boric acid

Boric acid CAS NO 10043-35-3		
	Results/remarks	Ref.
Macro-molecular description	White crystalline solid	
Molecular Weight	61.83	
Melting and Boiling Points	Not applicable. If heated above above 100 °C it loses water and is converted to metaboric acid and, on further heating, it is converted to boric oxide.	Mellor 1980
Vapour Pressure	9.9×10^{-6} Pa @ 25 °C	Tremain, 1998
Octanol-water Partition Coefficient (Log Pow)	-1.09 @ 22 ± 1 °C	Cordia, 2003a
Water Solubility	49.20 g/l @ 20 ± 0.5 °C	Cordia, 2003°
K_{oc} - soil	62 to 438	deVette et al. 2000
K_{oc} - sediment	68 to 120	Hanstveit et al. 2001

Density D 23/4	1.489	Cordia, 2003a
Viscosity	Not relevant	
pH-Value	4.05 @ 20 °C at a concentration of 32.969 g/l	Cordia, 2003°
pK _a	9.15 @ 20 °C	Dawber and Matusin, 1982
Oxidation	No oxidising properties	

Table 3: Physico-chemical data for borax

Borax CAS NO 1303-96-4 EINECs No 214-540-4		
	Results/remarks	Ref.
Macro-molecular description	White crystalline solid	
Molecular Weight	381.37	
Melting Point and boiling Point	Not applicable. Dehydrates on heating above 50 °C to pentahydrate and then to anhydrous borax. Anhydrous borax melts at 742 °C.	Mellor 1980
Vapour Pressure	Negligible @ 20°C	Based on data for boric acid
Octanol-water Partition Coefficient (Log Pow)	-1.53 @ 22 ± 1 °C	Cordia, 2003b
Water Solubility	49.74 ± 3.63 @ 20 ± 0.5 °C	Cordia, 2003b
K _{oc}	See boric acid	
Density D23/4	1.742	Cordia, 2003b
Viscosity	Not relevant	
pH-Value	9.32 at concentration of 40.004 g/l	Cordia, 2003b
pK _a		
Oxidation	No oxidising properties	

For comparative purposes, exposures to borates are often expressed in terms of boron (B) equivalents based on the fraction of boron in the source substance on a molecular weight basis. Conversion factors are given in Table 4 below. The B equivalents used are a generic designation rather than a designation of the element boron. As noted previously, only the boric acid and borate ion are present at environmentally and physiologically relevant concentrations, so presentation of concentrations as boron equivalents is appropriate.

Table 4: Conversion factors to Boron Equivalents

		Conversion factor for Equivalent dose of B
Boric acid	H ₃ BO ₃	0.1748
Disodium tetraborate decahydrate	Na ₂ B ₄ O ₇ • 10H ₂ O	0.1134
Disodium tetraborate pentahydrate	Na ₂ B ₄ O ₇ • 5H ₂ O	0.1484

3.3 MANUFACTURING ROUTE & PRODUCTION/VOLUME STATISTICS

The majority of boric acid is manufactured by reacting inorganic borate minerals with sulphuric acid in an aqueous solution. Sodium borates are the principle source in the US and calcium borates are the principle source in Turkey. Borax decahydrate is manufactured by dissolving the sodium borate mineral in hot liquor and recrystallizing. There are no European primary manufacturers of boric acid or borax.

The annual consumption of boric acid and borax as enzyme stabilizers in detergents in the European market was estimated to be 3,000 tonnes B₂O₃ equivalent (CEH, 2003) in 2004, equivalent to 932 tonnes of boron. This use represents approximately 1% of total borate consumption in Europe. The more significant use of borates in the European detergent market is for the manufacture of sodium perborate and is the subject of a separate HERA assessment. The major uses of borates in Europe are for insulation and textile fibreglass (34%), frit and glazes for ceramics (23%), cleaning and bleaching (12%) and borosilicate glass (7%), (CEH, 2003), with smaller markets in metal and alloy manufacture, agriculture, flame retardants and biocides.

3.4 USE APPLICATIONS SUMMARY

Boric acid and borax are added to some liquid fabric detergents up to 2% concentration to stabilise the protease and other enzymes in the formulation. Boric acid and disodium tetraborate decahydrate are also used at concentrations of 5% in cosmetics in the US and in talc in Europe; up to 3% in other cosmetics in Europe; and up to 0.5% in oral hygiene products in Europe and elsewhere (Beyer et al., 1983; EC, 2000).

4 ENVIRONMENTAL ASSESSMENT

4.1 ENVIRONMENTAL EXPOSURE ASSESSMENT

Boron is ubiquitous and widely distributed in the environment in rocks, soil and water and is released into the environment primarily by weathering of rock and soil, volatilisation of sea water, and anthropogenic activity. It is estimated that 2×10^9 kg of boron is released into the environment through natural events (Park and Schlesinger, 2002). Boron mining for all uses is estimated to be about 3 to 4×10^8 kg/yr (Argust, 1998). The amount of boron mined is about equal to the amount generated by volcanoes to the atmosphere. Exposure to boric acid and borax from liquid laundry products must consequently be evaluated against background concentrations and natural flows.

When used in laundry and cleaning products, boric acid and borax are diluted by water. Such down-the-drain products typically enter sewage treatment plants (STP) which produce sewage sludge and treated effluent. Most of the borate remains with the treated effluent and is released to the aquatic environment. Some borate may remain with the sewage sludge and may enter the terrestrial environment via soil application of sludge. If the treated effluent is used for irrigation, borate will enter the terrestrial environment with the irrigation water. Because borates are imported into Europe and incorporated directly into laundry and cleaning products, environmental exposures from production and manufacturing in Europe are not addressed in this assessment.

Boric acid and borax are used in a large number of applications and products. Agricultural applications, as a micronutrient fertilizer for plants, directly apply borates into the environment. Human wastes will also introduce borates from foods into the treated effluent. Borates in many products and articles are immobile and unlikely to contribute to significant environmental exposures. To predict environmental exposures, this assessment uses tonnage values, physico-chemical properties, environmental models, and monitoring data. .

4.1.1 Environmental Fate

Borates entering the aquatic environment will form undissociated boric acid (H_3BO_3) and the borate anion. Their solubility defines that borates will be diluted and dispersed throughout the aquatic environment ultimately reaching the sea.

Recent studies of adsorption of boric acid on soils (Table 2, deVette et al, 2000) and sediments (Hanstveit et al., 2001) demonstrate that boric acid is not strongly nor extensively adsorbed to soil or sediment and that adsorption is not related to organic matter content. The Koc values reported by deVette et al. indicate that boron should be considered mobile in soil, according to the classification scheme in ASTM (2001). There is some evidence that water-soluble borates have a slight tendency for adsorption to soil, sediment particles and sewage sludge, depending e.g. on pH, organic matter content and the number of active adsorption sites (Butterwick et al., 1989). Significant adsorption, however, was only detected at alkaline pH levels of up to 9.5 when boron is mainly present as the borate ion (WHO, 1998; Blume et al., 1980).

Greatest adsorption was found in soils with high amounts of fine particles particularly with iron and aluminium compounds on the surface (Sprague, 1972). Depending on soil properties the adsorption of boron was mostly found to be reversible and the compound was easily leached. Boric acid, the predominant borate species present at acidic pH levels, was found to be mobile in soil and sediment. At relevant environmental pH values of ≤ 7 no significant adsorption of boron compounds in soil and the aquatic compartments are to be expected (EPA, 1975; Koehnlein, 1972.) Goldberg et al. (2000) reviewed boron binding and characterized boron adsorption as being maximal around pH 9 and exhibiting a parabolic shape around that maximum.

The vapour pressure for boric acid is extremely low (see Table 2) so volatilization is expected to be minimal. The exception is over the oceans, where evaporation of aerosols leads to small but measured quantities of boric acid vapour in the marine atmosphere. The solubility of such materials means that they would quickly be washed out of the atmosphere in precipitation.

4.1.2 Removal

Boron is not removed by conventional sewage treatment, although there is some evidence to suggest that trace quantities may be associated with sewage sludge (see section 4.1.3.5). A review of removal technologies suggested that conventional approaches were not effective at removing boron to sub-parts-per-million concentrations or would be associated with high costs (such as high amounts of sorptive materials, e.g., grams/liter) (Park and Edwards, 2005). While some technologies were seen as meriting further research, none was seen as ready for widespread application.

A limited study looking for evidence of boron removal was done at four water treatment facilities in the UK (Ashact Ltd, 1996). Boron levels were measured at the inlet and outlet of the treatment units such that the same mass of water was monitored at the inlet and outlet. Significant boron removal was noted at one plant. A mechanism for the removal was not identified.

Removal from wastewater using a weak-base anion exchange resin was reported by Yilmaz et al. (2005) to reach 99% from synthetic wastewater. However, the initial boron concentrations ranged from 250 to 100 mg-B/L, so it is not clear how applicable this study would be to typical wastewater boron concentrations.

4.1.3 Monitoring Studies

4.1.3.1 Water

Extensive environmental monitoring data exists for boron. However, much of the data have been collected as spot samples rather than as part of a more extensive monitoring programme. Only data that can be statistically evaluated is used for the risk assessment.

There are some areas in Europe where boron levels are high due to local geological conditions and any risk assessment needs to take account of natural background levels. In addition, rainwater, carrying boron from adjacent oceans, may contribute boron to surface waters: by comparing the ratios of ^{11}B and ^{10}B in the Seine River (France) and in sources (perborate, borax

from Turkey, borax from the U.S., fertilizer, rainwater, local rocks), Chetelat and Gaillardet (2005) suggested that about 25% of boron in the Seine at Paris was due to rainwater contribution, 10% was due to agricultural-affected waters, and about 65% due to urban effluents. Mean boron discharge at Paris was 4.6 $\mu\text{mol/L}$ or 50 $\mu\text{g-B/L}$. In the Seine system, geological sources (dissolution of borate from rocks) appeared to contribute less than 1% of total boron except for spring when it reached 10% of total.

A recent analysis of surface water quality data from European countries (Wyness et al., 2003) is summarised in table 5. The study reported the average 95th percentile for every monitoring point, reported as “Mean 95 percentile.” This provides a more conservative estimate of the mean concentration than the recommended 90th percentile (ECB, 2003).

Table 5. Boron Concentration ($\mu\text{g-B/L}$) – Summary of data (Wyness et al., 2003)

Country	No. of Monitoring Points	Date Coverage	Total No. Values	Arithmetic Mean	Range	Mean site 95% percentile
Austria	30	1998-2000	712	44	nd-690	80
Belgium	651	1998-2000	5,056	239	25-2,029	410
Denmark	0					
Finland (lakes only)	463	1995	463	3.3	<1-46	44
France	25	1995-2000	1,304	146	nd-2,670	261
Germany	197	1980-95	197	171	nd-1,300	632
Greece	28	1997-99	Not known	144	4-2,330	-
Luxembourg	0					
Ireland	185	1999-2000	185	26	nd-1,630	101
Italy	64	1998-1999	926	114	nd-894	84
Netherlands	9	1986-1999	1,842	111	38-878	218
Portugal	8	1999-2000	129	367	30-3,860	534
Spain	328	1991-2000	4,272	137	nd-7,490	288
Sweden	0					
UK-England	98	1974-2000	22,329	65	nd-1,121	95
UK-Northern Ireland	0					
UK-Scotland	10	1976-1997	3,437	9.7	nd-230	17
UK-Wales	39	1975-1999	4,965	13.0	nd-292	22

Boron data was also collected as part of the GREATER project and this data is summarised in Table 6.

Table 6. UK Boron monitoring data from the GREATER project

River	Year	No. of sites (No. of samples per site)	Range of site Mean boron concs ($\mu\text{g/L}$)	Mean of site mean boron concs (+/- 1 SD ¹) ($\mu\text{g/L}$)	Mean of site 90%ile boron concs (+/- 1 SD ¹) ($\mu\text{g/L}$)
R. Aire (UK)	1996-1998	15 (9 -38)	² L.D. - 280	247 (+/- 75)	236 (+/- 117)
R,Calder (UK) ³	1996-1998	18 (18 -27)	26 -417	163 (+/- 94)	274 (+/- 152)

R. Rother (UK) ⁴	1996-1998	15 (18 -21)	106 -512	317 (+/- 97)	506 (+/- 178)
R. Went (UK) ⁵	1996-1998	8 (19 -24)	179 -530	296 (+/- 108)	442 (+/- 173)

¹ SD is the standard deviation.

² L.D. = at the limit of detection (20µg/L). 20 µg/L has been used for the one site to which this applies, in the calculations of overall catchment means. A 90thile value of 20 µg/L has also been used for this site, in the calculations of overall catchment 90thiles.

³ Includes 1 small tributary with significant STW effluent influence, and two other tributaries.

⁴ Includes 2 tributaries, and also the River Don upstream and downstream of the confluence with the Rother.

⁵ Includes 1 small tributary with significant STW effluent influence.

The monitoring data summarised in Table 6 has been collected at standard Environment Agency monitoring sites, all of which are located at river sites specifically intended to monitor the effects of inputs from sewage works and other anthropogenic discharges. In the rivers Aire and Calder, the natural upstream and background boron levels are negligible. In the stretch of the river Rother which has been monitored, background boron levels in excess of 100 µg/L are present. These may have resulted from upstream and instream anthropogenic inputs, including leakage from fly ash tipping sites. Background boron levels in excess of 100 µg/L are also present in the river Went, due to exchange with groundwater which has incorporated boron leached from marine sediments exposed in flooded former coal mines. The 90th percentile concentrations from each site (see Fox et al., 2000, Holt et al., 2003) represent the concentrations at low water levels, which are used as a reasonable worst case in environmental risk assessment in Europe. The means of these site-specific 90th percentiles are given in Table 6, along with the standard deviations which are due to different boron levels at different sites within the catchment. The means of the 90th percentiles of specific site concentrations are recommended for use in regional risk assessment in Europe (ECB, 2003).

Table 7: Examples of Boron Concentrations in Surface Waters

Country	No. sites/ samples	Concentration range (mg/L)	Year	Reference
Austria		< 0.02 – 0.6	1985-1989	Schöller and Bolzer 1989
France	>300	98% < 0.1	1986-89	DDASS de l'Oise, 1990
Germany	7 rivers, 17 sites, 360 samples	0.013 – 0.372	1991-95	Metzner <i>et al</i> 1999
Italy	19 sites 166 sites 5 sites	< 0.002 < 0.01 – 0.5 0.1- 0.2	1989 1983-84 1997-98	Benfenati <i>et al</i> 1992 Tartari and Camusso, 1988 Gandolfi <i>et al</i> . 2000
Luxembourg		0.11 – 0.39	1993	Unilever 1994
Netherlands	22 analyses	0.04 – 0.09 0.09 – 0.145	1981 1992	Mance <i>et al</i> 1988 Unilever 1994
Spain	5 sites	0.20- 0.30	1986	Garcia <i>et al</i> 1987
Sweden		<0.005 – 0.069 <0.05	1990 1991	Sveriges Geologiska AB Analys, 1991 KM Lab, 1991
England Scotland	15 sites 59 sites (236 samples)	0.011 – 0.311 (mean values) <0.005 – 0.035	1993-96	Neal <i>et al</i> , 1998
Switzerland	8 sites	<0.004 – 0.26	1990	EAWAG, 1990

4.1.3.2 Air

The major source of boron in the atmosphere is from marine evaporation estimated as 1.3 to 4.5 x 10⁹ kg-boron per year globally (Argust, 1998, Park and Schlesinger, 2002). Most of this is re-deposited into the oceans or as precipitation in coastal areas. Volcanoes are estimated to contribute about 3 x 10⁸ kg-boron per year. Total industrial air emissions are estimated as approximately 1 x 10⁷ kg-boron per year, or < 0.6% of total flows (Argust, 1998). Processes such as fibreglass manufacture and ceramics involve high temperatures, so some volatilization of boron is likely. Gomez et al. (2004) reported that boron content of particulates in a ceramic producing region of northeast Spain (average 65 ng/m³) reflected boron vaporization or volatilization during high temperature ceramic processes. Combustion of coal also may release boron, especially to fly ash.

The total global removal of boron from the atmosphere through both wet and dry deposition has been estimated to be 5.3 to 7.0 million tonnes per year (Argust, 1998). There are limited data available on levels of boron in the atmosphere. 85% of the total atmospheric boron has been reported (Anderson et al 1994) in the gas phase at a level of 16ng/B/m³ at three continental sites. A more general measurement of atmospheric boron levels comes from the analysis of rain water where levels show wide variation (0.002 to 0.0045 mgB/L in France and 0.1 mgB/L in Japan). An analysis of boron concentrations in rainwater from various regions by Park and Schlesinger identifies that rainwater from continental sites contain less boron than that from coastal and marine sites. A median value of 6.6 ppb is used with mean values of 4.89 (continental sites) and 10.06 ppb (marine sites).

4.1.3.3 Soil

Boron occurs naturally in the soil and levels will reflect rock and soil type, weathering and climate. Sedimentary rocks typically have a higher concentration of boron compared to igneous rocks with rock originating from marine sediments containing borate concentrations of 15-300 mg B/kg while the borate concentration in carbonate sediments is around 10 mg B/kg. (ECETOC 1997). Highly concentrated deposits of boron minerals are generally found in arid areas with a history of volcanism or hydrothermal activity (Woods, 1994). There are many reported ranges of boron concentrations although typically soil boron concentrations range between 10-20 mg B/kg (ECETOC 1997).

Table 8: Soil boron levels (dry weight basis)

Region	Range	Mean	Reference
US	10- 300 mg/kg	30 mg/kg	Eisler, 2000
Worldwide	45-124 mg/kg		Eisler , 2000

A more relevant factor is the bioavailable boron. Most of the B available to plants comes from decomposition of organic matter and from B adsorbed and precipitated on the surfaces of soil particles (Gupta et al., 1985). Typically less than 5% of total soil B is available, with values ranging from 0.4% to 4.7% (Gupta, 1968). Measurement of the soil solution concentration of B would be the preferred method of determining the bioavailable concentration. Two procedures to estimate soil solution concentrations are used: the hot water soluble boron (HWS) and the saturation extract concentration. Neither is seen as universally applicable (Gupta et al., 1985),

although the HWS procedure appears to be used more often. Values of HWS boron normally lie between 0.1 mg/L and 3 mg/L (Shorrocks, 1989).

Boron introduced with irrigation water will equilibrate between soil solution and soil particles. The most important factors influencing adsorption are the pH of the system, the amount and type of clay minerals present and the exchangeable minerals in the soil. Soil adsorption of boron is maximal at alkaline pH. Of the clays, illite is the most reactive and kaolinite the least reactive. Liming soils replaces exchangeable aluminium cations with calcium, precipitating aluminium hydroxides which appears to increase B adsorption in limed soils (Gupta et al., 1985). Goldberg et al. (2000) modelled boron binding to soil as a constant capacitance model, with binding as a function of surface hydroxyl groups on oxides and clay minerals. Boron adsorption was characterized as being maximal around pH 9 and exhibited a parabolic shape around that maximum. The model used boron surface complexation constants that were obtained from easily measured soil properties: soil surface area, organic carbon content, inorganic carbon content and free aluminium oxide content (Goldberg and Su, 2005).

Boron adsorption has been reported as varying from fully reversible to irreversible, depending on soil type and environmental conditions (IPCS 1998). Goldberg and Su (2005) reported that infrared spectroscopy found boron in two types of complexes: inner-sphere complexes with no water between the adsorbed boron and the surface functional groups on the soil minerals and outer-sphere complexes with some water between the adsorbed boron and the surface functional groups on amorphous iron oxide.

Eventually adsorption to soil particles will equal desorption, such that the soil solution concentration will equal the irrigation water concentration. If excess irrigation water is applied, boron will be leached downward below the root zone, minimizing root zone concentrations. If insufficient water is applied, evapotranspiration of soil moisture can result in increased boron concentrations that are phytotoxic in the root zone (Gupta et al., 1985). This pattern is consistent with observations that surface concentrations of boron in arid regions are typically higher than in humid regions: movement of excess precipitation leaches boron downward, away from the root zone, leading to regions with boron deficient soils.

4.1.3.4 Sewage

Most boron is not removed by conventional sewage treatment and treated effluent will be discharged into surface waters or possibly as irrigation water. Monitoring studies under the GREATER project (Fox et al., 2000; Holt et al 2003; Gandolfi et al., 2000) show mean effluent concentrations in the range 0.5 to 2 mg-B/L, summarized in Table 9. Note that more recent data indicate lower concentrations than older data, suggesting an overall reduction in boron loading to sewage. Older reviews (Butterwick et al., 1989) suggested typical effluent values of 2 mg-B/L with levels up to 3 to 5 mg-B/L.

Table 9: Examples of boron concentrations in sewage waters

Country	No. sites /samples	Conc range (mg/L)	Mean (mg/L)	Year	Reference
Austria		< 0.02 – 0.8	-		Schöller and Bolzer, 1989; Schöller, 1990
Germany	27 STPs 1 STP	<1.5-4.5 0.50		1973 1993	Dietz, 1975 Metzner <i>et al</i> , 1999
Italy	7 STPs		1.0		Mezzanotte <i>et al</i> , 1995

	1 STP	0.23-0.66	0.42		Gandolfi <i>et al</i> , 2000
	1 STP	0.67-1.26	1.0		Gandolfi <i>et al</i> , 2000
	1 STP	0.73-2.86	1.90		Gandolfi <i>et al</i> , 2000
Netherlands	1 STP	0.39-0.75		1994	Feijtel <i>et al</i> , 1997
Spain	2 STPs		1.45-3.0		Navarro <i>et al</i> , 1992
Sweden	1 STP		0.4		Ahl and Jönssen 1972
UK	8 STPs/203	0.43-0.84	0.53	1996-1998	Fox <i>et al</i> 2000 Holt <i>et al</i> 2003
	14 STPs/307	0.22-1.12	0.48		
	7 STPs/138	0.72-1.16	0.92		
	6 STPs/156	0.70-1.06	0.93		
Egypt	4 STPs	0.11-1.67	0.08 – 0.2		El Kobbia and Ibrahim, 1989

4.1.3.5 Concentration in Dry Sewage Sludge

There has always been an assumption that boron is not significantly removed during the sewage treatment process. Nevertheless, some boron is associated with sewage sludge although data is scarce. Results of boron concentrations in sewage sludge from a study of 48 sewage treatment plants in Sweden (Eriksson, 2001) are detailed in Table 10.

Table 10: Concentration of boron (mg B/kg dw) in sewage sludge

Number of Samples	Mean	SD	Min	Percentile					Max
				10%	25%	Median	75%	90%	
48	61	81	2	8	18	32	58	150	390

Fujita *et al.* (2005) reported boron adsorption reaching sludge concentrations of 40 to 600 mg-B/kg-sludge (dry weight) when influent concentrations ranged from 0.3 to 30 mg-B/L. The Freundlich constant for activated sludge was 26 mg/kg and was less than for activated carbon (k=190 mg/kg) and activated alumina (k=440 mg/kg). The adsorption pattern was linear. They suggested that at typical wastewater concentrations in Japan of less than 0.1 mg-B/L, sludge concentrations would likely range from 20 to 60 mg-B/kg. This is in reasonable agreement with the results reported by Eriksson (2001).

4.1.4 PEC Calculations

4.1.4.1 Conceptual Model and Framework

Boron is present in the environment from both natural and anthropogenic sources. Consequently, the amount of boron measured in environmental samples represents all the multiple sources, as indicated in the following summation:

$$EC\text{-total boron} = EC\text{-background boron} + EC\text{-anthropogenic boron},$$

where: *EC-total boron* is the environmental concentration of boron from all sources,

EC-background boron is the boron from natural sources, such as rock and soil, and

EC-anthropogenic boron is the boron from all human uses and disposals of boron.

The total boron concentrations may be derived either by monitoring environmental media, or by quantifying inputs and using an environmental model to estimate concentrations in various media. Information from monitoring was presented in section 4.1.3. The model EUSES is recommended to estimate the local and regional exposure levels (ECB, 2003, HERA, 2005).

The anthropogenic boron may (in theory at least) be ascribed to each separate application. For purposes of this HERA risk assessment, it is useful to identify three categories: boron due to use of boric acid in detergents, boron from use of perborates in cleaning and laundry products, and boron from all other applications:

$$\textit{EC-anthropogenic boron} = \textit{EC-detergent boric acid} + \textit{EC-perborates} + \textit{EC-other uses}$$

To apportion the anthropogenic boron among various applications, the size of an activity (e.g., the market volume) and the emissions or release patterns (e.g., how much of a substance is released to specific environmental media) can be used. For consumer products such as addressed by HERA risk assessments (HERA 2005), simplifying assumptions can be used: (1) the market volume (kg of substance per year in European markets) is used to estimate the size of activity and (2) all consumer products are assumed to enter wastewater during use and disposal.

For substances such as boric acid in detergents and perborates in cleaning products, these assumptions are reasonable. Note that for other applications of borates, such as fibreglass and ceramics, these assumptions are not reasonable – borates in such applications are fully integrated into the product and are not released into the environment in any significant quantity. For some applications, such as fertilizers, some product may enter the environment from normal use.

Several types of conservative assumptions may be used to derive predicted environmental concentrations (PECs). When environmental monitoring data are used to estimate PEC-total boron, the boron due to background sources may be assumed to be zero, leading to the expression:

$$\textit{PEC-total boron} = \textit{PEC-anthropogenic boron}.$$

This clearly overestimates the amount of anthropogenic boron, but simplifies the PEC process by eliminating the need to evaluate the amount of background boron.

When evaluating individual applications, one may assume the entire PEC-anthropogenic boron is associated with the application under consideration. For many applications of boron, the environmental emissions may be minimal, leading to the assumption that PEC-other uses = 0. The resulting simplified model then becomes:

$$\textit{PEC-total boron} = \textit{PEC-detergent boric acid} + \textit{PEC-perborates}$$

by assuming that PEC-background boron = 0 and PEC-other uses = 0.

As stated in Section 3.3, the estimated annual consumption of boric acid and borax for the detergent uses which are the scope of this risk assessment were estimated to be 932 tonnes of

boron equivalent. In contrast, about 284,000 tonnes of perborate (19,900 tonnes boron equivalent) were estimated used in European detergent applications in 1997 (HERA, 2002). The subject uses (about 932 tonnes of boron) amount to about 4.7% of the perborate use or 4.5% of the total for both applications. Consequently, uses of boric acid and borax for detergents are much less likely to affect anthropogenic boron concentrations in the environment than perborate uses evaluated previously by HERA (2002).

To reflect the relative market volumes of boric acid and borax uses in detergents vs. uses of perborates, 5% of boron concentrations associated with wastewater effluents will be assumed to derive from boric acid and borax uses in detergents.

4.1.4.2 Modeling Environmental Concentrations: EUSES

EUSES 2.0 was used to estimate environmental concentrations as well as to calculate PEC, PNEC and risk ratios (RCR). Following HERA guidance (HERA 2005), the detergent use pattern was selected to represent the down-the-drain pathway to the environment.

Production and formulation releases at the local level were not considered because they fall outside the scope of HERA and because the subject material (boric acid) is considered as an import to the EU.

The EUSES program incorporates a number of default assumptions about environmental compartments, flows and processes. These were not modified unless specific data were available. HERA (2005) determined that, for a detergent scenario, it was appropriate to assign 7% of the EU tonnage to the standard EU region instead of the default value of 10%. HERA also determined that the local emissions scenario should use an increase factor of 1.5x, instead of the default 4x factor. These reflect evaluations of boron use in detergents (Fox, 2001). Values for physico-chemical properties of boric acid and results of monitored environmental calculations (see previous section) were entered as shown in Table 11 below. PEC estimates from the EUSES model are shown in Table 12 below.

Table 11. Data used for EUSES calculations.

(Values shown are for boric acid unless otherwise noted.)

Name of Field	Value	Source
Molecular weight (Boric acid)	61.83 g/mol	Table 2
Melting point	742.5 °C	Table 2
Boiling point	1575 °C	Table 2
Vapour pressure at 25 °C	9.9E-06 Pa	Tremain, 1998
Octanol-water partition coefficient	-1.09	Cordia, 2003a
Water solubility at 25 °C	59400 mg/L	Cordia, 2003a
Chemical class for Koc-QSAR	Non-hydrophobics	
Organic carbon-water partition coefficient	62 L/kg	deVette et al. 2000
Solids-water partition coefficient in soil	1.77 L/kg	deVette et al 2000
Solids-water partition coefficient in sediment	4.33 L/kg	Hanstveit et al 2001
Characterization of biodegradability	Not biodegradable	

Volume of chemical imported to EU	5300 tonnes/yr	Section 3.3
Fraction of emission directed to water	100%	
Concentration in untreated wastewater	0.447 mg-B/L	Heijerick and Van Sprang 2004
Concentration in dry sewage sludge	32 mg/kg	Ericksson 2001
Regional tonnage of substance for private use	7%	HERA 2005, section 2.2.3.1
Local release to wastewater treatment	1.5-fold	HERA 2005, section 2.2.3.2

Table 12. PEC-calculations using the EUSES model

Predicted Environmental Concentration	Value as B	Value as Boric Acid
Regional PEC in surface water (total)	0.45 mg/L	2.6 mg/L
Continental PEC in surface water (total)	0.0013 mg/L	0.0074 mg/L
Local PEC in surface water (average annual)	0.45 mg/L	2.6 mg/L
Regional PEC in sediment	0.0080 mg/kgwwt	0.046 mg/kgwwt
Local PEC in fresh-water sediment	0.96 mg/kgwwt	5.5 mg/kgwwt
Regional PEC in agricultural soil	<0.00008 mg/kgwwt	<0.00046 mg/kgwwt
Continental PEC in agricultural soil	<0.00002 mg/kgwwt	<0.00011 mg/kgwwt
Local PEC in agricultural soil (averaged over 30 days)	0.029 mg/kgwwt	0.17 mg/kgwwt
Local PEC in agricultural soil (averaged over 180 days)	0.028 mg/kgwwt	0.16 mg/kgwwt
Local PEC in grassland (averaged over 180 days)	0.006 mg/kgwwt	0.037 mg/kgwwt
Local PEC in pore water of agricultural soil	0.016 mg/L	0.091 mg/L
Local PEC in STP effluent	0.044 mg/L	0.25 mg/L

4.1.4.3 PEC Water

According to the TGD, a 90th percentile of measured environmental concentrations can be taken as the PEC-water (ECB, 2003). Using recent monitoring data, Heijerick and Van Sprang (2004) derived PEC-country values using the median value of all 90th percentiles that were measured for different sites, rivers/catchments or regions in EU countries. Table 13 shows the resulting Ambient PEC values, ranging from 7.4 to 447 µg-B/L. In some cases, the 90th percentiles are calculated from data for river systems within a country because full country-wide data were not available. The use of median is seen as more appropriate than the use of mean (average) values because the median value is less influenced when sites with elevated (possibly contaminated) boron concentrations are present in the data set (Heijerick and Van Sprang, 2004). The highest 90th percentile value from this analysis is 447 µg-B/L.

Heijerick and Van Sprang compared their results with those reported by Wyness et al. (2003, see Table 5 above) and noted that the Wyness results were generally a factor of 2 higher. They suggested several reasons for the systematic differences: the Wyness et al. analysis

- was based on 95th percentile values instead of 90th percentile values;
- used the mean of site-specific 95th percentile values instead of the median values;
- did not perform an evaluation of outliers; and

- included older data in all cases, with no preference for using most recent data set. The highest 95th percentile value in the Wyness et al. analysis was 632 µg-B/L.

HERA (2002) estimated the local PEC in surface water associated with uses of perborates in household cleaning products to be 0.204 mg-B/L. This was calculated using the EUSES model and the HERA exposure scenario of 7% of EU tonnage to the standard EU region, a perborate tonnage of 19,900 kg-B/year, and a local usage factor of 1.5. Boron concentration in the sewage plant influent was estimated as 1.43 mg-B/L with 100% of the influent boron remaining with the effluent. HERA used a conservative estimate of PEC-water of 0.8 mg-B/L.

Fox et al. (2000) used the GREAT-ER model in conjunction with river monitoring data from the Aire and Calder catchments (UK), concluding that the estimated regional PEC values calculated using only the mean of the 90% percentile monitoring data were higher than values calculated using normalized flow volumes, especially when upstream site values were excluded. This reflects a sampling bias whereby most monitoring samples are obtained from downstream, more contaminated locations. The mean 90th percentile of monitoring data was 0.242 mg-B/L; when normalized by site flow volume including upstream sites, the mean 90th percentile of the GREAT-ER data was 0.186 mg-B/L; the resulting PEC estimate would be about 24% lower. If the values were normalized by length of river stretch, then the mean 90th percentile of the GREAT-ER data was 0.028 mg-B/L, about 88% lower than a PEC based on monitoring data alone. This analysis pointed out that the more conservative PEC estimates may not be appropriate; if the intent of the exposure assessment is to identify the portion of a water body that experiences a given maximum concentration, then normalizing by flow volume and including upstream portions of the water body is justified. If upstream flow and distance are not considered in the calculations of PEC, then the resulting estimate has an unknown conservative factor and represents some value other than the intended 90th percentile.

The EUSES model predicted the Continental PEC in surface water associated the detergent use as 0.0013 mg-B/L. The Regional PEC was set to 0.45 mg-B/L, reflecting the monitoring data, and the predicted local PEC reflected this, calculated as 0.45 mg-B/L.

The market volume of boron used for liquid detergent applications was estimated to constitute about 5% of the market volume of boron used in perborates (section 3.3). If monitoring data is used to estimate a PEC-water, then logically the PEC associated with detergent applications is a similar fraction of monitored concentrations.

The Heijerick and Van Sprang (2004) analysis follows TGD guidance and incorporates data quality review to derive a PEC-water of 0.447 mg-B/L as the maximum regional value. **This value (0.447 mg-B/L) is recommended as a conservative PEC value for the use of borates in liquid detergents** because:

- the detergent uses of borates are a small fraction of perborate uses and the monitored data likely reflects the much greater amount of perborate use;
- the estimated PEC may overestimate actual boron concentrations throughout a region because the procedure did not normalize for upstream (non-monitored) sites by flow or river length;
- the procedure did not separate background boron from anthropogenic boron, but made the conservative assumption that all measured boron was anthropogenic; and
- the procedures screened for outlier values, gave preference to recent data, and provided specific rules for managing data quality issues.

The use of this value reflects total uses of borates and so significantly overestimates the PEC-water ascribable only to liquid detergents.

Table 13: Data-derived PECs for European Countries (Heijerick and van Sprang, 2004)

Country	Ambient PEC ($\mu\text{g/L}$)
Austria	31.2 $\mu\text{g/L}$
Belgium	
Flanders	447 $\mu\text{g B}_{\text{total}}/\text{L}$
Rupel catchment	106 $\mu\text{g B/L}$
Brussels	347 $\mu\text{g B/L}$
Walloon Region	95.8 $\mu\text{g B/L}$
Finland	7.4 – 9.3 $\mu\text{g/L}$
France	167 $\mu\text{g B}_{\text{total}}/\text{L}$ 97.6 $\mu\text{g B}_{\text{diss}}/\text{L}$
Germany	General: 125 – 384 $\mu\text{g/L}$ Baden-Wurttemberg: 60 – 132 $\mu\text{g B/L}$ Large rivers - 1997: 226 $\mu\text{g B/L}$ Large rivers – 1998: 216 $\mu\text{g B/L}$ Bavarian rivers: 58 – 270 $\mu\text{g B/L}$
Greece	191 – 261 $\mu\text{g B/L}$
Ireland	47.3 – 62.1 $\mu\text{g B/L}$
Italy	108.1 $\mu\text{g B/L}$ (Po river)
The Netherlands	137.1 $\mu\text{g B/L}$
River Rhine	130.5 $\mu\text{g B/L}$
River Meuse	140.1 $\mu\text{g B/L}$
Portugal	356 $\mu\text{g B/L}$
Spain	--
United Kingdom	
England	301 (156 – 405) $\mu\text{g B/L}$
Wales	19.7 $\mu\text{g B/L}$
Scotland	125 $\mu\text{g B/L}$
UK – General	200 $\mu\text{g B/L}$
Range	7.4 – 447 $\mu\text{g B/L}$

4.1.4.4 PEC Soil

There is a natural level of boron in the soil derived from boron-bearing rocks as well as from decomposition of soil organic matter. The world-wide range is reported as 45 to 124 mg-B/kg soil (dry weight basis, Eisler 2000). Less than 5% of total soil boron is available for plant uptake, i.e., it is not bioavailable (Gupta et al., 1985). As discussed in Section 4.1.3.3, soil boron may be reported as the extractable portion, but no one procedure for measuring boron in soil solution is universally accepted. The wide variability of soil types within Europe makes the determination of a single “background” boron level inappropriate.

The application of borates as essential micronutrients for plants is probably a significant anthropogenic source of boron to soil. The current annual consumption in Europe for this use is

about 25,000 tonnes of B₂O₃. This is many orders of magnitude greater than the amount of boric acid used in detergents. Shorrocks (1997) observed that clear evidence of boron deficiency has been reported in over 80 countries and on 132 crops, as evidenced by positive responses to boron application. Application rates vary with crop species, but recommended rates are usually 1 to 2 kg-B/ha for annual plants. Using standard factors for soil bulk density and depth of agricultural mixing, this is equivalent to 0.3 mg-B/kg-soil.²

The conceptual model for this risk assessment includes the pathway from wastewater to soil by application of sewage sludge containing borates to agricultural soils (HERA 2004). This pathway is modelled in the EUSES program. The estimated PEC-soil values from EUSES were 0.029 mg-B/kg-wet weight for agricultural soil averaged over 30 days, 0.028 mg-B/kg-wwt for agricultural soil averaged over 180 days, and 0.006 mg/kg-wwt for grassland averaged over 180 days (values for Local PECs). Values for Regional and Continental PEC-soil were much smaller, as shown on Table 12.

Secondly, boron may be introduced into soils by the use of irrigation water containing sewage effluent with its associated boron. The extent to which sewage effluent is used for irrigation of agricultural crops within Europe has not been determined but it is anticipated that higher use will be in Mediterranean countries rather than the wetter countries in Northern Europe. The irrigation pathway is not within the EUSES model so will be considered separately by evaluating the PEC for soil porewater.

In general, boron is mobile with water in soils. In wetter areas, boron is unlikely to accumulate in soils, but will move with surface and groundwater flows. In drier areas, however, evaporation of soil moisture may lead to accumulations of borates and other salts in surface soils. Consequently, boron concentrations in wastewaters used for irrigation have been of concern to governments in arid regions. To reduce boron content of wastewaters, Israel and Cyprus have restricted boron use in detergents (Vengosh et al., 2004; Nurizzo, 2003), with goals of keeping boron levels below 1.0 mg-B/L (the EU drinking water standard) or 0.5 mg-B/L.

The EUSES estimate of PEC-soil porewater associated with liquid detergent products was 0.016 mg-B/L. As a more conservative estimate, the river monitoring data (which includes all anthropogenic sources of boron) will be used as an additional PEC-soil porewater (0.447 mg-B/L).

4.1.4.5 PEC Sediment

There are few available data on boron levels in European river sediments. A laboratory study of sorption to sediments showed that boric acid is mobile in sediments (K values of 3.96 to 4.70) and so the absence of monitoring survey data is not critical because the PEC-aquatic will address the same pathway. An estimate of the PEC-sediment can be made based on equilibrium partitioning. The estimated PEC-sediment from EUSES is 0.0080 mg-B/kg for the Regional PEC, 0.0033 mg-B/kg for the Continental PEC and 0.96 mg-B/kg for the Local PEC. For this risk assessment, the PEC-sediment of 0.96 mg-B/kg will be used

4.1.4.6 PEC STP

² The concentration is estimated as the application rate (1 kg-B/ha) x (bulk density of soil, 1700 kg/m³)⁻¹ x (depth of agricultural soil mixing of 0.2 m)⁻¹ x (10000 m²/ha)⁻¹ using EUSES default values.

The concentration of boron in sewage effluent arising from the use of boric acid in detergents is small compared to the contribution from the use of sodium perborate. The Perborate risk assessment (HERA, 2004) states that a conservative estimate of boron concentration in the sewage from the use of perborate as a bleaching agent is 2.3 mg B/L. This can be compared to monitoring data (Section 4.1.3.4) reporting a range from 0.5 mg B/L to 2 mg B/L. Using the fraction of anthropogenic boron associated with use of borates in liquid detergents (5%) with the upper value, the estimated boron in STP effluent would be approximately 0.1 mg-B/L or less.

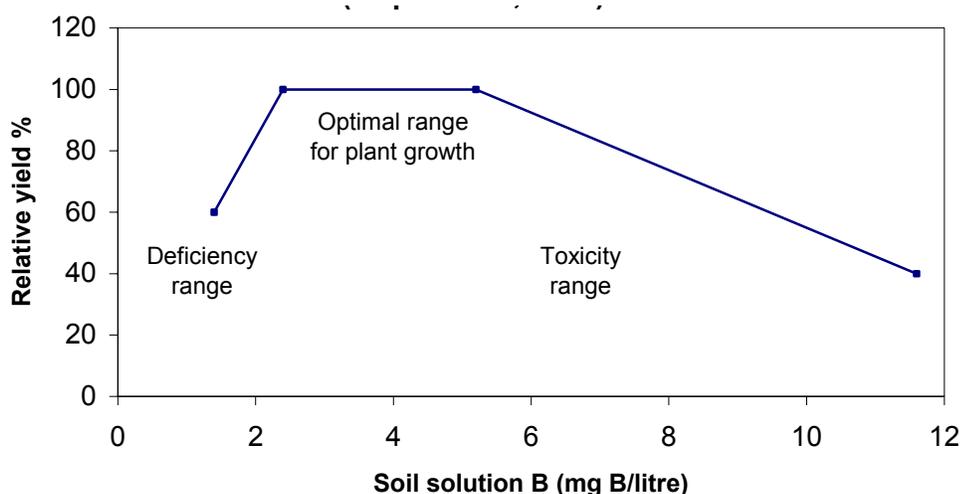
The PEC-STP estimated using EUSES arising from use of boric acid in liquid detergents is 0.044 mg-B/L. This estimate will be used for the risk assessment.

4.2 ENVIRONMENTAL EFFECTS ASSESSMENT

Discussion of the environmental effects of boron must reflect that boron is an important, if not essential, micronutrient to many species. Boron is known to be an essential micronutrient for terrestrial plants (Butterwick et al., 1989, Eisler, 2000). Shorrocks (1997) documented the use of boron applications for 132 crops in over 80 countries, demonstrating the widespread nature of agricultural use of boron. Boron has also been found to be an essential element to a variety of aquatic species. These include some fungi and bacteria (Saiki et al., 1993, Fernandez et al., 1984), some diatoms and algae (Smyth and Dugger, 1981), and macrophytes (Eisler, 2000). Work with rainbow trout and zebrafish has shown that embryo-larval development was adversely affected in waters deficient in boron (Rowe et al., 1998, Eckhert, 1998). Fort et al. (1998) reported that abnormal development in frog embryos (*Xenopus laevis*) was observed when larval stages were exposed to 0.003 mg-B/L or less. Boron does not appear to be essential for all species, however.

The concentration-response curve for boron is likely to be U-shaped for many species, with adverse effects observed at very high and very low concentrations, while no adverse effects are observed at the intermediate concentrations (Lowengart, 2001). Figure 1 illustrates such a pattern for plants (Gupta et al., 1985) although the response has been normalized to 100%, making the curve an inverted-U shape.

Figure 1. U-Shaped Toxicity Pattern: Plant yield as influenced by soil boron concentrations (Gupta et al., 1985)



Plant and animal species vary in the concentrations associated with deficiency and toxicity. Monocotyledons (e.g., corn and grasses) require about one-quarter as much boron as dicotyledons (e.g., tomatoes, carrots, clovers, beets) (Butterwick et al., 1989). The mobility of boron within the plant may help explain the observed deficiency and toxicity patterns. Boron is more mobile in plants that produce the simple sugars known as polyols (e.g., sorbitol and mannitol) than in species that do not produce polyols. In polyol-producing species, boron is translocated from one part of the plant to another and so may reach the meristem and affect growth. In the absence of polyols, boron is relatively immobile within the plant (Brown et al., 2002). A polyol-producing plant may be both more tolerant of boron deficiency and more sensitive to higher boron concentrations because of the mobility of boron within the plant. This is important in agricultural applications of boron, which may be applied as a soil treatment or as foliar spray.

Agricultural application of boron depends on the plant and cultivar, as well as the local soil. Recommended application rates range from 0.5 to 7.6 kg-B/ha (Borax, 2002), but typically are in the range of 1 to 2 kg-B/ha (Shorrocks, 1997). If one assumes typical soil densities of 1700 kg/cubic meter and a mixing depth of 20 cm (default values used in the EUSES model), an application rate of 1 to 2 kg-B/ha results in an estimated soil concentration of 0.3 to 0.6 mg-B/kg-soil. Mortvedt et al. (1992) estimated soil concentrations of 0.16 to 2.0 mg-B/kg-soil for several crops with application rates of 0.45 to 5.7 kg/ha. The intentional application of borates to achieve such soil concentrations should be acknowledged in the risk assessment process.

Work with rainbow trout and zebrafish has demonstrated boron deficiencies: embryo-larval development was adversely affected in waters with very low boron concentrations. Rowe et al. (1998) concluded that embryonic growth of rainbow trout was reduced below 0.1 mg-B/L³ and that zygote development was affected in zebrafish at concentrations below 0.002 mg-B/L. Zebrafish development was normal at 0.5 mg-B/L. When zebrafish embryos from parent fish exposed to low boron concentrations were placed in 0.5 mg-B/L, development was normal, as embryos appeared able to replenish boron levels. These data demonstrate that extremely low boron concentrations can cause adverse effects through boron deficiency, i.e., the left-hand part of the curve in Fig. 1.

4.2.1 Toxicity

The ecotoxicity of boron has been evaluated by a variety of techniques, including laboratory and field tests. Many studies pre-date current standard ecotoxicity test protocols and other relevant data come from studies that are not carried out in accordance with traditional toxicity test designs. Evaluations of test reliability were made for the studies discussed in this section following the Klimisch et al. (1997) codes. The studies most closely following standard protocols were rated “1. *Reliable without restriction*” with the descriptive qualifiers:

- (a) Guideline study
- (b) Comparable to guideline study

High quality studies but that did not strictly follow standard protocols were rated “2. *Reliable with restriction*” with the descriptive qualifiers:

³ For simplicity, boron values are expressed as boron equivalents even though the tested substance was boric acid or another borate. To convert boron equivalents to boric acid concentrations, divide the boron equivalent by 17.5% (see Table 4). For example, 0.1 mg-B/L is equivalent to 0.6 mg-boric acid/L.

- (c) Well-done study and report that meets basic scientific principles
- (d) Peer-reviewed technical publication
- (e) Comparable to guideline study with acceptable restrictions

Studies with significant deviations from current scientific or protocol practices were rated “3. *Not reliable*” with the descriptive qualifiers:

- (f) Method not validated
- (g) Documentation insufficient for assessment
- (h) Does not meet important criteria of current standard methods
- (i) Methods deficient in critical aspects
- (j) Test system unsuited for standard method

Some reported test results could not be evaluated because of limited information and were rated “4. *Not assignable*” with the descriptive qualifiers:

- (k) Insufficient documentation to permit review
- (l) Secondary literature citing some other primary source
- (m) Only reports an endpoint value or summary statement

4.2.2 Aquatic Acute Test Results

A summary of appropriate acute test results are detailed in Table 14. Eisler (2000) and Dyer et al (2001) have compiled numerous literature values. The most sensitive tests report that acute effects on fish are in the range of 10-20 mg-B/L although the quality of these studies was rated low (Reliability code 4). The lowest daphnid acute value is 133 mg-B/L. Algal and microbial inhibition studies (Table 15) suggest less toxicity: *Selenastrum* growth was not affected at 93 mg-B/L and activated sludge respiration showed minimal effects at 683 mg/L boric acid (119 mg-B/L).

Other results showed substantially higher values (less toxicity) with fish acute values often exceeding 100 mg-B/L. Juveniles and fry appear to be the most sensitive fish life-stage (Hamilton, 1995; Hamilton and Buhl, 1990).

Aquatic studies have been used to create species sensitivity distributions (SSD). SSD incorporate all available information into a summary statistic by calculating a designated percentile of the distribution, such as the 5th percentile. Such values indicate a concentration that is predicted to protect 95% of all species (included those not tested) (Cardwell et al., 1993). Dyer et al. (2001) calculated the Acute 5th percentile concentration for aquatic species. Using the procedure of Aldenberg and Slob (1993), the acute 5th percentile SSD concentration is 43 mg-B/L (246 mg-boric acid/L). Using a similar procedure of Stephan et al. (1985) produces a similar value, 46 mg-B/L (263 mg-boric acid/L).

Table 14: Acute toxicity for boron ⁴
(For algal and protozoan data, see Table 15)

Guideline or method	Species	Endpoint	Duration	Result (LC ₅₀) in mg-B/L	Reference (Reliability Code ⁵)
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⁴ For simplicity, boron values are expressed as boron equivalents even though the tested substance was boric acid or another borate. To convert boron equivalents to boric acid concentrations, divide the boron equivalent by 17.5% (see Table 4).

ASTM E729-80	<i>Daphnia magna</i> (invertebrate)	Mortality	48 hr	133	Gersich, 1984 (1b)
US EPA 1975	<i>Daphnia magna</i> (invertebrate)	Mortality	48 hr	226	Lewis and Valentine, 1981 (1b)
US EPA 1975	<i>Daphnia magna</i> (invertebrate)	Mortality	48 hr	141	Maier and Knight, 1991 (1b)
US EPA 1975	<i>Chironomus decorus</i> (midge)	Mortality	48 hr	1376	Maier and Knight, 1991 (1b)
ASTM E729-88	<i>Ptychocheilus lucius</i> (Colorado squawfish)	Mortality of swimup fry	96 hr	279	Hamilton 1995 (1b)
ASTM E729-88	<i>Xyrauchen texanu</i> (Razorback sucker)	Mortality of swimup fry	96 hr	233	Hamilton 1995 (1b)
ASTM E729-88	<i>Gila elegans</i> (Bonytail)	Mortality of swimup fry	96 hr	280	Hamilton 1995 (1b)
ASTM E729-88	<i>Catostomus latipinnis</i> (Flannelmouth sucker)	Mortality	96 hr	125	Hamilton and Buhl 1997 (1b)
ISO 7346/II	<i>Brachydanio rerio</i> (Zebrafish)	Mortality	96 hr	14.2	Guhl, 1992 (4k,l,m)
ASTM E729-80	<i>Oncorhynchus tshawytscha</i> (Chinook salmon)	Mortality	96 hr	600 (freshwater) 725 (brackish water)	Hamilton and Buhl, 1990 (1b)
ASTM E729-80	<i>O. kisutch</i> (Coho salmon)	Mortality	96 hr	447 (freshwater) 600 (brackish water)	Hamilton and Buhl, 1990 (1b)

4.2.3 Aquatic: Chronic Test Results

A list of scientifically defensible chronic data is detailed in table 15. Most of these studies were included in the probabilistic analysis carried out by Dyer (2001) on 18 species. Dyer calculated the Chronic 5th percentile concentration for aquatic species to be 3.45 mg-B/L. The chronic values used by Dyer are shown in Table 15, along with other results.

Table 15: Chronic test results for boron ⁶

Guideline /Method	Species	Endpoint	Duration	Result (mg-B/L)	Reference (Reliability ⁷)
OECD 209	Activated sludge, domestic sewage treatment plant	Respiration inhibition	3 hr	>1001	Hanstvelt and Schoonmade, 2000 (1a)
DIN 38412 T.8	<i>Pseudomonas putida</i> (microbe)	Growth	16 hr	59 (NOEC, species mean of 2 tests)	Dyer 2001 (2c,d)
	<i>Entosiphon sulcatum</i> (protozoan)	Growth	72 hr	15 (NOEC)	Dyer 2001 (2c,d)

⁵ See Section 4.2.1 for description of reliability codes and qualifiers.

⁶ For simplicity, boron values are expressed as boron equivalents even though the tested substance was boric acid or another borate. To convert boron equivalents to boric acid concentrations, divide the boron equivalent by 17.5% (see Table 4).

⁷ See Section 4.2.1 for description of reliability codes and qualifiers.

OECD 201	<i>Selenastrum capricornutum</i> (alga)	Growth Biomass	74.5 hr 74.5 hr	212 (E ₆ C ₅₀) 277 (E _r C ₅₀) 93 (NOE _r C)	Hansveit and Oldersma, 2000 (1a)
	<i>Anacystis nidulans</i> (bluegreen alga)	Growth, chlorophyll, protein	96 hr	50 (NOEC) 75 (LOEC)	Martinez et al., 1986 (2c,d,e)
	<i>Anabaena PCC7119</i>	Growth	96 hr	50 (LOEC)	Mateo et al. 1987 (2c,d,e)
	<i>Chlorella pyrenoidosa</i>	Growth	96 hr	10 (NOEC)	Fernandex et al 1984 (2c,d,e)
	<i>Chlorella pyrenoidosa</i>	Growth	96 hr	50 (NOEC)	Maeso et al, 1985 (2c,d,e)
	<i>Lemna minor</i> (duckweed)	Growth	7 day	60 (NOEC) >60 (LOEC)	Wang, 1986 (2d,e)
	<i>Phragmites australis</i> (reed)	Growth (height, biomass)	4 month	>4 (NOEC)	Bergmann et al., 1995 (4k,l)
	<i>Paramecium caudatum</i> (protozoan)	Growth, reproduction	72 hr	20 (NOEC)	Dyer 2001 (2c,d)
	<i>Opercularia bimarginata</i> (protozoan)	Growth, reproduction	72 hr	10 (NOEC)	Dyer 2001 (2c,d)
DIN 38412 T.9	<i>Scenedesmus subspicatus</i> (alga)	Growth	96 hr	10 (NOEC) 30 (EC10)	Guhl 1992 (4k,l,m) ⁸
US EPA, 1996	<i>Spirodella polyrhiza</i> (duckweed)	Growth rate	10 day	6.1 (NOEC)	Davis et al. 2002 (1b)
	<i>Phragmites australis</i> (reed)	Growth (height, biomass)	4 month	>4 (NOEC)	Bergmann et al., 1995 (2c,d)
ASTM E729-80	<i>Daphnia magna</i> (daphnid)	Growth, reproduction	21 day	6.4 (NOEC)	Gersich, 1984 (1b) ⁹
	<i>Daphnia magna</i> (daphnid)	Growth, reproduction	14 to 21 days	9.1 (NOEC, species mean of 4 tests)	Dyer 2001 (2c,d)
OECD, US EPA	<i>Ceriodaphnia dubia</i>	Growth, reproduction	14 day	10 (NOEC) 18 (LOEC)	Hickey 1989 (2c,d,e) ⁹
OECD 211	<i>Daphnia magna</i> (daphnid)	Growth, reproduction	21 day	10 (NOEC) 18 (LOEC)	Hoofman et al 2000c (1a)
Draft OECD	<i>Chironomus riparius</i> (midge)	Growth, emergence	28 day	180 (NOEC) using spiked sediments	Hoofman et al 2000b (1a)
US EPA	<i>Chironomus decorus</i> (midge)	Growth	96 hr	10 (NOEC)	Maier and Knight 1991 ⁹ (2c,d,e)

⁸ Data also used by Dyer (2001) to calculate SSD.

	<i>Brachydanio rerio</i> (non-salmonid fish)	Mortality of embryo, Growth	6 month	10 (LOEC) 0.0002 (deficiency LOEC)*	Rowe et al. 1998 ⁹ (2c,d)
OECD 210	<i>Brachydanio rerio</i> (non-salmonid fish)	Mortality, growth, condition	34 day	5.6 (NOEC) 18 (LOEC)	Hoofman et al 2000a (1a)
	<i>Onchorhynchus mykiss</i> (rainbow trout)	Mortality of embryo, growth	>2 weeks	11 (LOEC) 0.5 (deficiency NOEC*) 0.1 (deficiency LOEC*)	Rowe et al, 1998 (2c,d)
	<i>Onchorhynchus mykiss</i> (rainbow trout)	Mortality of embryo, growth	28 day	5.5 (LC10, species mean of 5 tests)	Dyer 2001 (2c,d)
	<i>Ictalurus punctatus</i> (non-salmonid fish)	Mortality of embryo, growth	9 day	13.8 (LC10, species mean of 3 tests)	Dyer 2001 (2c,d)
	<i>Carassius auratus</i> (non-salmonid fish)	Mortality of embryo, growth	7 day	16.7 (LC10, species mean of 4 tests)	Dyer 2001 (2c,d)
	<i>Micropterus salmoides</i> (non-salmonid fish)	Mortality of embryo, growth	9 day	6 (LC10)	Dyer 2001 (2c,d)
	<i>Rana pipiens</i> (frog)	Mortality, larval development	7.5 day	29 (LC10, species mean of 4 tests)	Dyer 2001 (2c,d)
	<i>Rana sylvatica</i> (frog)	Mortality, larval development	23 day	49.5 (NOEC)	Laposata and Dunson 1998 ⁹ (2c,d)
	<i>Bufo fowleri</i> (toad)	Mortality, larval development	7.5 day	41 (LC10, species mean of 2 tests)	Dyer 2001 (2c,d)
	<i>Ambystoma jeffersonian</i> (amphibian)	Larval deformities	23-day	<49.5 (NOEC)	Laposata and Dunson 1998 ⁹ (2c,d)
	<i>Ambystoma maculatum</i> (amphibian)	Larval deformities	23-day	<49.5 (NOEC)	Laposata and Dunson 1998 ⁹ (2c,d)

* Adverse effects (embryo mortality or growth inhibition) were observed at concentrations less than specified value, indicating deficiency.

Sub-chronic studies by Birge and Black (1977) produced the lowest reported boron toxicity values for rainbow trout (*Oncorhynchus mykiss*), an LC1 of 0.01 mg-B/L and an LC50 of 79 mg B/L based upon embryonic mortality and teratogenesis in a 28-day test. The extremely low LC1 value was derived by extrapolation. Unfortunately, the results were not repeatable in other laboratories or

in the original laboratory when using natural waters or when testing rainbow trout from a different hatchery (Black et al. 1993). The extrapolation relied on results that were within the range of variability seen in controls with this type of test and the magnitude of response was so small as to likely be of no consequence to natural fish populations. A re-evaluation by the same authors suggested that reasonable, environmentally acceptable limits for boron in aquatic systems would be much greater than the original LC1 value (Black et al. 1993). The test conditions used by this research team have not been adopted as a standard method. Because of this and other limitations, the study was rated “3. Not reliable” and not used in derivation of a PNEC.⁹

Rowe et al. (1998) reported that rainbow trout (*O. mykiss*) was affected by lack of boron at 9 µmol B/L (0.1 mg-B/L) and zebrafish (*Danio rerio*) were affected by lack of boron at 0.2 µmol B/L (0.002 mg-B/L). The lack of boron elicited impaired growth and embryonic death. Fort et al (1998) reported adverse effects on embryo-larval development in *Xenopus* cultured in 3 µg-B/L or less. These studies showing essentiality suggest that problems seen by some researchers at very low boron concentrations may reflect deficiency from too little boron rather than toxicity from too much boron. Loewengart (2001) concluded that some of the early low values may have been due to deficiency of boron, rather than toxicity.

Awareness of the early trout studies led to studies of wild trout population data and these reviews suggest that boron is not very toxic to wild trout where boron occurs naturally. Loewengart (2001) pointed out that nearly half of streams in California (USA) with viable populations of wild trout have boron concentrations equal to or above 0.1 mg-B/L. One stream (Little Warm Springs Creek, California) had a boron concentration of 13 mg/L.

The Firehole River (Wyoming, USA) has a world-renowned trout fishery, even though it has elevated boron concentrations. The river receives geothermal input from geysers and hot springs, so has warm waters as well as elevated boron. Studies of trout reproduction in the Firehole River system reported that trout delayed spawning until winter, presumably to reduce stress from high summer temperatures, but in doing so, reproduce successfully in stream areas where boron is highest, ranging from 0.4 to 1.2 mg-B/L (Meyer et al. 1998).

Similar results are reported by Guhl (1992) for other trout species in German surface waters and hatcheries, with trout populations in waters of 0.1 mg-B/L (Taubergerien area in southern Baden), in waters of 0.8 to 1.2 mg-B/L (Schilling lake in upper Bavaria) and in hatcheries with 0.01 to 0.08 mg-B/L (Albaum and Lohmar facilities). These studies provide an additional line of evidence regarding environmentally acceptable boron concentrations.

A number of biocenosis (multispecies) studies have been carried out (Guhl, 1992). In a laboratory microcosm test using abundance and presences of prokaryotes and micro-eucaryotes of six trophic stages, the NOEC for borate was found to be 2.5 mg-B/L and LOEC of 5 mg-B/L. A laboratory river model, consisting of sequence of several vessels fed a mixture of treated wastewater and drinking water was monitored for biotic indices of the prokaryotes and micro-eucaryotes. No adverse effect was found at 1 mg-B/L so the the threshold for effect is greater

⁹ The European Union member states have reviewed other data on fish early-life-stage tests and decided not to use data from Birge’s test method if other fish data are available. See, for example, page 40 of http://ecb.jrc.it/DOCUMENTS/Existing-Chemicals/RISK_ASSESSMENT/DRAFT/R307_0403_env.pdf and page 29 of <http://chimie.ineris.fr/fr/lespdf/metodexpchron/naphtalene.pdf>. These and other sources note that the results from Birge’s studies are consistently an order of magnitude below studies from other researchers with no clear explanation for the discrepancies.

than 1 mg-B/L. Studies of outdoor ponds with up to 29 species over two years showed no significant difference when treated with 0.7 mg-B/L. Field studies in outdoor ponds over two vegetation periods showed no toxic effects of borate at concentrations between 0.16 and 1.52 mg-B/L. A summary of these studies is detailed in Table 16 (Guhl, 1992).

Table 16: Borate toxicity to biocenotic systems

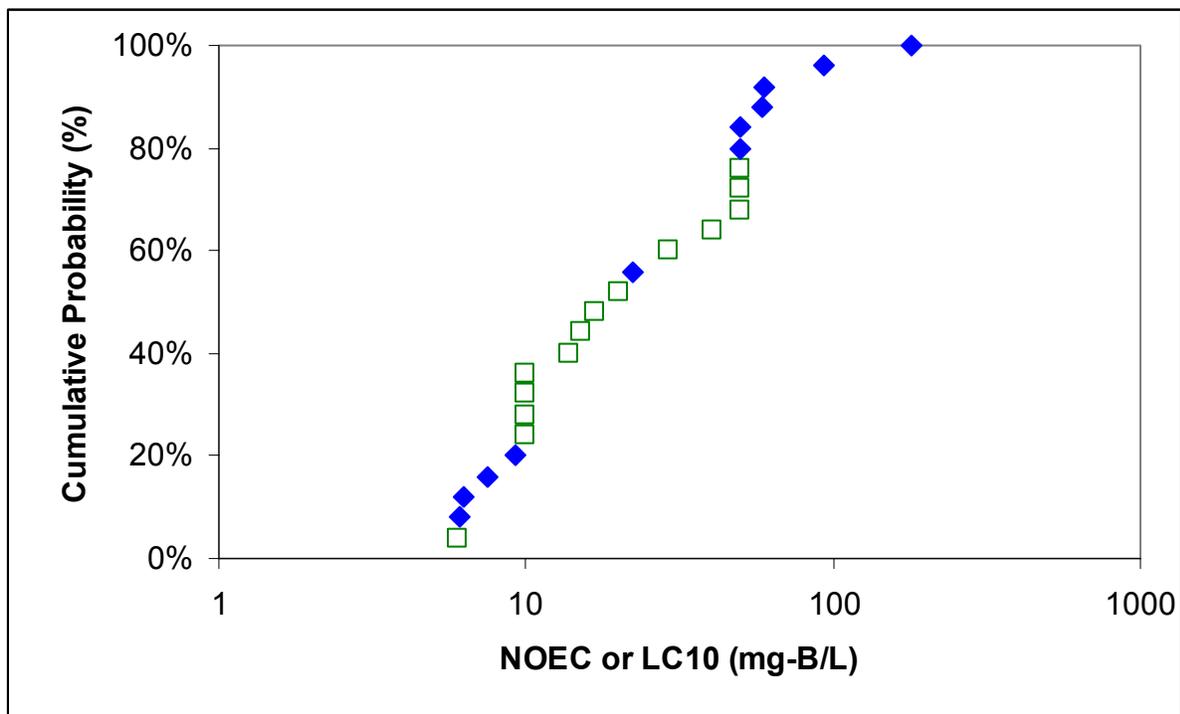
Biocenosis	Test type	Duration	Effect	Borate in solution (mg-B/L)	Reference (Reliability)
Activated sludge community	Chronic	72 h	NOEC/LOEC No function damage	20/50 110	Guhl 1992 (4k,m)
Biocenosis	Microcosm	28 d	NOEC/LOEC	2.5/ 5	Guhl, 1992 (4k,m)
	Outdoor pond	2 years	CWE ¹	0.7	Guhl, 1992 (4k,m)
	Field study	5 months	CWE	0.16 1.52	Guhl, 1992 (4k,m)
	Stair case river model	6 weeks	CWE	1	Guhl, 1992 (4k,m)

¹ Concentration without effect

Dyer (2001) based the Chronic 5th percentile concentration on species mean acute values if multiple tests were available. The HC₅ value reflected tests on *Pseudomonas putida*, *Entosiphon sulcatum*, *Paramecium caudatum*, *Opercularia bimarginata*, *Scenedesmus subspicatus*, *Daphnia magna*, *Ceriodaphnia dubia*, *Chironomus decorus*, *Oncorhynchus mykiss*, *Ictalurus punctatus*, *Carassius auratus*, *Micropterus salmoides*, *Brachydanio rerio*, *Rana pipiens*, *Rana sylvatica*, *Bufo fowleri*, *Ambystoma jeffersonian*, and *Ambystoma maculatum*.

Some data shown in Table 15 were not available to Dyer. Additional studies on *Daphnia magna* modify the species mean value from 9.1 to 9.3 mg-B/L. Additional studies on *Oncorhynchus mykiss* modify the species mean value from 5.5 to 6.2 mg-B/L. A value used by Dyer for *Brachydanio rerio* appeared to be incorrect (75 mg-B/L); the species mean value from 2 tests is 7.5 mg-B/L. Inclusion of several additional algal species leads to data points at the higher end of the distribution. One additional algae was among the more sensitive data points at the lower end of the distribution (*Spirodella*). In general, however, the calculated 95th percentile value from Dyer is consistent with the revised data and will be used.

Figure 2. Chronic Aquatic Toxicity: Species Sensitivity Distribution (Values shown in open squares were used by Dyer 2001. Other values are newer additional species or are revised species mean values using recent test results.)



4.2.4 Terrestrial – Acute Test Results

Boron is naturally present in soil at levels of between 10-30 ppm although there are geographical areas that are much higher. It is only the water soluble boron content of the soil that is available to the plant (Campbell, 1989). The available boron is further restricted in high pH soils. Boron is an essential micronutrient for all plants and in most parts of the world boron is added to address deficiency in soil. However an excess of boron can lead to phytotoxicity. Symptoms of boron toxicity are similar across species and consist of a marginal and tip chlorosis which is quickly followed by a necrosis. Most research on plants has been associated with agricultural applications and crop yield. Such studies are usually longer term and are discussed in Section 4.2.5.

4.2.4.1 Plants

Environment Canada (2005) has recently published a biological test method for measuring emergence and growth of terrestrial plants that recommends use of boric acid as a reference toxicant. Environment Canada reported that endpoints (7- and 10-day IC50s for shoot length) for the 12 plant species tested ranged from 452 mg-boric acid/kg-soil (dry wt) for carrot (*Daucus carota*) to 1603 mg-boric acid/kg-soil (dry wt) for alfalfa (*Medicago sativa*). In an interlaboratory study, 6 laboratories tested cucumber (*Cucumis sativus* var. Marketmore 76) and found the mean 7-day IC50 for shoot length was 693 mg-boric acid/kg-soil (dry wt). The range of values was 379 to 961 mg-boric acid/kg with a coefficient of variation of 30%.¹⁰

Aitken and McCallum (1988) evaluated toxicity of boron in soil porewater to sunflower (*Helianthus annuus*) over 14 days, reporting a toxicity threshold of 1.9 to 2.4 mg-B/L, depending

¹⁰ Boric acid is 17.5% boron by weight. Boron equivalents to the given boric acid values are: 452 mg boric acid = 79 mg-B, 1603 mg boric acid = 281 mg-B, 693 mg boric acid = 121 mg-B, 379 mg boric acid = 66 mg-B, and 961 mg boric acid = 168mg-B.

on which model was fitted to the data. The measured endpoint was dry weight of above-ground biomass. However, toxicity was not observed in all soil types tested. Plants were transplanted to soils with boric acid, so germination was not evaluated and plants were actually more than 14 days beyond germination.

Other plant studies are discussed in the section on Plants under Terrestrial - chronic test results. Chronic test results will be used to establish PNEC-soil values.

4.2.4.2 Invertebrates

Table 17 summarizes available data on acute toxicity to invertebrates. Borates are used as effective pesticides for termites, ants, cockroaches due to the interference with metabolic pathways causing toxicity. These pesticidal treatments are carried out at percentage levels of borates and are summarized as chronic results in Section 4.2.5.2.

Table 17: Boron toxicity to terrestrial invertebrates

Species	Test Substance	Exposure	LC/LD50	NOEC	Reference (Reliability ¹¹)
<i>Apis mellifera</i> (honeybee)	Boric acid	96-h	>363 ug B/Bee		Atkins 1987 (4k)
<i>Apis mellifera</i>	Boric acid	Not reported	175,000 mg B/L	87,000 mg B/L	Ostrovskii 1955 (4k)
<i>Eisenia fetida</i> (earthworm)	Boric acid	14-d	>175 mg B/kg dry soil	>175 mg B/kg dry soil	Henzen 2000 (1a)
<i>Eisenia andrei</i> (earthworm)	Boric acid	14-d	568-689 mg B/kg dry ref soil, 581-694 mg B/kg dry artificial soil	350 (est.) mg-B/kg dry artificial and reference soils	Stantec, 2004 (2e)
<i>Lumbricus terrestris</i> (earthworm)	Boric acid	14-d	501 mg-B/kg dry ref soil; 301 mg-B/kg dry artificial soil	875 (est.) mg-B/kg dry ref soil; 350 (est.) mg-B/kg dry artificial soil	Stantec, 2004 (2 ^e)
<i>Folsomia candida</i> (collembollan)	Boric acid	14-d	116 mg-B/kg dry ref soil; 140 mg-B/kg dry artificial soil	Not reported	Becker-van Slooten et al. 2003 (2e)
<i>Onychiurus folsomi</i> (collembollan)	Boric acid	14-d	248 mg-B/kg dry reference soil ^a	Not reported	ESG International 2003 (2e)

^a Endpoint: number of juveniles

As shown in Table 17, acute ecotoxicity values are typically in the range of 100-600 mg-B/kg dry soil.

¹¹ See Section 4.2.1 for description of reliability codes and qualifiers.

4.2.5 Terrestrial Chronic Results

Terrestrial studies have mostly involved plants, reflecting the widespread boron deficiencies observed in certain agricultural regions. As detailed below, studies of terrestrial invertebrates suggest that plant toxicity is the more sensitive endpoint. As noted above, agricultural application rates of 1-2 kg-B/ha translate to soil concentration estimates of 0.3 to 0.6 mg-B/kg. Plants designated as “sensitive” to boron are those where some injury is anticipated at 1 to 5 mg-B/L-soil solution (Sprague, 1972; Eisler, 2000). No SSD or similar statistical distribution appears in the literature.

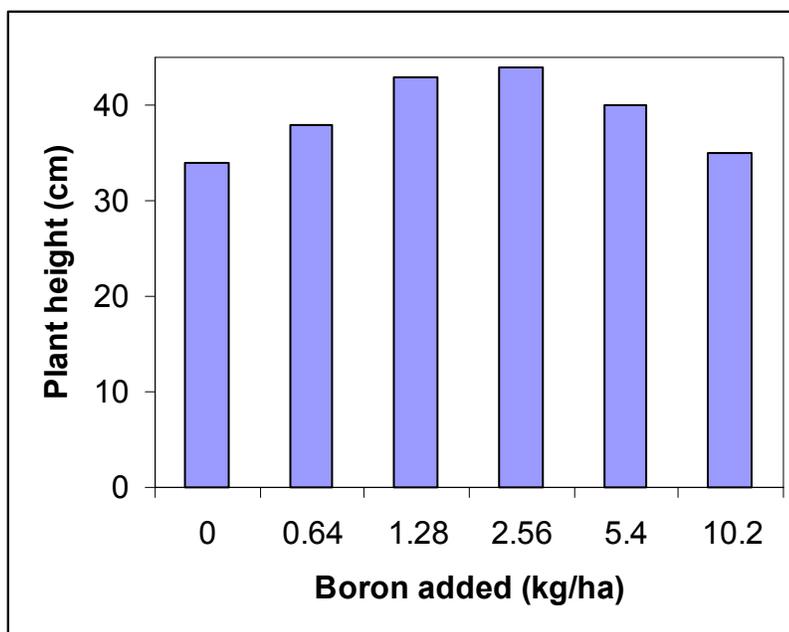
4.2.5.1 Plants

Boron is an essential micronutrient for all plants and borates are added to agricultural land in amounts determined by the needs of the crop. Boron deficiency in soil is more prevalent than boron toxicity (Gupta 1985). However, boron is phytotoxic at higher concentrations.

An illustration of a deficiency-toxicity pattern is shown in Fig. 2. Shuxiang et al. (2002) measured oil rape (*Brassica oleracea* cv “Zhongyou 119”) growth in B-deficient soil from southeast China. Plant height showed optimal growth at 1.28-2.56 kg-B/ha addition. Biomass was significantly increased at the 2.56 kg-B/ha addition relative to other treatments. Symptoms of boron toxicity (scorching of older leaf margins) were seen at the highest addition level.

Figure 2. Boron deficiency and toxicity in oil rape (*Brassica oleracea*)

Plant height at harvest in pot experiments using a B-deficient soil (after Shuxiang et al., 2002).



The band between essentiality and toxicity is typically narrow (e.g., less than 10-fold). Symptoms of boron toxicity are similar in most plants and consist of chlorosis of the tips and margins of older leaves (Shorrocks, 1984). Leaves normally contain 40-100 mg B/kg dry weight, rising to 250 mg B/kg dry weight when soils approach toxic levels. A level of between 700-1000 mg/B/kg will occur in cases of extreme toxicity (Nable et al, 1997). However, most studies of

plants focus on yield which is the endpoint of agricultural interest. This may be considered a chronic, sub-lethal endpoint.

Table 18 summarizes chronic plant studies arranged in approximate order of decreasing sensitivity. For experimental convenience, tests of boron have frequently used water-only or water-plus-sand test systems (resulting in endpoints expressed as mg-B/L) or soil application rates (expressed as kg-B/ha). There are no simple translator relationships to predict soil porewater concentrations from soil boron content or vice versa (Goldberg et al. 2000). Consequently, attention must be paid to the type of exposure media and analysis used in different studies.

The initial work was reported by Eaton in 1944, testing 50 species in soil solution; only the two most sensitive test results are shown in Table 18. Eaton's results have been used by Sprague (1972) and Eisler (2000) as the basis of tolerance groupings. Butterwick et al (1989) observed that the range of concentrations within which boron is essential to some plants overlaps the range where it is toxic to other species. Sprague noted that over 70% of the plants tested by Eaton did best with more than a trace of boron, and 46% did best with more than 1 mg-B/L.

Plants have been divided into sensitive, semi tolerant and tolerant (Eisler, 2000). Sensitive plants show optimal growth at trace to 1 mg B/L in soil water, with injury at 1-5 mg B/L, whilst tolerant plants show optimal growth at 5 to 10 mg B/L with indications of damage at 5 to 25 mg B/L. Blackberry (*Rubus* sp.), Lemon (*Citrus limonin*) and big leaf Maple (*Acer macrophyllum*) are among the species characterised as sensitive. Turnip (*Brassica rapa*), cotton (*Gossypium hirsutum*) and asparagus (*Asparagus officinalis*) are among the tolerant species.

Based on the soil solution test results, Eisler (2000) suggested that 1 mg-B/L be considered a likely guideline for protection of sensitive plant species. Eisler (2000) and Gupta (1985) suggested that concentrations of 5 to 10 mg-B/L are consistently associated with toxic effects.

Agricultural practice applies boron to soil at rates varying with crop, but generally in the range of 0.5 to 7.6 kg-B/ha. This corresponds to a soil concentration of 0.15 to 2.3 mg-B/kg. Mortvedt et al. (1992) reported applications rates resulting in 0.16 to 2.0 mg-B/L. Van de Plassche et al. (1999) used a smaller soil density (1400 kg/m³) but obtained approximately the same results. Van de Plassche et al. then concluded that 0.1 mg-B/kg could be added without concern for ecotoxicological effects (the "maximum permissible addition" value). This is a very conservative proposal and would appear to result in likely boron deficiencies to many plant species.

Table 18: Chronic Toxicity of Boron in Soil to Plants¹²

Plant Species	Boron Compound	Overt Toxicity	Yield Reduction	Analysis	Reference (Reliability ¹³)
<i>Acer macrophyllum</i> Pursh (big leaf Maple)	Boron (compound not specified)	0.9 ppm-B	0.5-0.9 ppm-B	Extractable B	Glaubig and Bingham 1985 (2c,d)
<i>Rubus</i> sp.	Boric acid	5 mg-B/L	1 mg-B/L	Soil solution	Eaton 1944 (2c,d)

¹² For simplicity, boron values are expressed as boron equivalents even though the tested substance was boric acid or another borate. To convert boron equivalents to boric acid concentrations, divide the boron equivalent by 17.5% (see Table 4).

¹³ See Section 4.2.1 for description of reliability codes and qualifiers.

(Blackberry)					
<i>Citrus limona</i> (lemon)	Boric acid	5 mg-B/L	1 mg-B/L	Soil solution	Eaton 1944 (2c,d)
<i>Helianthus annuus</i> (Sunflower)	Boric acid	8 to 12 kg-B/ha (ca. 2.3 to 3.5 mg-B/kg)	1.9 to 2.4 mg-B/kg (Toxicity thresholds)	Porewater	Aitken and McCallum 1988 (2c,d)
<i>Arbutus menziesii Pursh</i> (Madrone)	Boron (compound not specified)	5 ppm-B	2-5.4 ppm-B	Extractable B	Glaubig and Bingham 1985 (2c,d)
<i>Umbellularia Californica</i> (California Laurel)	Boron (compound not specified)	4 ppm-B	3-4 ppm-B	Extractable B	Glaubig and Bingham 1985 (2c,d)
<i>Phaseolus vulgaris</i> (field beans)	Sodium borate		3.2 mg-B/kg 1.6 mg-B/kg (NOEC)	Extractable B (hot water)	Gupta and Cutcliffe 1984 (2c,d)
<i>Phaseolus vulgaris</i> (Snap Beans)	Sodium borate	2-4 ppm-B	>4 ppm-B	Bulk soil	Gupta 1983 (2d,e)
<i>Zea Mays</i> (Corn)	Sodium borate	2-4 ppm-B		Bulk soil	Gupta 1983 (2c,d)
<i>Lycopersicon esculentum</i> (Tomatoes)	Sodium Borate	4 ppm-B	>4 ppm-B	Bulk soil	Gupta 1983 (2c,d)
<i>Brassica oleracea var. Capitata</i> (cabbage)	Sodium borate	None	None at 6.3 mg-B/kg	Extractable B (hot water)	Gupta and Cutcliffe 1984 (2c,d)
<i>Hordeum vulgare</i> (barley)	Boric acid	2 mg-B/kg	8 mg-B/kg	Extractable B (mannitol)	Riley et al. 1994 (2c,d)
<i>Psium salivum</i> (Pea)	Boron (compound not specified)	20 mg/kg	20-50 mg/kg	Bulk soil	Bagheri et al., 1994 (2c,d)
<i>Hibiscus cannabinus</i> (Kenaf)	Boric acid	45 mg-B /kg	45 mg-B /kg	Bulk soil	Banuelos et al., 1996 (2c,d)
<i>Gossipium hirsutum</i> (Cotton)	Boric acid	45 mg-B /kg	45 mg-B /kg	Bulk soil	Banuelos et al., 1996 (2c,d)

Values for plant tests in soil or soil extracts will be used to determine a PNEC for soil, while tests using soil solution (e.g., Eaton) will be used to determine a PNEC for irrigation water.

4.2.5.2 Invertebrates

Terrestrial invertebrate chronic values were approximately 10 times lower than acute values, as shown in Table 19. The lowest chronic NOEC reported was 5.2 mg-B/kg dry artificial soil from an earthworm test (*Eisenia andrei*) reported by Stantac (2004). However, this result was significantly lower than a simultaneous test using the OECD draft method, 52 mg-B/kg in the 8-week protocol, and also much lower than a test using the same protocol but over a longer time (9-weeks), which gave a NOEC of 20 mg-B/kg dry soil (114 mg-boric acid/kg dry soil).

Comparison of Tables 18 and 19 shows that invertebrate were, as a group, less sensitive than plants..

Table 19. Chronic Toxicity of Boron in Soil to Terrestrial Invertebrates¹⁴

Species	Test Substance	Exposure	LC/LD50	NOEC	Reference (Reliability ¹⁵)
<i>Eisenia andrei</i>	Boric acid	63-d, Env. Canada draft protocol	77-99 mg-B/kg dry artificial soil ^a	20 mg-B/kg dry artificial soil ^b	Stantac 2004 (2e)
<i>Eisenia andrei</i>	Boric acid	56-d, Env. Canada draft protocol	26 mg-B/kg dry artificial soil ^c	5.2 mg-B/kg dry artificial soil ^c	Stantac 2004 (2e)
<i>Eisenia andrei</i>	Boric acid	56-d, OECD draft protocol	59 mg-B/kg dry artificial soil ^c	52 mg-B/kg dry artificial soil ^{a,b,c}	Stantac 2004 (2e)
<i>Folsomia candida</i>	Boric acid	28-d	26 mg-B/kg dry ref soil; 30 mg-B/kg dry artificial soil	Not reported	Becker-van Slooten et al. 2003 (2e)
<i>Onychiurus folsomi</i>	Boric acid	35-d	20 mg-B/kg dry reference soil; 88 mg-B/kg dry artificial soil ^a	22 mg-B/kg dry reference soil; 44 mg-B/kg dry artificial soil ^a	ESG International 2003 (2e)

^a Endpoint: number of juveniles

^b Endpoint: number of unhatched cocoons

^c Endpoint: juvenile dry mass

4.2.5.3 Micro-organisms

Effects of boric acid on micro-organisms are summarized in Table 20. Using the standardized OECD method, Hanstvelt and Schoonmade (2001) found the EC₂₀ for activated sludge to be 112 mg-B/L. This is consistent with earlier tests of activated sludge.

Bowen and Gauch (1966) evaluated fungi and found toxic effects at 50 to 4000 mg-B/kg using solid culture media. They reported a strong inhibition in micromycetes at concentrations above 1000 mg-B/kg.

Crommentuijn *et al* (1995), studied the effect of boron on a range of microbial processes including nitrification and dehydrogenase, arylsulfatase and urease enzyme activity. A range of soil types were tested with organic matter and clay contents ranging from 2.27 to 9.27% and 17 to 45% respectively. No differences in effects were observed between the different soils. Interpretation of the effect data is difficult because of poor concentration-response relationships. However, the studies do indicate that nitrification was more sensitive than dehydrogenase and arylsulfatase activity and of similar sensitivity to urease activity. The lowest effect concentration was reported as an EC₁₁ of 5.4 mg/kg boron (dry weight) for urease activity.

¹⁴ For simplicity, boron values are expressed as boron equivalents even though the tested substance was boric acid or another borate. To convert boron equivalents to boric acid concentrations, divide the boron equivalent by 17.5% (see Table 4).

¹⁵ See Section 4.2.1 for description of reliability codes and qualifiers.

Boron compounds historically have been used against bacteria in the form of antiseptics and as preservatives in cosmetics and food. Some species of fungi exhibit effects of boron toxicity, resulting in the aborted growth of hyphae, perithecia and ascospores (Bowen & Gauch, 1966). The use of borates as preservatives in foods has been largely discontinued.

Borates are extensively used in biodeterioration control and wood preservation. These applications are regulated as pesticides for control of wood rotting fungi and wood-boring beetles and termites. Application rates up to about 1.2% (w/w) are required to be effective.

Table 20: Effects on Micro-organisms ¹⁶

Guideline /Method	Species	Endpoint	Duration	Result (mg-B/L)	Reference (Reliability ¹⁷)
OECD 209	Activated Sludge, domestic sewage treatment plant*	Respiration inhibition	3 hr	112 (EC ₂₀)	Hanstvelt and Schoonmade, 2000 (1a)
OECD 1971	Activated sludge treatment plant*	Performance		20 (NOEC) 120 (LOEC)	Gerike et al 1976 (2d,g)
	Activated sludge*	Respiratory inhibition		110 (EC ₀)	Guhl 1992 (4k,l,m)
	<i>Pseudomonas putida</i> (microbe)*	Growth		59.5 (NOEC, species mean of 2 tests)	Dyer 2001 (2c,d)
	<i>Pseudomonas putida</i> (microbe)*	Growth		291 (NOEC)	Guhl 1992 (4k,l,m)
	Nitrification in soil	Process	20 day	54 (EC7)	Crommentijn 1995 (4k,l,m)
	Dehydrogenase in soil	Process	24 hr	176 (EC50)	Crommentijn 1995 (4k,l,m)
	Arylsulfatase in soil	Process	30 min	270 (EC60)	Crommentijn 1995 (4k,l,m)
	Urease in soil	Process	2 hr	54 (EC13) 5.4 (EC11)	Crommentijn 1995 (4k,l,m)
	<i>Aspergillus niger</i> (black mould)	Yield (dry wt.)		1200 (NOEC) 1300 (LOEC)	Bowen and Gauch 1966 (2c,d)
	<i>Neurospora crassa</i> (bread mould)	Yield (dry wt.)		100 (NOEC) 250 (LOEC)	Bowen and Gauch 1966 (2c,d)
	<i>Penicillium chrysogenum</i> (fungi)	Yield (dry wt.)		500 (NOEC) 4000 (LOEC)	Bowen and Gauch 1966 (2c,d)
	<i>Saccharomyces cerevisia</i> (yeast)	Growth		5 (NOEC) 50 (LOEC)	Bowen and Gauch 1966 (2c,d)
	<i>Saccharomyces cerevisia</i> (yeast)	CO ₂ evolution		<150 (NOEC) 150 (LOEC)	Bowen and Gauch 1966 (2c,d)

*Used to estimate PNEC-STP

¹⁶ For simplicity, boron values are expressed as boron equivalents even though the tested substance was boric acid or another borate. To convert boron equivalents to boric acid concentrations, divide the boron equivalent by 17.5% (see Table 4).

¹⁷ See Section 4.2.1 for description of reliability codes and qualifiers.

The recommended PNEC-STP value uses the Hanstvelt and Schoonmade study result of 112 mg-B/L. The data for mould and fungi and soil processes suggest that micro-organisms are less sensitive than plants, so will not be used to calculate the PNEC-soil.

4.2.6 PNEC Calculations

4.2.6.1 PNEC aquatic

The EUSES model calculated a PNEC-aquatic based only on the rainbow trout data with an assessment factor of 10, resulting in a value of 0.55 mg-B/L. However, field data on trout in natural river systems suggests that this value is over-protective and a statistical approach is more appropriate.

Based on the statistical distribution of chronic laboratory studies (see Sections 4.2.2 and 4.2.3), the recommended PNEC-aquatic is 3.45 mg-B/L. This value was derived by Dyer (2001) as the PNEC_{0.05} (Predicted No Effect Concentration for 95% of the species) from chronic studies that were available for boron for all trophic levels. This value will be used for the risk assessment.

4.2.6.2 PNEC sediment

EUSES calculated a PNEC-freshwater sediment based on the single sediment test of the midge, *Chironomus decorus* (Hooftmann et al 2000b, see Table 15) with an assessment factor of 100, resulting in a value of 3.29 mg-B/kgwwt. A PNEC-freshwater sediment based on equilibrium partitioning was calculated as 1.2 mg-B/kgwwt, but this was not recommended by EUSES.

The recommended value of PNEC-sediment 3.29 mg-B/kgwwt will be used in the risk assessment.

4.2.6.3 PNEC terrestrial

Based on the effects data shown in Section 4.2.5, effects on plants appear the most sensitive taxa so will be used to recommend PNEC-terrestrial values. Two PNEC values will be used – a value for soil concentrations (mg-B/kg-soil) and a value for soil pore-water concentrations (mg-B/L). The second will be used to evaluate the risks associated with irrigation using wastewater effluent.

The EUSES model calculated a PNEC-for terrestrial organisms based on the Gupta and Cutcliffe (1984) result with field bean (*Phaseolus vulgaris*) with a NOEC of 1.6 mg-B/kg and an assessment factor of 10. This gave a PNEC-terrestrial of 0.16 mg-B/kg.

As discussed in Section 4.2.5.1, minimal agricultural application rates of boron would add about 0.15 mg-B/kg. The very conservative approach developed by van de Plassche et al. (1999) suggests that 0.1 mg-B/kg would pose no ecotoxicological risk.

The EUSES-based value of 0.16 mg-B/kg is used for evaluation of terrestrial ecotoxicity based on bulk soil concentrations, i.e., the PNEC-soil.

For irrigation, tests using soil solutions suggest that 1 mg-B/L represents a reasonable concentration of soluble boron in soil pore-water or soil solution that would not have adverse impacts. In fact, it might be sub-optimal for species that require relatively large amounts of boron. This value is below the threshold of toxicity observed in recent tests using extractable boron. The value of 1 mg-B/L is therefore recommended as the PNEC-soil porewater.

4.2.6.4 PNEC-STP

The recommended PNEC-STP value is the Hanstvelt and Schoonmade study result of 112 mg-B/L. This is consistent with other test results, such as from Guhl (1992) and Gerike et al. (1976) using activated sludge test systems.

4.3 ENVIRONMENTAL RISK CALCULATIONS

A comparison of predicted exposures with ecotoxicological effects thresholds allows evaluation of the relative risk. If the quotient of PEC/PNEC is less than 1, no significant environmental risk is evident. If the quotient (also termed the “risk characterization ratio”, RCR) exceeds one, then further evaluation may be needed. Ecological risk assessment also requires evaluation of the uncertainties to determine how confident one may be of the estimated risks and whether the limitations of the data used affect the reliability of the assessment.

4.3.1. Risk Characterization

Table 21 presents the PEC and PNEC values derived in earlier sections and the calculated ration of PEC/PNEC for the different environmental compartments. In every instance, the ratio is less than 1, suggesting no significant environmental risks are apparent from the borates used in liquid laundry and dishwashing products.

Table 21: Risk Characterization Ratios

Environmental Compartment	PEC Value as B	PNEC Value as B	PEC/PNEC
<i>Surface Water</i>	(see 4.1.4.c)	(see 4.2.6.a)	
Regional	0.45 mg/L	3.45 mg/L	0.13
Continental	0.0013 mg/L		<0.01
Local	0.45 mg/L		0.13
River Monitoring Data	0.447 mg/L		0.13
<i>Freshwater Sediment</i>	(see 4.1.4.e)	(see 4.2.6.b)	
Regional	0.008 mg/kg	3.29 mg/kgwwt	<0.01
Continental	0.003 mg/kg		<0.01
Local	0.96 mg/kg		0.29
<i>Agricultural Soil</i>	(see 4.1.4.d)	(see 4.2.6.c)	
Regional	<0.00008 mg/kg	0.16 mg/kgwwt	<0.01
Continental	<0.00002 mg/kg		<0.01
Local – 30 day	0.029 mg/kg		0.18
Local – 180 day	0.028 mg/kg		0.17
<i>Grassland Soil</i>	(see 4.1.4.d)	(see 4.2.6.c)	
Local – 180 day	0.006 mg/kg	0.16 mg/kgwwt	0.04
<i>Irrigation</i>	(see 4.1.4.d)	(see 4.2.6.c)	
Soil Porewater	0.016 mg/L	1 mg/L	0.02
STP effluent	0.044 mg/L		0.04
<i>Sewage Treatment Plant</i>	(see 4.1.4.f)	(see 4.2.6.d)	
Local	0.044 mg/L	112 mg/L	<0.01

4.3.2 Uncertainties

Limitations in the data or models used in an assessment may be minimal, resulting in relatively high confidence in the assessment, or may be substantial, suggesting that any conclusions should be considered tentative. Such uncertainties might result from use of inappropriate models or gaps in important data. A discussion of both the exposure and effects assessments helps address the strengths and limitations of the risk assessment.

The exposure assessment of borates was based on both monitoring of borate in European surface waters and modelling of fate and transport using the EUSES model. Some assumptions or limitations associated with the exposure assessment are:

1. The environmental concentrations associated with background levels of borates and uses other than the subject liquid detergent used and perborate uses were assumed to be zero. This allowed the monitored concentrations of boron in European surface waters to be used as the PEC-aquatic. This overestimates the actual PEC and would overestimate risk.
2. The use of perborates in laundry applications is known to be declining in Europe, so the associated wastewater concentrations are also declining. The monitoring data represents older use patterns of perborates and so is likely to overestimate current or near-future concentrations. This would overestimate the actual PEC.
3. The 90th percentile of monitored concentrations was used in derivation of the PEC-aquatic. This is accepted practice, but should be recognized as a conservative approach for estimating typical or average exposure.
4. The EUSES model incorporates a number of fate models that are driven by physico-chemical parameters. Some of the parameters for boric acid (such as octanol/water partitioning, melting point, boiling point) were flagged by EUSES as being outside the normal range. Many fate models are designed for organic chemicals. These factors contribute to some uncertainty about the accuracy of the EUSES model.
5. The EUSES model appears to have no mechanism to incorporate background concentrations. Seawater contains significant boron concentration (about 4.5 mg-B/L). Consequently, marine exposures were not considered. However, this pathway seems of minor importance, given the likely large dilution factor for wastewaters introduced into marine environments.
6. Equilibrium partitioning (EqP) is one model useful to estimate the relative distribution of a chemical between water, sediment or soil. Some components of the EUSES model appear to use EqP approaches. The behaviour of borates is not clearly in accord with EqP modelling: some literature is available on adsorption to clay or organic matter, but no strong patterns are evident. The application of EqP to borate distribution in the modelled environment may be uncertain.
7. The PEC-aquatic was based on the total environmental concentration from monitoring studies. The environmental concentration was derived using accepted procedures from field sampling, so the confidence in the PEC-aquatic is good.
8. The PEC-soil was driven by the amount of borate in sewage sludge. This was obtained from a single publication so confidence in this value is limited.
9. The PEC-irrigation used the PEC-aquatic. While confidence in the PEC-aquatic is good, irrigation patterns may not parallel the boron use patterns that drove the PEC-aquatic. For example, irrigation may be a regional activity that emphasizes southern Europe. The

Regional PEC derived by EUSES may not reflect the appropriate regional use of irrigation water.

10. The PEC-STP is based on detergent-specific use patterns, with good confidence.

The environmental effects assessment was based on laboratory and field data for plants, animals and microorganisms. Some assumptions or limitations of the assessment included:

1. The conventional concept of a PNEC assumes that there is a threshold concentration associated with ecotoxicity and that concentrations below the PNEC have no adverse effects, i.e., a zero concentration is ecologically fine. For essential substances, this concept is incorrect as deficiencies can affect species. Boron is essential for plants and many other organisms, so the conventional dose-response concept does not fully apply.
2. The PNEC-aquatic was derived using the Species-Sensitivity-Distribution (SSD) technique based on chronic studies of 18 species. Confidence in the results should be high because this uses a large data set.
3. Some early aquatic toxicity studies suggested extreme toxicity to trout. Subsequent laboratory and field studies do not support the early work. Boron has also been shown to be essential for trout, suggesting that boron deficiency might have influenced the early studies at low concentrations. The PNEC-aquatic (3.45 mg/L) uses data from the early studies but this is balanced by use of later studies. If the early studies were used uncritically, the SSD technique would produce a slightly lower PNEC-aquatic (1.3 mg/L). The alternative PEC/PNEC-aquatic ratio would still not exceed 1.
4. The number of terrestrial invertebrate studies has been increased recently, so this data set is substantially improved. The new data are consistent with previous values.
5. The PNEC-soil is driven by plant toxicity estimates. However, many of the available data use soil solutions, with results expressed as mg-B/L. There is no simple way to translate soil solution concentrations to bulk soil concentrations (or vice versa), so these data are difficult to use. These studies have been used in evaluation of irrigation water and with estimated soil pore-water concentrations.
6. Boron is essential for plants but many agricultural soils are boron-deficient. Many of the available plant studies were conducted to optimize boron application rates. These studies do not follow typical plant toxicity methods but have been used in this assessment. Some approaches to data quality review for risk assessment might exclude such studies. This would reduce the number of “acceptable” studies and would likely lead to use of a larger uncertainty factor.
7. Boron is known to be phytotoxic in excess. The variability between species is such that boron-sensitive species are likely to show toxic effects at concentrations where other species show deficiency symptoms. This reflects the conceptual limitation of the PNEC process that does not address risk of essential nutrients. A SSD technique thus does not appear suitable, and the PNEC-soil was therefore derived from the more sensitive species. The resulting conservative PNEC-soil might be below soil concentrations that cause deficiency symptoms in some crops.
8. The data for STP includes several studies with activated sludge systems. The most recent and OECD-compliant test is used for the PNEC-STP, giving good confidence in the results.

Overall, there are extensive data on borate concentrations in the aquatic environment and on the effects of borate on plants, animals and micro-organisms. The major limitations appear to be in quantitative models of boron transport and availability in soil: general patterns are known, but

detailed models to describe adsorption and desorption are not available for all soil types. The narrow range between boron deficiency and toxicity in plants poses some uncertainties in determination of appropriate assessment factors: if the range between toxicity and deficiency is less than 10, than use of 10-fold factors is inappropriate. These, however, reflect limitations in the ecological risk assessment framework more than uncertainties about the information available for borates.

Finally, the relatively small market volume of this application combines with the dispersed use pattern to suggest that overall uncertainty with the assessment results is low and the risk characterization ratios can be accepted with a high level of confidence. The market volume is quite small relative to the market for perborates and agricultural applications, so the influence of this application on environmental concentrations is expected to be small. The use as a laundry product means that environmental introductions are proportional to population and therefore dispersed throughout Europe.

4.4 DISCUSSIONS AND CONCLUSIONS

The use of boric acid and borax in consumer cleaning products is minor, representing less than 1% of the market, compared to other uses of borates and the use of borax in the manufacture of sodium perborate bleach. Other uses of borates such as agricultural applications as an essential plant micronutrient are likely to contribute to anthropogenic releases of borates into the environment. However, the major sources of borates are natural weathering of rocks and soils, volatilization of boric acid from seawater and volcanic activity. Variability in geological levels of boron results in considerable variability in soil and aquatic levels.

The conceptual framework of this environmental risk assessment is use of boric acid and borax in consumer cleaning products that enter the environment via wastewater. Most of the borate remains with the treated effluent and is released to the aquatic environment. Some borate may remain with the sewage sludge and may enter the terrestrial environment via soil application of sludge. If the treated effluent is used for irrigation, borate will enter the terrestrial environment with the irrigation water. Because borates are imported into Europe and incorporated directly into laundry and cleaning products, environmental exposures from production and manufacturing in Europe are not addressed in this assessment. Marine exposures were not addressed because seawater has a high natural level of boron (about 5 mg/L) and wastewater effluents would be widely dispersed in marine environments

Extensive monitoring data for European surface waters was used to determine a 90th percentile PEC. Although this value (0.447 mg-B/L) is the result of all natural and anthropogenic emissions of boron, it was used as a conservative estimate of the PEC-aquatic. Monitoring data are more limited for sediment, soil or wastewater treatment plants, so PEC estimates for these compartments used the EUSES program. To evaluate irrigation waters, both the monitoring data for surface waters and the EUSES-modelled soil porewater values were used as PEC-irrigation/soil porewater estimates.

Considerable toxicity data exists for aquatic species enabling a probabilistic PNEC to be calculated for borates. For terrestrial species, plants appear to be the most sensitive group. However, boron is essential to plants and the literature reveals that exposures that may result in phytotoxicity to sensitive species would result in deficiency symptoms in other species. This type

of U-shaped exposure/response curve is characteristic of essential nutrients, but is not easily addressed in the typical ecological risk assessment framework. Therefore, even though terrestrial species data are abundant, a probabilistic PNEC was not seen as appropriate and the PNEC-soil was based on a sensitive species test result with an application factor. Standard microbial data were used to derive a PNEC-STP.

Without exception, the calculated PEC/PNEC ratios are well below 1. A number of uncertainty factors were discussed; probably the most influential on the results were the use of monitored values as an estimate of the PEC for the subject use and the difficulty of estimating a PNEC for terrestrial plants. The use of the surface water monitoring value led to a conservative estimate of risk: exposures associated with only the subject use would be much lower. The use of a single species endpoint with application factor is probably also a conservative approach, overestimating the possibility of phytotoxicity in an irrigation scenario.

In conclusion, all evaluations lead to the finding that use of boric acid and borax in liquid detergent applications will pose no significant risk to the environment. All calculated PEC/PNEC ratios were well below 1. There is a reasonable amount of data available, both on the existing concentrations of boron in European surface waters and on the ecotoxicity of borates.

5 HUMAN HEALTH ASSESSMENT

5.1 CONSUMER EXPOSURE

Boric acid and borax primary use in household cleaning products is in liquid laundry detergent products and to a far lesser extent automatic dishwashing liquid; the levels of boric acid in household cleaning products are low (AISE 2002), types and concentrations are detailed in Table 22. Primary exposure will therefore be through skin contact. In addition to consumer product exposure, dietary exposure will occur through consumption of food and drinking water. Borates are essential to plant growth and fruit, vegetables and nuts are rich sources of boron in the daily diet. Dietary intake has been estimated to be in the ranges of 0.5 - 3 mg B/day (Rainey et al., 2002). In January 2001, the U.S. Food and Nutrition Board (FNB), while not suggesting that boron is essential for humans, accepted the nutritional importance for boron and determined a safe Tolerable Upper Intake Level, of 20 mg boron /day. This implies that the average person can safely ingest 20 mg boron/day in food (U.S. Food and Nutrition Board 2001). The EU safe drinking water standard for boron is 1 mg/B/l (EU,1998) although environmental levels are generally well below this limit.

Table 22: Concentrations of boric acid in Household cleaning products (AISE)

Product	Typical content	Maximum
Laundry – regular liquid	1%	1%
Laundry – compact liquid/gel	1%	1%
Laundry – compact gel	1%	1%
Dishwashing Liquid – Automatic	2%	

5.1.1 Consumer Exposure via direct skin contact

Consumers may be exposed to boric acid through solutions used in hand washing of clothes or in some cases through direct contact of the neat liquid product during pre-treatment of clothes. Due to its high water solubility, no residual boric acid is expected to remain on the fabric. The intended use of automatic dishwashing liquid does not result in skin contact, however occasional misuse of this product for hand dishwashing cannot be ruled out and may result in skin exposure. AISE habits and practices data for consumer exposure data in Europe are used for this risk assessment (AISE 2002a).

5.1.2 Consumer Exposure Estimates

Hand Laundry Washing

The highest concentration of laundry detergent used in the hand washing solution is approximately 1% (10 g/l); a typical amount is 3.7 g/l. The highest concentration of boric acid in the liquid laundry detergent is 1%.

For the exposure calculations the maximum concentrations in the products are used. These exposures can be considered a reasonable worst-case estimate of the laundry hand washing exposure.

Worst-case estimate for hand washing scenario:

Contact time is usually 10 minutes (AISE (2002a). Frequency of tasks per week is typically 4 (AISE (2002a) with a maximum of 10 tasks per week. Using the equations of the HERA guidance document (2002) the following exposure can be derived:

$C_{\text{boric acid}}$ = Maximum concentration of boric acid: 0.1 g/l (= mg/ml)

T_{der} = Thickness of layer on skin: 100 μm = 0.01 cm (HERA 2002, EU-TGD, 1996)

S_{der} = Exposed Area (hands and forearms according to EPA, 1997 EU-TGD 1996): 1980 cm^2 (adult male)

F = Fraction absorbed: 0.004 in (24 h exposure time) derived from percutaneous absorption for worst case: 0.4 %, (Section 5.2.8)

$EXP_{\text{sys}} = C_{\text{boric acid}} \times T_{\text{der}} \times S_{\text{der}} \times F$

$EXP_{\text{sys}} = 0.1 \text{ mg/ml (cm}^3) \times 0.01 \text{ cm} \times 1980 \text{ cm}^2 \times 0.004 = \mathbf{0.008 \text{ mg boric acid or a maximum of 0.0014 mg B absorbed in 24 hours}}$

Assuming 10 min contact time per task and a worse case or maximum task frequency of 10 washes per week (AISE 2002a) the total daily contact time adds up to approximately 14 min. Assuming such a worse case scenario for daily duration of exposure the amount of absorbed boric acid per day can be calculated as $[(0.008 \text{ mg/day}) \times (10/7) \times (10/60 \text{ hr}) \times (1/24 \text{ day/hr}) \times (1000 \mu\text{g/mg})] = 0.08 \mu\text{g}$. This would correspond to a maximum of 0.014 μg of boron. Assuming a body weight of 60 kg, the resulting estimated systemic dose is $[(0.08 \mu\text{g}) \times (1/60 \text{ kg BW})] = 0.0013 \mu\text{g boric acid /kg BW/day}$

Worst-case estimate:

$Exp_{\text{sys (direct skin contact)}} = 0.0013 \mu\text{g boric acid/kg BW/day}$ and $0.00023 \mu\text{g B/kg BW/day}$

A more realistic case estimate would use the typical use frequency of 4 times per week for 10 min, this would result in an exposure of $[(0.008 \text{ mg/day}) \times (4/7) \times (10/60 \text{ hr}) \times (1/24 \text{ day/hr}) \times (1000 \mu\text{g/mg})] = 0.03 \mu\text{g}$ of boric acid/day and 0.006 μg boron per day, and for a 60 kg individual, 0.0005 $\mu\text{g/kg/day}$ as boric acid or 0.0001 $\mu\text{g B/kg}$ per day.

Typical frequency and exposure, realistic case estimate:

$Exp_{\text{sys (direct skin contact)}} = 0.0005 \mu\text{g boric acid/kg BW/day}$ and $0.0001 \mu\text{g B/kg BW/day}$

Direct skin contact from pre-treatment of clothes

Direct skin contact with laundry product is possible when clothing stains are being removed by spot-treatment with neat liquid. As only a fraction of the skin surface area of the hands (840 cm^2) (TGD, 2003) is exposed and the treatment time is very short (10 min. or less) (THPCPWE, 2002), it can be assumed that the amount of boric acid systemically available via percutaneous absorption is very low.

The following worst case should address this scenario:

$C_{\text{boric acid}}$ = Maximum concentration of boric acid in liquid laundry detergent = 10mg/ml (internal AISE data). Because liquid detergents may be used neat for pre-treatment, the worst case value of 10 mg/ml will be used in the calculation.

T_{der} = Thickness of layer on skin: 100 μm = 0.01 cm (HERA 2002, TGD, 1996)

S_{der} = Exposed Area (hands and forearms according to EPA, 1997 EU-TGD 1996): 840 (cm^2)

F = Fraction absorbed: 0.004 in (24 h exposure time) derived from percutaneous absorption for worst case: 0.4 %, (Section 5.2.8)

$$\text{EXP}_{\text{sys}} = C_{\text{boric acid}} \times T_{\text{der}} \times S_{\text{der}} \times F$$

$\text{EXP}_{\text{sys (direct skin contact)}} = 10 \text{ mg/ml (cm}^3) \times 0.01 \text{ cm} \times 840 \text{ cm}^2 \times 0.004 \text{ (fraction absorbed)} = \mathbf{0.34 \text{ mg boric acid (0.059 mg B) absorbed in 24 hours.}}$

Under the very conservative assumptions of 10 min highest contact time per task and a maximum task frequency of 1 wash pre-treatment per day, the total daily contact time adds up to 10 min. assuming such very conservative daily duration of exposure the amount of absorbed boric acid per day can be calculated as:

$$0.34 \text{ (mg boric acid/day)} \times 10/60 \text{ (hr)} \times 1/24 \text{ (day/hr)} \times 1000 \text{ (\mu g/mg)} = 2.4 \text{ \mu g boric acid}$$

Assuming a body weight of 60 kg, the resulting estimated systemic dose is [2.4 μg x 1/60 kg BW] = 0.04 μg boric acid/kg bw/day:

Worst-case estimate

$\text{Exp}_{\text{sys (direct skin contact)}} = \mathbf{0.04 \text{ \mu g boric acid/kg bw/day and } 0.007 \text{ \mu g B/kg bw/day}}$

Hand Dishwashing

The intended use of automatic dishwashing liquid does not result in skin contact, however occasional misuse for hand dishwashing cannot be ruled out and may result in skin exposure. To estimate a worse case exposure that might derive from this misuse of the product, the standard scenario for hand dishwashing is used with the assumption that the frequency will be once per week, all other assumptions remain the same (AISE 2002a). The assumptions made are that 5 grams of liquid detergent, containing 2% boric acid is added to 5 litres of water, 1 wash per week, of 45 minutes duration.

Using the equations of the HERA guidance document (2002) the following exposure can be derived:

$$C_{\text{boric acid}} = \text{Maximum concentration of boric acid: } (5 \text{ g liquid detergent} \times 2\% \text{ boric acid}) / 5 \text{ L} \\ = 0.02 \text{ g/l (} = 0.02 \text{ mg/ml)}$$

T_{der} = Thickness of layer on skin: 100 μm = 0.01 cm (HERA 2002, TGD, 1996)

S_{der} = Exposed Area (hands and forearms according to EPA, 1997 EU-TGD 1996): 1980 cm^2 (adult male)

Percutaneous absorption worst case derived from data: 0.4 %, (Section 5.2.8)

F = Fraction absorbed: 0.004 in (24 h exposure time)

$$EXP_{sys} = C_{boric\ acid} \times T_{der} \times S_{der} \times F$$

$$EXP_{sys} = 0.02\text{ mg/ml (cm}^3\text{)} \times 0.01\text{ cm} \times 1980\text{ cm}^2 \times 0.004 = \mathbf{0.0016\text{ mg boric acid or a maximum of 0.00028 mg B absorbed in 24 hours}}$$

Assuming a worse case scenario or maximum contact time of 45 min per task and a task frequency of 1 wash per week (AISE 2002a) the total daily contact time adds up to 45 minutes. Assuming such duration of exposure the amount of absorbed boric acid per day can be calculated as $[(0.0016\text{ mg/day}) \times (0.75\text{hrs}) \times (1/24\text{ day/hr}) \times (1000\ \mu\text{g/mg})] = 0.05\ \mu\text{g}$. This would correspond to a maximum of 0.009 μg of boron. Assuming a body weight of 60 kg, the resulting estimated systemic dose is $[0.05\ \mu\text{g} \times 1/60\text{ kg BW}] = 0.0008\ \mu\text{g boric acid/kg bw/day}$:

Worst-case estimate

$$Exp_{sys\ (direct\ skin\ contact)} = \mathbf{0.0008\ \mu\text{g boric acid /kg BW /day}} \text{ and } \mathbf{0.00015\ \mu\text{g B/ kg BW/day}}$$

Indirect exposure via skin contact

Exposure from wearing of fabrics washed with detergents containing boric acid is expected to be negligible. This is because no residues of boric acid are expected to remain on the fabric due to its physical properties, high water solubility and low concentration levels.

Consumer exposure via inhalation route

It can be assumed that there will be no inhalation exposure from liquid detergents. There are no spray products and aerosols will not be formed during pouring of the liquid. Furthermore borates have negligible volatility at room temperature.

Consumer exposure via the oral route

Ingestion of liquid detergents is considered negligible under conditions of normal handling and use. Borates are not expected to be retained on dishes or cutlery due to its physical properties, high water solubility and low concentration levels.

Indirect Exposure via environment

The most relevant indirect exposure will be from the boric acid content of drinking water. The uptake of boron (in form of boric acid) via drinking water is reported in the literature without specifying the underlying sources. For Germany, drinking water concentrations of $< 0.2\text{ mg boron/l}$ (with a median of 0.02 mg/l) were measured in 1985/86 (Krause et al., 1991) In a world-wide data compilation of WHO (1998) it was found that in most areas boron content in drinking water was clearly below 0.4 mg/l . In contrast, bottled mineral water of different origin showed in a number of cases significantly higher concentrations (up to 4 mg/l) (Allen et al., 1989). These higher levels are caused by boron containing minerals in the surroundings of the springs. Boron content of drinking water is limited by the European Drinking Water Directive to 1 mg boron/l (EU, 1998).

Accidental or intentional exposure

Accidental swallowing of liquid detergents would lead to an intake of 20 ml of liquid (200 mg of boric acid or 35 mg B). The German Federal Institute for Health Protection of Consumers and Veterinary Medicine (BgVV) published recently a report on products involved in poisoning cases. No fatal case of poisoning with detergents was reported in this report. Detergent products were not mentioned as dangerous products with a high incidence of poisoning (BgVV, 1999).

Equally, in the UK, the Department of Trade and Industry (DTI) produces an annual report of the home accident surveillance system (HASS). The data in this report summarizes the information recorded at accident and emergency (A&E) units at a sample of hospitals across the UK. It also includes death statistics produced by the Office for National Statistics for England and Wales. The figures for 1998 show that for the representative sample of hospitals surveyed, there were 33 reported accidents involving detergent washing powder (the national estimate being 644) with none of these resulting in fatalities (DTI, 1998). In 1996 and 1997, despite their being 43 and 50 reported cases, respectively, no fatalities were reported either.

In summary the hypothetical total exposure to boric acid from all potential laundry and cleaning scenarios is detailed in Table 23.

Table 23: Total exposure levels

Exposure Scenarios	Boric Acid ($\mu\text{g}/\text{kg BW}/\text{day}$)	Boron ($\mu\text{g}/\text{kg BW}/\text{day}$)
Hand Laundry washing	0.0013	0.00023
Laundry pretreatment with neat product	0.04	0.007
Misuse of product for hand dishwashing	0.0008	0.00015
Total Consumer exposure to boric acid in consumer detergent products	0.0421	0.00738

5.2 HAZARD ASSESSMENT

Additional Information

A number of detailed risk assessments and reviews of the toxicology of borates have been published (Culver et al, 1994a; ECETOC, 1995; Murray, 1995; European Commission, 1996; Culver and Hubbard, 1996; Hubbard and Sullivan, 1996, Hubbard, 1998; IPCS, 1998; WHO; 1998; Moore et al., 1998, U.S. Food and Nutrition Board. 2001, US EPA, 2004; EFSA, 2004)

Most of the simple inorganic borates exist predominantly as un-dissociated boric acid in dilute aqueous solution at physiological pH, leading to the conclusion that the main species in the plasma of mammals is un-dissociated boric acid.

For this reason, the majority of toxicological studies of borates have involved either boric acid (H_3BO_3) or disodium tetraborate decahydrate (i.e., borax, or $\text{Na}_2\text{B}_4\text{O}_7 \cdot 10\text{H}_2\text{O}$). Both acute and longer-term studies have been carried out on these two substances.

As already identified, for comparative purposes, dose levels of borates have been expressed in terms of boron (B) equivalents based on the fraction of boron on a molecular weight basis. Conversion factors are given in Table 24 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.

Table 24: Conversion factors to Boron Equivalents

		Conversion factor for Equivalent dose of B
Boric acid	H ₃ BO ₃	0.175
Disodium tetraborate decahydrate	Na ₂ B ₄ O ₇ • 10H ₂ O	0.113
Disodium tetraborate pentahydrate	Na ₂ B ₄ O ₇ • 5H ₂ O	0.148

5.2.1 Acute Toxicity

Acute Oral Toxicity

Boric acid and sodium tetraborates are in general of low acute oral toxicity in mammals, including rats and mice. The range of rat LD₅₀ values reported for the various borates are given in Table 25. No substantial differences in acute oral toxicity were seen in mice and dogs in the limited studies available. However, dogs exhibit an emetic effect in response to high doses of borates. The LD₅₀ in dogs was determined to be > 3980 mg boric acid/kg and > 6150 mg disodium tetraborate decahydrate /kg (administered in a capsule). The dogs vomited shortly after treatment at all doses (158 mg boric acid/kg and 246 mg disodium tetraborate decahydrate/kg were the lowest doses tested). No other adverse symptoms were seen (Keller, 1962; Weir & Fisher, 1972). The main symptoms of toxicity seen in all species tested were CNS depression, ataxia and convulsions.

Table 25: Acute Oral Rat LD₅₀ Values

	LD ₅₀ mg/kg rat	Reference
Boric acid	2660 - 4100	Weir & Fisher, 1972; Pfeiffer et al., 1945
Disodium tetraborate decahydrate	4500 - 6000	Weir & Fisher, 1972
Disodium tetraborate pentahydrate	3200 – 3400	Reagan and Becci, 1985a

Acute Inhalation Toxicity

Low acute inhalation toxicity was observed in those borates tested; the 4 hour LC₅₀ being > 2 mg/l for boric acid, disodium tetraborate decahydrate, disodium tetraborate pentahydrate. (Wnorowski 1994a, b, c,).

Acute Dermal Toxicity

As would be expected due to the low skin absorption, the acute dermal toxicity was low for those borates tested, i.e., LD₅₀s were >2 g/kg for boric acid, sodium tetraborate decahydrate and sodium tetraborate pentahydrate (Vernot et al., 1977; Reagan and Becci, 1985b.c).

Acute toxicity – other routes

The acute intravenous LD₅₀s of a 5 % aqueous solution of boric acid were 1.78 g/kg and 1.33 g/kg in mice and rats respectively and the subcutaneous LD₅₀s were 2.07 g/kg and 1.2 g/kg for mice and guinea pigs respectively (Pfeiffer et al., 1945).

Conclusion

Boric acid and the sodium tetraborates are of low acute toxicity. Although the acute oral studies were not of modern standards and were performed prior to the introduction of GLP, they are reproducible across a number of studies and species and of acceptable quality. For acute dermal and acute inhalation the studies are of modern GLP standard. LD₅₀ oral rat > 2000 mg/kg; LD₅₀ dermal rat > 2000 mg/kg; LC₅₀ inhalation rat > 2 mg/l.

5.2.2 Corrosiveness/Irritation

Skin Irritation

Inorganic borates are generally not skin irritants or are very mild irritants (Pfeiffer, 1945; Roudabush et al., 1965; Reagan and Becci, 1985, d, e; Young and Doyle, 1973).

Eye Irritation

Boric acid is not an eye irritant in rabbits. (Doyle, 1989b). With disodium tetraborate decahydrate, the eye irritancy observed was reduced significantly when the eyes were rinsed (Reagan and Becci, 1985f; Doyle, 1989c). For disodium tetraborate pentahydrate an early study indicated severe eye irritation. The initial irritation was thought to be due to the abrasive nature of this substance's crystals, rather than the result of a chemical effect. The sample was ground to a fine powder before instillation to reduce the sharp crystals in the sample. However, a sample that was produced by a new manufacturing process, which produced less glassy crystals, was tested in two subsequent studies, which revealed only mild irritation (Reagan and Becci, 1989f; Wnorowski, 1996; Cerven, 2000). This supports the view that the irritancy was due to the abrasive nature of the crystal rather than a chemical effect. The process of manufacture has now been changed to produce less glassy crystals. In fifty years of occupational exposure to sodium boric acid and sodium tetraborates, no significant adverse effects on the human eye have been observed. Rabbit eye studies are known to overestimate human eye hazard.

Conclusion

Boric acid and sodium tetraborates are not skin irritants. Boric acid is not an eye irritant. The initial irritation seen with sodium tetraborates can be attributed to the abrasive nature of the

crystals. No effects have been observed in humans and the sodium tetraborates can be considered as not being irritating to eye.

5.2.3 Sensitisation

No borate tested has displayed skin sensitisation in Bheuler studies (Wnorowski 1994 d, e, f). No evidence of skin sensitisation has been seen in humans exposed occupationally to sodium borates, or in a human patch test with a 3% aqueous boric acid solution (Bruze et al., 1995).

Conclusion

Boric acid and sodium tetraborates are not skin sensitisers on both human and animal studies.

5.2.4 Repeated Dose Toxicity

A number of studies in which rats were fed boric acid or disodium tetraborate decahydrate in their diet or drinking water for periods of 70 - 90 days indicated that the main target organ for toxicity is the testis. As well as testicular atrophy, animals receiving doses of 88 mg B/kg bw/day for 90 days in their diet exhibited weight loss and, at higher doses, rapid respiration, inflamed eyes, swollen paws and desquamation of the skin on the paws (Weir and Fisher, 1972; NTP, 1987). These studies are further discussed under Carcinogenicity and Toxicity to Reproduction.

Conclusion

The main effects observed were on the testis. These effects and the appropriate NOAEL are discussed under Carcinogenicity (Section 5.2.6) and Reproductive Toxicity (Section 5.2.7).

5.2.5 Genetic Toxicity

In vitro

A number of *in vitro* mutagenicity studies, including bacterial mutation assays in *Salmonella typhimurium* and *Escherichia coli*, gene mutation in mammalian cells (L5178Y mouse lymphoma, V79 Chinese hamster cells, C3H/10T1/2 cells), bacterial DNA-damage assay, unscheduled DNA synthesis (hepatocytes), chromosomal aberration and sister chromatid exchange in mammalian cell (Chinese hamster ovary, CHO cells) have been carried out on boric acid, disodium tetraborate decahydrate or disodium octaborate tetrahydrate. No evidence of mutagenic activity was observed (NTP, 1987; Haworth et al., 1983; Landolph, 1985; Bakke, 1991; Stewart, 1991).

In vivo

No mutagenic activity was seen *in vivo* in a mouse bone marrow micronucleus study on boric acid (O'Loughlin, 1991).

Conclusion

Neither boric acid nor the sodium tetraborates are mutagenic either in vitro or in vivo.

5.2.6 Carcinogenicity

In long term feeding studies on boric acid and disodium tetraborate decahydrate in both rats and dogs, no carcinogenic effects were observed (Weir and Fisher, 1972). In rats, diets contained disodium tetraborate decahydrate or boric acid at 0, 117, 350 and 1,170 ppm boron equivalents for 2 years; these doses were approximately 0, 5.9, 17.5 or 58.5 mg B/kg bw/day. Effects observed in these rat studies included lowered food consumption, retarded body weight gain, coarse hair coats, haunched position, swollen pads, inflamed bleeding eyes and changes in haematological parameters at the highest doses. (58.5 mg B/kg bw/day).

Dogs, were fed diets containing boric acid (0.033%, 0.067%, 0.2% in diet) or disodium tetraborate decahydrate at (0.051%, 0.103%, 0.309%). No evidence of toxicity was observed. Therefore, additional groups of dogs (4 male and 4 female) were fed diets containing 0.67% boric acid or 1.03% disodium tetraborate decahydrate. The estimated equivalent boron intakes from the boric acid diet were 1.7, 3.8, 10.9 and 40.8 mg B/kg bw/day and from the disodium tetraborate decahydrate diet were 1.9, 3.6, 9.6 and 38.1 mg B/kg bw/day.

In dogs diarrhoea was observed in some and soft stools in all dogs at the highest dose tested.

Testicular effects were observed in both rats and dogs. Testicular atrophy with some interstitial cell hyperplasia were the critical effects seen in a US National Toxicology Program (NTP) bioassay in mice (dose levels in food 0, 2500, 5000 ppm boric acid). No carcinogenic effects were observed at these doses estimated to be equivalent to 78 mg B/kg bw/day and 201 mg B/kg bw/day (NTP, 1987). Effects on survival rate and reduced body weight gain were seen at the high doses. The testicular effects noted in these studies are discussed in more detail in Toxicity to Reproduction

Conclusion

The studies carried out are not to modern standards, nor to GLP. However, they are well performed and reported and are more than adequate to evaluate the carcinogenicity of boric acid and sodium tetraborates. It can be concluded that boric acid and sodium tetraborates are not carcinogenic and there is no concern for a carcinogenic effects in humans.

5.2.7 Toxicity to Reproduction

Fertility

Effects on the testis have been observed in both sub-chronic and chronic studies in three species: rats, mice and limited studies in dogs. In rats, a single dose of 175 mg B/kg bw was found to cause reversible disruption of tubular spermiation (Linder et al., 1990), although no such effects were observed after a single dose of 350 mg B/kg (2000 mg boric acid/kg) (Bouissou and Castagnol, 1965).

A comparison of the key NOAELs and LOAELs for reproduction studies is given in Table 26. The effects tend to be similar in all three species, although most data comes from rat studies. The reproductive effects in rats at lower doses and shorter time periods start with reversible inhibition of spermiation. Early effects were seen after 14 days treatment, at doses around 39 mg B/kg, (217 mg boric acid/kg bw/day) but at a lower dose of 26 mg B/kg (149 mg boric acid/kg bw/day) the effects take about 28 days to manifest (Ku et al., 1993). In a rat three generation study of boric acid and disodium tetraborate decahydrate, doses equivalent to 58.5 mg B/kg bw/day led to testicular atrophy, degeneration of seminiferous tubules, reduced sperm count and a reduction in fertility, with a NOAEL of 17.5 mg B/kg bw/day (Weir and Fisher, 1972). Similar results were seen in a two-year study of boric acid and disodium tetraborate decahydrate at 58.5 mg B/kg bw/day where the NOAEL was also 17.5 mg B/kg bw/day. (Weir and Fisher, 1972). In male rats fed disodium tetraborate decahydrate for either 30 or 60 days at 100 or 200 mg B/kg bw/day testis weight was reduced, testicular germ cells were depleted, selected testicular enzymes were affected and fertility was reduced. The NOAEL was 50 mg B/kg bw/day (Lee et al., 1978). As might be expected, while recovery from inhibition of spermiation occurred at the lower doses, there was no recovery from testicular atrophy when the germ cells were lost.

Data in dogs derives from two very limited and unreliable two-year dietary studies. Unfortunately, the published study does not accurately reflect the original study reports (Weir and Fisher, 1972). In the published paper, the authors estimated the dietary intakes from standard intake figures. However, actual dietary intake was reported in the original study reports allowing a more accurate measure of the dietary intake to be made which are used in this review. Groups of only four male dogs were fed either boric acid or disodium tetraborate decahydrate at doses up to 10.2 mg B/kg bw/day (62.4 mg boric acid/kg bw/day and 84.7 mg disodium tetraborate decahydrate/kg bw/day) in one study and 39.5 mg B/kg bw/day (233.1 mg boric acid/kg bw/day and 373.2 mg disodium tetraborate decahydrate/kg bw/day) in a second study. The animals were sacrificed at various time periods such that observations were reported on only 1 or 2 animals. At 39.5 mg B/kg bw/day, testicular atrophy was observed, however the effects in the only one disodium tetraborate decahydrate treated dog investigated at 38 weeks were less severe than those seen in the control dog. Also, testicular atrophy was present in three out of four control dogs, so that the significance of the effect in the treated animals is difficult to assess. One boric acid treated and one disodium tetraborate decahydrate treated dog were allowed to recover for three weeks. Some recovery was observed in each dog. Minor histopathological changes such as decreased spermatogenesis remained which was less obvious in the disodium tetraborate decahydrate treated dog. The NOAEL was deemed to be the equivalent of 10.2 mg B/kg bw/day by the authors (Weir, 1966 a, b; 1967 a, b; Weir and Fisher, 1972). For the reasons given above (effects in control animals, insufficient group sizes, inaccurate dose reporting) this data is not reliable for risk assessment, but it does confirm the effects seen in other species. Due to the acute toxic effects of borates in dogs, had the LOAEL doses been administered as a single dose (i.e. by gavage) then vomiting would have occurred and the study would not have been possible.

Table 26: Comparison of NOAELs and LOAELs for Reproductive Effects

Species	Study type or duration	NOAEL (mg B/kg bw/day)	LOAEL (mg B/kg bw/day)	Effect at LOAEL	Reference
Rat	9 week dietary study	-	26	Mild reversible inhibition of spermiation	Ku et al., 1993

	3-generation dietary study and 2 year dietary study	17.5	58.5	Testicular atrophy; reduced fertility	Weir and Fisher, 1972
Mouse	Continuous breeding dietary study	27	111	Reduced fertility	Fail et al., 1991
Dog	2 year dietary study	10.2	39.4	Testicular atrophy (also present in control animals)	Weir, 1966a,b; 1967a,b

Conclusion

A dose related effect on the testis was observed in rats and mice with confirmation from limited and unreliable studies in dogs. Effects start with reversible inhibition of spermiation after 14 days treatment, at doses around 39 mg B/kg, (217 mg boric acid/kg bw/day) although at a lower dose of 26 mg B/kg (149 mg boric acid/kg bw/day) the effects take about 28 days to manifest. Higher doses (58.5 mg B/kg bw/day and above) lead to testicular atrophy, degeneration of seminiferous tubules, reduced sperm count and a reduction in fertility. No recovery from testicular atrophy was observed when the germ cells were lost.

The NOEL for this endpoint is 17.5 mg B/kg corresponding to 100 mg boric acid/kg/day; 155 mg disodium tetraborate decahydrate/kg and 118 mg disodium tetraborate pentahydrate/kg.

Developmental Toxicity

Only boric acid as been tested in developmental studies. Effects were observed at high doses in rats, mice and rabbits. A comparison of the key NOAELs and LOAELs for developmental studies is given in Table 27.

The majority of studies have been carried out in rats. In two separate dietary studies performed in the same laboratory, groups of rats were given dose levels of approximately 3.3, 6.3, 9.6, 13.7, 25, 28 and 59 mg B/kg bw/day on gestation days 0-20 and 94 mg B/kg bw/day on gestation days 6-15 in feed. The NOAELs for maternal toxicity and developmental effects were 13.7 mg/kg bw/day and 9.6 mg B/kg bw/day, respectively. A reduction in food intake and an increase in relative liver and kidney weight and a reduction in maternal body weight gain at higher doses indicated maternal toxicity. At non-maternally toxic doses, there was a reduction on foetal weight and some skeletal variations and malformations (increase in wavy ribs and short rib XIII and a decreased incidence of rudimentary extra rib on lumbar 1) which, had reversed by postnatal day 21 at 13.7 and also, with the exception of short rib XIII, had reversed at 28.6 mg B/kg bw/day in a study designed to look at postnatal recovery (Price et al., 1990, 1996). At higher maternally toxic doses, other indications of developmental effects were observed, including resorptions and visceral malformations (enlarged lateral ventricles; cardiovascular effects; anophthalmia and microphthalmia and short and curly tails). However, these are likely to have been secondary to the maternal toxicity (Price et al., 1990, 1996; Heindel et al., 1992).

Similar findings were observed in mice receiving estimated doses of 0, 43, 79, and 175 mg B/kg bw/day on gestation days 0-20 in feed. Maternal toxicity was indicated by a dose related incidence of renal tubule dilation/regeneration and at the highest dose increases food and water consumption in late gestation and in the relative kidney weight. A NOAEL was not determined

for maternal toxicity. The key developmental effects observed were similar to those seen in rats i.e. a reduction in foetal body weight at the mid dose (79 mg B/kg) and an increase in skeletal variations and malformations (missing lumbar vertebrae, fused vertebral arches and short rib XIII) and resorptions at the highest, more maternally toxic dose. The NOAEL for developmental effects in mice was 43 mg B/kg bw/day (Heindel et al., 1992), however, this dose was also a maternally toxic dose.

In rabbits receiving estimated doses of 0, 11, 22 and 44 mg B/kg bw/day by gavage on gestation days 6-19 maternal toxicity was indicated by effects such as an increase in relative kidney weight, increase food intake, vaginal bleeding and an increase in corrected weight gain. Developmental effects were seen only at the top dose, where the majority of the embryos were resorbed and malformations were primarily visceral (major heart and/or great vessel defects), however these effects are likely to be secondary to the maternal toxicity. The only skeletal effect observed was a decreased incidence of rudimentary extra rib on lumbar 1 which was not considered biologically significant. The NOAEL for both maternal and developmental toxicity in the rabbit was 21.8 mg B/kg bw/day (Price et al., 1991).

Table 27: Comparison of NOAELs and LOAELs for Developmental Effects

Species	Maternal NOAEL Mg/B/kg bw/day	NOAEL (mg B/kg bw/day)	LOAEL (mg B/kg bw/day)	Effect at LOAEL	Reference
Rat	13.7	9.6	13.7	Decreased foetal body weight; minor skeletal variations	Price et al., 1990, 1996
Mouse	No NOAEL	43	79	Maternal toxicity; decreased foetal body weight; minor skeletal variations	Heindel et al., 1992
Rabbit	21.8	21.8	43.5	Maternal toxicity; resorptions; Visceral malformations (cardiovascular defects)	Price et al., 1991

Conclusion

Developmental effects have been observed in three species, rats, mice and rabbits. The most sensitive species appears to be rats, in which the effects observed at non maternally toxic doses include a reduction in foetal body weight and minor skeletal variations which, with the exception of short rib XIII, had reversed by 21 days post natal. The NOAEL for developmental effects is 9.6 mg B/kg.

5.2.8 Additional Data

Toxicokinetic Information

The toxicokinetics of boric acid are similar in rats and humans with respect to absorption, distribution, and metabolism (Dourson et al., 1998; Murray, 1998).

Absorption

Boric acid and sodium borates given orally are readily and completely absorbed in humans and animals. Animals investigated include rats (Ku et al., 1991), rabbits (Draize & Kelly, 1959), sheep (Brown et al., 1989) and cattle (Owen, 1944; Weeth et al., 1981) as shown by the levels of boron in urine, blood or tissues. In adult human volunteers given a single oral dose of 131 mg B (as boric acid dissolved in water), 94% of the administered dose was excreted in the urine over a 96 hour period (Schou et al, 1984). Similar absorption was observed based on urinary excretion of boron in 6 volunteers drinking curative spa water with a high boron content (daily dose of 102 mg B) for two weeks (Job, 1973). In another study greater than 90% was absorbed in human volunteers taking in 3% boric acid in an aqueous solution or as a waterless emulsifying ointment spread onto biscuits Jansen, 1984a). In a series of human volunteer studies conducted in the early 1900s, in which large doses of boric acid were repeatedly administered orally, approximately 80% of an administered dose was recovered in the urine, while 1% was recovered in the faeces (Wiley, 1904). Reports involving accidental human ingestion, particularly in infants, where newborn infants died after accidentally ingesting boric acid, provide further evidence of oral absorption (Wong, 1964).

Inhaled sodium borate dust is readily absorbed as demonstrated by the blood and urine levels among groups of workers occupationally exposed to various levels of boron (Culver et al., 1993; 1994). In rats, inhaled boron oxide aerosol was readily absorbed, based on the increased levels of boron excreted in the urine following inhalation exposure (Wilding et al., 1959).

Dermal absorption of borates across intact skin is insignificant in all species evaluated, including human newborn infants (Friis-Hansen et al., 1982), adult humans (Beyer et al., 1983; Hui et al, 1996; Wester et al, 1998), rabbits (Draize and Kelley, 1959), and rats (Nielsen, 1970). Borates have been demonstrated to penetrate damaged or abraded skin (Draize and Kelley, 1959; Nielsen, 1970, Stüttgen et al., 1982). However, the use of an ointment-based vehicle may prevent or reduce the absorption through diseased skin compared to an aqueous jelly based vehicle (Nielsen, 1970 and Stüttgen et al, 1982), although the results by Stüttgen et al. (1982) have a number of flaws and are therefore not conclusive.

Skin absorption data was obtained in human volunteers. Volunteers were dosed on a 900 cm² area (30cm x 30 cm) area of the back with ¹⁰B enriched boric acid or borax (5% in aqueous solution), or disodium octaborate tetrahydrate (10% in aqueous solution). Twenty-four hours later the residual dose was removed by washing. Boron was measured in the urine (Hui et al, 1996; Wester et al, 1998). The absorption rates are given in Table 28.

Table 28: Dermal Absorption in Humans of boric acid and borax

	% Dose Absorbed ± SD	Rate of Absorption Flux µg/cm ² /hr	Permeability Constant (Kp) (cm/hr)
Boric Acid (5 %)	0.226 ± 0.125	0.009	1.9 x 10 ⁻⁷
Borax (5 %)	0.210 ± 0.194	0.00875	1.8 x 10 ⁻⁷

For the purposes of risk assessment, the mean percentage dose absorbed plus the standard deviation (overall 0.4%) is used for skin absorption.

Distribution

There is no substantiated evidence of boron accumulation in humans or other animals although bone contains higher levels than other tissues. (Alexander et al, 1951; Forbes et al., 1954; Forbes

and Mitchell, 1957; Jansen et al, 1984b; Ward, 1987; Treinen and Chapin, 1991; Ku et al., 1991, 1993; Culver et al., 1994).

Absorbed boron rapidly distributes throughout the body water in humans and animals. In a study of workers occupationally exposed to 10 mg/m³ of airborne borax (0.22 mg B/kg/day), there was no progressive accumulation of boron in soft tissues during the working week as measured by blood and urine levels (Culver et al., 1993; 1994). Similarly, Jansen et al. (1984a, b) concluded from pharmacokinetic studies of human volunteers that there was no tendency for boron to accumulate following a single i.v. dose of 600 mg of boric acid (approximately 105 mg B). Tissue levels of boron generally reached steady state within three to four days among rats fed boric acid in the diet or drinking water for 28 days (Treinen and Chapin, 1991) or 3 – 4 days (Ku et al., 1991). Thus, boron does not accumulate in soft tissues with time in either humans or animals.

In both humans and animals, boron levels in soft tissue are comparable to plasma levels, while a greater concentration of boron in bone is observed relative to other tissues. The most complete study of boron distribution conducted to date examined tissue disposition of boron in reproductive organs and other selected tissues in adult male rats fed boric acid, providing approximately 100 mg B/kg bw/day for up to seven days (Ku et al., 1991; 1993). All tissues examined, except bone and adipose tissue, appeared to reach steady state boron levels by three to four days. Bone achieved the highest concentration of boron (2 to 3 times plasma levels), and bone boron levels continued to increase throughout seven days of dietary administration (Ku et al., 1991). In contrast, adipose tissue concentration was approximately 20 % of the plasma level. No other tissues showed any appreciable accumulation of boron over plasma levels. In dogs, an accumulation in the brain, liver and fat was reported after a high single dose of 2000 mg/kg bw boric acid (Pfeiffer et al., 1945). However, the accuracy of the analytical procedures in that study is questionable.

Previous studies also show a greater concentration of boron in bone relative to other tissues in humans (Alexander et al., 1951; Forbes et al., 1954;) and rats (Forbes and Mitchell, 1957). Boron levels in a number of tissues have been measured (Abou-Shakra, 1989; Ciba and Chrusciel, 1992; Ward et al, 1987; Sabbioni et al., 1990; Shuler et al., 1990; Minoia et al., 1990; 1994). In mice, boron distribution appeared to be homogenous in the tissues examined, except for higher levels in the kidney (bone was not analysed) (Locksley and Sweet, 1954; Laurent-Pettersson et al., 1992), but higher levels were found in bone in another study (Massie et al., 1990). In vivo and in vitro studies indicate that boric acid has a strong affinity for cis -hydroxyl groups. This may explain the higher concentrations of boric acid in bone, owing to the binding of to the cis -hydroxyl groups of hydroxyapatite.

Metabolism

Boric acid is not metabolised in either animals or humans, owing to the high energy level required (523kJ/mol) to break the B - O bond (Emsley, 1989). Other inorganic borates convert to boric acid at physiological pH in the aqueous layer overlying the mucosal surfaces prior to absorption. Additional support for this derives from studies in which more than 90% of administered doses of inorganic borates are excreted in the urine as boric acid. Boric acid is a very weak and exclusively monobasic acid that is believed to act, not as a proton donor, but as a Lewis acid, i.e., it accepts OH⁻. Because of the high pK_a, regardless of the form of inorganic

borate ingested (e.g., boric acid, borax or boron associated with animal or plant tissues), uptake is almost exclusively (>98%) as undissociated boric acid.

Excretion

In both humans and animals, boron is excreted in the urine regardless of the route of administration. It is excreted with a half-life of < 24 hours in humans and animals. Boric acid is slowly eliminated from bone.

In humans, 99 % of a single i.v. dose of boric acid was excreted in the urine; the plasma half-life was calculated to be 21 hours using a three compartment toxicokinetic model (Jansen et al., 1984b). Following oral intake of an aqueous solution of boric acid, the urinary recovery was 94 % (Jansen et al., 1984a); more than 50 % of the oral dose was eliminated in the first 24 hours, consistent with the 21 hour half-life in the i.v. study. Sutherland et al. (1998) showed in a boron balance study that only 8% of dietary boron is excreted in faeces. Half-lives ranging 13-28.7 hours have also been reported from various poisoning cases (Astier et al., 1988; Litovitz et al., 1988).

Elimination half-lives for animals have not been stated explicitly in the scientific literature, but they can be calculated or estimated from the data in the literature. In mice, assuming first order kinetics for elimination, the half-life was estimated to be approximately one hour, and in rat < 12 hours (Farr and Konikowski, 1963; Ku et al. 1991; 1993). In rabbits, 50 to 66% of an orally administered dose of boric acid was excreted in the urine in the first 24 hours after dosing (Draize and Kelley, 1959). A recent study indicated that the half-life may be only 3 hours (Vaziri et al., 2001) in both pregnant and non-pregnant rats.

The major determinant of boric acid excretion is expected to be renal clearance since boric acid is excreted unchanged in the urine. Rats and mice generally have faster rates of renal clearance than humans since the glomerular filtration rates as a function of body mass are generally higher in rats and mice than in humans.

Clearances of 40.4 ± 3.2 ml/min/1.73m² for sodium tetraborate in male rats and 40 ml/min/1.73m² for boron in mice (Usuda et al., 1998; Farr and Konikowski, 1963) have been reported, although there are methodological and/or analytical limitations in both studies. In more recent studies boric acid clearance rates in non-pregnant rats and pregnant rats ranged from 29.0 ± 5.7 to 31.0 ± 4.5 and from 32.2 ± 5.1 to 35.6 ± 5.7 ml/min/1.73m², respectively (Vaziri et al., 2001).

In humans, Jansen et al (1984b) determined a clearance rate of 55 ml/min/1.73m² following an i.v. dose of 600 mg of boric acid (105 mg B). Farr and Konikowski (1963) also reported a similar value of 39 ml/min/1.73m² in humans given 35 mg B/kg intravenously as sodium pentaborate, although there are methodological and analytical limitations to this 40 year old study. In a more recent study, renal clearance rates in humans were 68.30 ± 35.0 ml/min/1.73m² for pregnant subjects and 54.31 ± 19.35 ml/min/1.73m² for non-pregnant subjects (Pahl et al., 2001). This indicates about 20 –25% greater clearance in pregnant humans.

Pharmacokinetic clearance data is normally quoted in terms of body surface area (m²). A comparison of the renal clearance between rats and humans in terms of body surface area indicated that humans clear boric acid slightly faster than rats (~1.7 -1.9 times as fast). However,

toxicological comparisons are normally related to body weight (kg) and a comparison on that basis indicates that humans may clear boric acid more slowly than rats (~ 3 - 4 times slower). (Pahl et al., 2001; Vaziri et al., 2001).

Table 29: Summary of Toxicokinetics of Inorganic Borates in rats and humans

Absorption	<ul style="list-style-type: none"> • Readily absorbed orally and by inhalation (of respirable particles) • No dermal absorption except through severely damaged skin
Distribution	<ul style="list-style-type: none"> • Rapidly distributed through body water • No accumulation in tissues
Metabolism	<ul style="list-style-type: none"> • Not metabolised • Exists mainly as boric acid in whole blood
Excretion	<ul style="list-style-type: none"> • Excreted almost exclusively in the urine • Half-life < 24 hours • Renal clearance is approximately 3 times faster in rats than humans based on a body weight comparison

Conclusion

There is little difference between animals and humans in absorption, distribution, and metabolism. Differences in renal clearance is the major determinant in the differences between animals and humans, there being an approximate 3 fold difference between rats and humans.

Absorption via the oral route is nearly 100%. Similarly, 100% of inhaled (respired) borates are absorbed across the lung. Dermal absorption through intact skin is extremely low. A figure of 0.4% for boric acid and borax has been used for this risk assessment as a conservative worst case approach.

Essentiality and Nutritional Importance

Studies of animals given boron deficient diets have shown that boron is critical for normal reproduction and embryonic development. The reproductive capacity of the frog *Xenopus laevis* can be completely eliminated by removing boric acid from the diet and water, and boric acid deficiency interferes with foetal development (Fort et al, 1998, 1999). The embryo-larval stage of fish development is sensitive to boron deficiency (Rowe and Eckhert, 1999). In rats, maternal exposure to a low boron diet was associated with a reduction in embryo implantation sites (Lanoue et al, 1998). In vitro exposures of mouse embryos to low B growth medium showed reduced blastocyst formation and increased embryo degeneration (Lanoue et al.1999) Additional studies on effects of low boron diets to embryonic development and embryo membrane function in rats, mice, and frogs are currently being conducted.

Boric acid displays similar toxicity to other essential elements as demonstrated by Rowe et al. (1998). There is also wide database of references relating to the nutritional importance of boron. The U.S. Food and Nutrition Board (2001) determined a Tolerable Upper Intake Level (UL) for

boron of 20 mg/day, which confirms the nutritional importance for humans. In addition the UK Expert Committee on Minerals and Vitamins also determined an acceptable daily intake for boron (0.16 mg /kg/day) (UK Expert Group on Minerals and Vitamins, 2002).

5.2.9 Experience with Human Exposure

Data from Epidemiology

Inhalation and Respiratory Irritation

A study of workers exposed occupationally to sodium borates up to levels of 14 mg sodium borates/m³ (the nuisance dust level is 10 mg/m³) indicated no significant respiratory effects (i.e., nose, eye and throat irritation). No significant difference in response was found between workers exposed to different types of sodium borate dusts. No effect on pulmonary function or other health effects was observed in workers exposed chronically to borates (Wegman et al, 1994).

The results of Wegman et al were confirmed in a recent human study in which the sensory perception of dusts of sodium tetraborate pentahydrate (Na₂B₄O₇·5H₂O), calcium sulphate (CaSO₄), and calcium oxide (CaO) was investigated. Twelve subjects were exposed to dust particles for 25 min while performing moderate exercise (i.e., riding an exercise bike set at a load of 60 watts). During exposure, subjects judged level of feel or irritation in the eye, nose, and throat (nasopharynx) at 5-min intervals. The subjects indicated the absence of any feel or irritation by a judgement of zero. At the intervals indicated, heart rate, oxygen saturation, minute ventilation and respiration rate were recorded as well. The results indicated no significant respiratory effects at 14-15 mg/m³ sodium borate (Cain et al., 2002).

Effects on Reproduction

The potential reproductive effects of inorganic borate exposure to a population of workers at a large mining and production facility was assessed using the Standardised Birth Ratio (SBR), a measure of the ratio of observed to expected births. A total of 542 workers completed a reproductive questionnaire. The average total boron exposure for the highest exposure group was 28.4 mg B/day (approximately 0.4 mg B/kg bw/day) for two or more years. This represents both occupational and dietary exposures since it is based on biological sample data. The average duration of exposure was 16 years. The number of offspring was actually greater than the US national average, indicating no adverse effects on reproduction in these workers (Whorton et al., 1994).

In a study of a highly exposed population in Turkey, where exposure comes mainly from naturally high levels of B in drinking water (up to 29 mg B/l) as well as from mining and production, no adverse effect has been reported on fertility over three generations (Sayli, 1998; 2001).

Data from poison control centre

There is a large database of accidental or intentional poisoning incidents for humans. Many were the result of accidental use as an antiseptic for irrigating body cavities, treating wounds or as a

treatment for conditions such as epilepsy. Such medical uses are now obsolete. Also, accidental misuse in the preparation of baby formula (1 – 14 g in boric acid in the formula) and the topical use of pure boric acid powder for infants has led to poisonings in the past. This database is reviewed in several papers of data from poisoning centres as well as a detailed review of the literature cases from the mid 1800s to the 1970s by Kliegel (Kliegel, 1980; Wong et al. 1964, Litovitz et al, 1988; Goldbloom and Goldbloom, 1953; Valdes-Dapena and Arey, 1962). Humans display different acute symptoms compared with most animals. In the literature, the human oral lethal dose is regularly quoted as 2--3 g boric acid for infants, 5-6 g boric acid for children and 15-30 g boric acid for adults. This data is largely unsubstantiated. In most cases it is difficult to make a good quantitative judgement particularly since medical intervention occurred in most cases and there were often other unrelated medical conditions (Culver and Hubbard, 1996). Of 784 more recent reports of accidental ingestion, none were reported as fatal and 88.3% were asymptomatic. The estimated dose range was 10 mg to 88.8 g (Litovitz et al, 1988). However, a single intake of 30 g of boric acid was fatal in one case (Yoshitaka et al., 1993). Symptoms of acute effects may include nausea, vomiting, gastric discomfort, skin flushing, excitation, convulsions, depression and vascular collapse.

In humans multiple exposure (high levels > 1g) results in various symptoms which may appear singly or together and include dermatitis, alopecia, loss of appetite, nausea, vomiting, diarrhoea, and focal or generalised central nervous system irritation or convulsions. Much data comes from the mid 1800s to around 1940, when boric acid and disodium tetraborate decahydrate were used systematically for a variety of medical conditions including amenorrhoea, malaria, epilepsy, urinary tract infection and exudative pleuritis (Kliegel, 1980). Daily oral doses in adults ranged from 1-14 g per day. Repeated doses in the 6 - 10 g/day range were given for as long as several weeks. In one extreme case a 28 year old women ingested around 0.5 g of boric acid (in baby powder) every day for two years and suffered anaemia, which reversed on ceasing ingestion (Adelhardt and Fogh, 1983). Doses greater than 3 –5 g/day regularly caused vomiting and/or diarrhoea in the first instance often accompanied by dermatitis and appetite suppression. As the dose became higher and the dosing period longer, symptoms included alopecia, disseminated maculopapular eruption followed by widespread desquamation, focal or generalised central nervous system irritation, and convulsions. The symptoms of dermatitis, nausea, diarrhoea and vomiting symptoms also occurred in some patients receiving doses of 2 g boric acid/day (29 mg boric acid/kg/day) and above. In one such case, reduction of the dose from 2 g/day of boric (29 mg boric acid/kg/day) acid to 1g/day (14 mg boric acid/kg/day) resulted in resolution of the effects (vomiting and dermatitis). In all cases where withdrawal of treatment was reported, recovery occurred with no lasting effects. The lowest recorded adult dose causing symptoms was 2 g/day boric acid (Kliegel, 1980).

In children, where low levels can be estimated (Gordon et al, 1973 and O'Sullivan and Taylor, 1983), infants aged from 6 to 19.5 weeks ingested borax (as a honey-borax mixture which had been applied to pacifiers) for periods of 4 to 12 weeks. The mean intake was 0.98 g boric acid/day (range 0.55g to 2 g) for a 10 kg child. The effects seen, which disappeared on withdrawal of the honey borax mixture, relate to effects on CNS such as convulsions, generalised seizures and focal seizures. There were no dermal effects. Minor occurrences of vomiting and loose stools were also described.

Conclusions

An oral no effect level for humans based on the acute and chronic symptoms of nausea, vomiting and diarrhoea can be established at about 1 g of boric acid/day (2.5 mg B/kg/day) The level at which adverse effects of anorexia, indigestion and exfoliative dermatitis will be seen is 5.0 mg boric acid/kg/day. Although chronic absorption data at these levels is not available in the literature for infants, their responses at high doses are similar enough to the human adult to assume that children are not more sensitive to the effects of borates.

5.2.10 Identification of Critical Endpoints

Boron is a ubiquitous element found widely distributed in the environment and is a normal component of a healthy diet. It is an essential micronutrient for plants, and there is evidence to indicate that B is of nutritional importance, if not essential, for mammals. Boron is essential for normal reproduction and embryonic development in frogs and fish (Fort et al., 1999, 2002; Rowe et al., 1998), and mechanisms for this essentiality are beginning to be revealed (Fort 2002).

Boric acid and sodium borates have low acute toxicity. They are not skin irritants, nor skin sensitizers. Some borates cause eye irritancy in animals, but in 50 years of occupational exposure no adverse ocular effects have been seen in humans. Borates are absorbed orally and by inhalation. They are very poorly absorbed dermally except through severely damaged skin. They are not carcinogenic or mutagenic.

The most critical endpoints of toxicity are considered to be (1) effects on the testis and fertility in males and (2) developmental effects (in particular, foetal weight reduction). The effects seen occur in three species, rats, mice and dogs for reproductive effects; rats, mice and rabbits for developmental effects. There is good agreement between these species, which indicates that there is little species variation in the response. This may be due to the lack of metabolism of boric acid and borates, which tends to reduce interspecies variation.

Determination of NOAEL or quantitative evaluation of data

The critical lowest No Observed Adverse Effect (NOAEL) level for the purposes of risk assessment is 9.6 mg B/kg/day (54 mg boric acid/kg/day; 85 mg disodium tetraborate decahydrate), from feeding (dietary intake) studies based on developmental effects. This NOAEL is universally accepted for systemic exposure in all the risk assessment published (see references in section 5.2).

5.3 RISK ASSESSMENT

Borates are naturally occurring minerals and essential for the healthy development of plants and probably essential to humans. They form a natural part of a healthy diet of fresh fruit vegetables and nuts. Dietary intake is approximately 1-3 mg B/day. The U.S. Food and Nutrition Board (2001) published a Tolerable Upper Intake Level (UL) for boron of 20 mg/day. Borates do not accumulate in the body and are rapidly excreted with a half-life less than 24 hours.

5.3.1 Margin of Exposure Calculation

The Margin of Exposure (MOE) is the ratio of the No Observed Adverse Effect Level (NOAEL) or an appropriate substitute to the estimated or actual level of human exposure to a substance. The critical lowest No Observed Adverse Effect (NOAEL) level for the purposes of risk assessment is 9.6 mg B/kg/day (54 mg boric acid/kg/day) based on developmental effects.

Exposure scenario: direct skin contact from hand laundry washing

For calculation of the MOE, the NOAEL of 54 mg boric acid/kg bw/day was divided by the daily systemic dose of 0.0013 µg boric acid/kg bw/day estimated for the dermal exposure to boric acid from hand laundry washing.

$$\text{MOE}_{\text{direct skin}} = 54000/0.0013 = 41500000$$

Exposure scenario: direct skin contact from laundry pretreatment with neat product

For calculation of the MOE, the NOAEL of 54 mg boric acid/kg bw/day was divided by the daily systemic dose of 0.04 µg boric acid/kg bw/day estimated for the dermal exposure to boric acid from direct skin contact from laundry pretreatment with neat product.

$$\text{MOE}_{\text{direct skin}} = 54000/0.04 = 1350000$$

Exposure scenario: direct skin contact from misuse of product for hand dishwashing

For calculation of the MOE, the NOAEL of 54 mg boric acid/kg bw/day was divided by the daily systemic dose of 0.04 µg boric acid/kg bw/day estimated for the dermal exposure to boric acid from direct skin contact from direct skin contact from misuse of product for hand dishwashing.

$$\text{MOE}_{\text{direct skin}} = 54000/0.004 = 13500000$$

Total Consumer Exposure

The total consumer exposure from direct and indirect skin contact with laundry cleaning products is 0.0453µg boric acid/kg BW/day.

$$\text{MOE}_{\text{total consumer}} = 54000/0.0453 = 1192053$$

The far greater consumer exposure will come from daily diet (1-3 mg B/day), which is equivalent to between 95 to 290 µg boric acid/ kg BW/day for a 60kg person. Consumer exposure to boric acid from laundry cleaning products is over 2000 - 6000 times less than dietary intake.

Exposure Scenario: oral route from accidental Exposure via ingestion

Accidental swallowing is considered an acute exposure. The maximum likely intake through this route is estimated to be 0.2 g boric acid. In the literature, the human oral lethal dose is regularly quoted as 2-3 g boric acid for infants, 5-6 g boric acid for children although this is difficult to substantiate. A no effect level for humans based on the acute symptoms of nausea, vomiting and diarrhoea can be established at about 1 g of boric acid/day (2.5 mg B/kg/day based on a 70 kg male) (Culver and Hubbard, 1996). The level at which adverse effects of anorexia, indigestion and exfoliative dermatitis will be seen is 5.0 mg boric acid/kg/day. Although chronic absorption

data at these levels is not available in the literature for infants, their responses at high doses are similar enough to the human adult to assume that children are not more sensitive to the effects of borates.

There is a clear margin of safety should accidental ingestion occur. These acute effects demonstrate that it is not possible for humans to be exposed to the high doses that could give rise to reproductive effects. Furthermore nausea, vomiting and diarrhoea would prevent repeated exposure through accidental misuse.

5.3.2 Risk Characterisation

The availability of data on borates is comprehensive. However the animal feeding studies do not represent human exposure to borates under conditions of normal handling and use. The primary route of exposure to borates through skin contact with detergent liquids containing boric acid is extremely low and far below levels found in a healthy diet.

Acute Effects

Accidental ingestion may lead to acute and chronic symptoms of nausea, vomiting and diarrhoea, which would mitigate against repeated dose exposure.

The doses that cause these effects are far higher than any levels to which the human population could be exposed. A 60 kg person would need to consume daily some 3.3 g of boric acid (5.0 g disodium tetraborate decahydrate) to ingest the same dose level as the lowest animal NOAEL.

The greatest exposure of the general population to borates is through a healthy diet of fresh fruit, vegetables nuts and, in adults, wine.

Reproductive and Developmental Effects

The critical lowest No Observed Adverse Effect (NOAEL) level for the purposes of this risk assessment is 9.6 mg B/kg/day (54 mg boric acid/kg/day) based on developmental effects.

Local effects

Skin or eye contact with the liquid detergent

Boric acid is not an eye irritant in humans and is used commercially in eye solutions (Beyer et al., 1983). This provides confirmation that the use of boric acid in household laundry and cleaning detergents raises no concerns for skin or eye irritation.

Inhalation exposure

There will be no significant consumer exposure via inhalation from the use in liquid laundry detergents due to their low volatility and lack of aerosols during their application and use.

5.4 DISCUSSION AND CONCLUSIONS

Boric acid has a long history of safe use in detergents. Exposure from detergent use is far below normal dietary levels and such use will not constitute a risk to the consumer. The use of boric acid in detergents represents only a small percentage (approximately 1%) of the wide use of borates in industrial and consumer applications.

Boric acid has low acute toxicity and is not irritant to the skin or eyes. Borates are rapidly excreted from the body and do not bioaccumulate. The toxicological endpoint of concern for boric acid from studies in rodents were effects on fertility with the most sensitive endpoint being histopathological changes in male sex organs and developmental toxicity at high dose levels. Such doses are not possible under conditions of normal handling and use. Consumer exposure to borates from use of detergents is limited to dermal contact and boric acid is poorly absorbed through intact skin.

Consumer exposure to detergent products containing boric acid under conditions of normal handling and use are very low (0.0453 μg boric acid/kg bw/day) and will not cause systemic effects. The margin of safety is several orders of magnitude 10^7 for possible developmental effects. Exposure levels are also between 2000 to 6000 times below normal background levels in the diet and together several orders of magnitude below the tolerable intake level.

It can be concluded that the use of boric acid in liquid detergents poses no risk to human health under conditions of normal handling and use.

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7 CONTRIBUTORS TO THE REPORT

This report has been prepared by Rio Tinto Borax, and has been reviewed by the experts of the HERA Human Health and Environment Task Force.