

Borax (B₄Na₂O₇·10H₂O): Human health tier II assessment

29 June 2018

CAS Number: 1303-96-4



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Preface

This assessment was carried out by staff of the National Industrial Chemicals Notification and Assessment Scheme (NICNAS) using the Inventory Multi-tiered Assessment and Prioritisation (IMAP) framework.

The IMAP framework addresses the human health and environmental impacts of previously unassessed industrial chemicals listed on the Australian Inventory of Chemical Substances (the Inventory).

The framework was developed with significant input from stakeholders and provides a more rapid, flexible and transparent approach for the assessment of chemicals listed on the Inventory.

Stage One of the implementation of this framework, which lasted four years from 1 July 2012, examined 3000 chemicals meeting characteristics identified by stakeholders as needing priority assessment. This included chemicals for which NICNAS already held exposure information, chemicals identified as a concern or for which regulatory action had been taken overseas, and chemicals detected in international studies analysing chemicals present in babies' umbilical cord blood.

Stage Two of IMAP began in July 2016. We are continuing to assess chemicals on the Inventory, including chemicals identified as a concern for which action has been taken overseas and chemicals that can be rapidly identified and assessed by using Stage One information. We are also continuing to publish information for chemicals on the Inventory that pose a low risk to human health or the environment or both. This work provides efficiencies and enables us to identify higher risk chemicals requiring assessment.

The IMAP framework is a science and risk-based model designed to align the assessment effort with the human health and environmental impacts of chemicals. It has three tiers of assessment, with the assessment effort increasing with each tier. The Tier I assessment is a high throughput approach using tabulated electronic data. The Tier II assessment is an evaluation of risk on a substance-by-substance or chemical category-by-category basis. Tier III assessments are conducted to address specific concerns that could not be resolved during the Tier II assessment.

These assessments are carried out by staff employed by the Australian Government Department of Health and the Australian Government Department of the Environment and Energy. The human health and environment risk assessments are conducted and published separately, using information available at the time, and may be undertaken at different tiers.

This chemical or group of chemicals are being assessed at Tier II because the Tier I assessment indicated that it needed further investigation.

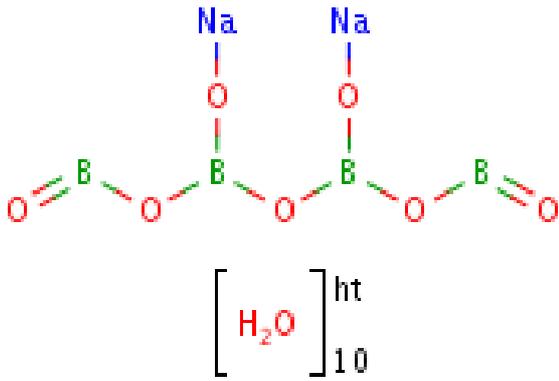
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Acronyms & Abbreviations

Chemical Identity

Synonyms	sodium tetraborate decahydrate sodium tetraborate sodium borate, decahydrate disodium tetraborate decahydrate borax decahydrate
Structural Formula	
Molecular Formula	B ₄ Na ₂ O ₇ ·10H ₂ O
Molecular Weight (g/mol)	381.37
Appearance and Odour (where available)	White crystalline solid. Odourless.
SMILES	<chem>O O O O O O O O O O O O=BOB(OB(OB=O)O{-}.[Na]{+})O{-}.[Na]{+}</chem>

Import, Manufacture and Use

Australian

The following Australian industrial uses were reported under previous mandatory and/or voluntary calls for information.

The chemical has reported domestic uses including:

- in consumer cleaning products such as laundry and dishwashing products; and
- as a deodoriser.

The chemical has reported commercial uses including in:

- flame retardants and fire-preventing agents;
- welding and soldering agents;
- manufacturing glazes and enamels for covering refrigerators and washing machines steel;
- artificially ageing wood; and
- as preservative and tanning agents.

Non-industrial uses identified in Australia include as a pesticide to control ants, fleas, cockroaches, termites and silverfish.

The chemical is listed on the 2006 High Volume Industrial Chemicals List (HVICL) with a total reported volume of between 1000 and 9999 tonnes. The chemical is available to consumers in 100 % powder form.

The National Pollutant Inventory (NPI) holds data for all sources of the chemical in Australia.

International

The following international uses have been identified through European Union Registration, Evaluation, Authorisation and Restriction of Chemicals (EU REACH) dossiers; the Organisation for Economic Cooperation and Development Screening Information Dataset Initial Assessment Report (OECD SIAR); Galleria Chemica; Substances and Preparations in the Nordic countries (SPIN) database; the European Commission Cosmetic Ingredients and Substances (CosIng) database; United States (US) Personal Care Product Council International Nomenclature of Cosmetic Ingredients (INCI) dictionary; and eChemPortal: OECD High Production Volume chemical program (OECD HPV), the US Environmental Protection Agency's Aggregated Computational Toxicology Resource (ACToR), and the US National Library of Medicine's Hazardous Substances Data Bank (HSDB).

The chemical has reported cosmetic use as a buffering agent.

The US Cosmetic Ingredient Review (CIR) expert panel stated that there were 280 uses of the chemical in cosmetic products in 2002 with use concentrations ranging between 0.1 % to 3 % (CIR, 2006). Borax (CAS No. 1303-96-4) has also been reported as present in a number of personal care products, with a concentration of up to 1 % only stated for a personal care cream (Household Products Database, US Department of Health and Human Services).

The chemical has reported domestic uses, including in:

- adhesives (binding agents);
- colouring agents;
- cleaning/washing agents;

- paints, lacquers and varnishes;
- fillers;
- fertilisers;
- surface-active agents; and
- surface treatment.

Borax (CAS No. 1303-96-4) has been reported as present in a range of domestic products including various home maintenance products (including landscape/yard) at varied concentrations. A concentration of up to 100 % has been reported for various hand soap products (Household Products Database, US Department of Health and Human Services).

The chemical has reported commercial uses, including in:

- anti-freezing agents;
- anti-set-off and anti-adhesive agents;
- conductive agents;
- construction materials;
- cutting fluids;
- corrosion inhibitors;
- fixing agents;
- impregnation materials;
- flame retardants and extinguishing agents including in heat-resistant glassware and as a fire-resistant additive for paints;
- formulating cellulose insulation for textiles, leather, fur, wood and wood products, paper and paper products, and building and construction materials including plaster board and wood;
- lubricants and additives;
- photo chemicals;
- process regulators;
- reprographic agents; and
- welding and soldering agents.

The chemical has reported site-limited uses, including:

- as an intermediate;
- as a heat transferring agent; and
- in an electroplating agent.

The following non-industrial uses have been identified internationally for the chemical including in:

- non-agricultural pesticides and preservatives; and
- agricultural pesticides.

Restrictions

Australian

Borax is listed in the *Poisons Standard* (Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP, 2014)) in Schedule 5 as follows:

'BORIC ACID (excluding its salts) and BORAX **except**:

- (a) when included in Schedule 4;
- (b) in preparations, other than insect baits, containing 1 per cent or less of boron; or
- (c) in hand cleaning preparations'.

BORON, including boric acid and borax, is also listed in Schedule 4 for non-industrial uses.

Schedule 5 chemicals are labelled with 'Caution'. These are substances with a low potential for causing harm, the extent of which can be reduced through the use of appropriate packaging with simple warnings and safety directions on the label.

International

Borax (CAS No. 1303-96-4) is listed on the following (Galleria Chemica):

- EU Regulation (EC) No 1223/2009 of the European Parliament and of the Council of 30 November 2009 on cosmetic products—Annex III—List of substances which cosmetic products must not contain except subject to the restrictions laid down;
- New Zealand Cosmetic Products Group Standard—Schedule 5—Table 1: List of substances which cosmetic products must not contain except subject to restrictions and conditions laid down;
- Health Canada List of prohibited and restricted cosmetic ingredients (The Cosmetic Ingredient "Hotlist"); and
- The US CIR expert panel did not express any concern for the use of the chemical in cosmetic products with the stated use concentrations of 0.1–3 %, considering the low dermal absorption through intact skin. However, using the chemical on damaged skin, in which the barrier function of the skin has been compromised, was not recommended (CIR, 2006).

Restrictions for borax for certain types of cosmetic products according to the European Commission Cosmetics Directive Annex III (List of restricted substances) and New Zealand Cosmetic Products Group Standard (Schedule 5) are:

- 'the maximum concentration for borax in talc cosmetic products is 5% (as boric acid). These are not to be used in products for children under 3 years of age and not to be used on peeling or irritated skin if the concentration of free soluble borates exceeds 1.5% (as boric acid);
- oral hygiene and other hygiene products, the maximum concentration is 0.1% (as boric acid). These are not to be used in products for children under 3 years of age;
- for other cosmetic products (excluding bath products and hair waving products), the maximum concentration is 3% (as boric acid). These are not to be used in products for children under 3 years of age and not to be used on peeling or irritated skin if the concentration of free soluble borates exceeds 1.5% (as boric acid); and
- the maximum concentration for borax in bath products is 18% (as boric acid). These are not to be used in products for children under 3 years of age. The maximum concentration for borax in hair waving products is 8% (as boric acid)'.

Existing Work Health and Safety Controls

Hazard Classification

Borax (CAS No: 1303-96-4) is classified as hazardous, with the following risk phrases for human health in the Hazardous Substances Information System (HSIS) (Safe Work Australia):

- T; R60 (Reproductive Category 2) (Reproductive toxicity)
- T; R61 (Reproductive Category 2) (Developmental toxicity).

Exposure Standards

Australian

The chemical has an exposure standard of 5 mg/m³ time weighted average (TWA).

International

The following exposure standards are identified for the chemical (Galleria Chemica):

- Canada 1–5 mg/m³ TWA, 6 mg/m³ short-term exposure limit (STEL) (inorganic borate compounds);
- Denmark 1–2 mg/m³ TWA;
- Germany 0.5 mg/m³ TWA;
- Spain 5 mg/m³ TWA;
- Sweden and UK 2 mg/m³ TWA.

Health Hazard Information

Borax (CAS No. 1303-96-4) is a boron-containing compound; its toxicity is driven predominantly by boron. Borax and other simple inorganic borates will exist predominantly as undissociated boric acid (H₃BO₃) in dilute aqueous solutions at physiological and acidic pH. As boric acid is a very weak acid with a pKa of 9.2, undissociated boric acid is the main species present in mammal blood following exposure to inorganic borates, including borax. For this reason, the majority of toxicological studies (acute and longer-term) of borates have involved either boric acid or borax.

Since inorganic borate toxicity is driven predominantly by boron, the toxicokinetics and toxicological effects of inorganic borates, including borax, are expected to be similar on a boron-equivalent basis. Therefore, the data obtained from studies on other inorganic borates can be read across for human health risk assessment of different boron-containing compounds, including borax.

Boron is considered to be an essential nutrient and an acceptable daily intake (ADI) of 0.32 mg/kg bw/day has been assigned. This ADI would amount to 22.4 mg boron/day for a 70 kg adult human (Australian Government Department of Health, 2008).

Toxicokinetics

As stated above, undissociated boric acid is the main species present in mammal blood following exposure to simple inorganic borates, including borax and boric acid. Therefore, the toxicokinetics of simple inorganic borates, including borax and boric acid,

is similar in rats and humans with respect to absorption, distribution, and metabolism. The major difference between animals and humans is with respect to renal clearance, which is approximately three times faster in rats than in humans.

Simple inorganic borates are readily and completely absorbed in humans and animals following oral administration as shown by the levels of boric acid in urine, blood or tissues. Several studies of boric acid uptake following oral ingestion in human volunteers, and reports of human ingestion of boric acid with fatal consequences, also provided evidence of rapid and complete oral absorption.

Dermal absorption of simple inorganic borates through intact skin is insignificant (very low) in all species evaluated, including rats, rabbits, new-born infants and adult humans, although penetration through damaged or abraded skin has been demonstrated. A dermal absorption rate of 0.5 % is assumed for borates as a worst case scenario.

Inhalation absorption is also assumed to be 100 %, as a worst case scenario.

Absorbed boric acid is distributed rapidly and evenly throughout the body water in humans and animals. There is no evidence of boric acid accumulation in humans or animals. It is noted that boron levels in bones were approximately three-fold higher than in soft tissue.

Boric acid is the main species present in the blood and is not further metabolised due to the high energy required (523 kJ/mol) to break the B–O bond. Boric acid is excreted rapidly with a half-life of <24 hours in humans and animals and is mainly excreted in the urine (>90 %), regardless of the route of administration (WHO, 1998; US EPA, 2004; EU RAR, 2009; ATSDR, 2010; REACH).

Acute Toxicity

Oral

The chemical has low acute toxicity in animal tests following oral exposure. The median lethal dose (LD50) in rats is >2000 mg/kg bw. Observed sub-lethal effects included central nervous system (CNS) depression, ataxia and convulsions (WHO, 1998; HERA, 2005; EU RAR, 2009; ATSDR, 2010).

Dermal

The chemical has low acute toxicity in animal tests following dermal exposure. The LD50 in rats is >2000 mg/kg bw. It is also noted that the dermal absorption through intact skin is very low; a dermal absorption rate of 0.5 % is assumed (see **Toxicokinetics**) (WHO, 1998; HERA, 2005; EU RAR, 2009).

Inhalation

The chemical has low acute toxicity in animal tests following inhalation exposure. The median lethal concentration (LC50) in rats is >2 mg/L (HERA, 2005; EU RAR, 2009; ATSDR, 2010).

Observation in humans

There is a large database of accidental or intentional boron poisoning incidents in humans following exposure to simple inorganic borates. A review of more than 700 cases of acute boric acid exposures in adults and children found that 88.3 % of cases were without symptoms. Although the report provided only limited information on dose response, dose ranges of 100 mg to 55 g boric acid, and 10 mg to 89 g of boric acid were reported for symptomatic and asymptomatic cases, respectively (Litovitz et al., 1988).

There are case reports of lethal oral exposures of humans involving accidental or intentional ingestion of high doses of boric acid. While oral lethal doses for boron (as boric acid) have been quoted as 2–3 g for infants, 5–6 g for children, and 15–20 g for

adults, the data are largely unsubstantiated. Difficulty in making appropriate quantitative judgment about lethal dose was also noted due to medical intervention in most cases and the unsubstantiated data.

Following ingestion of a formula accidentally prepared with a 2.5 % aqueous solution of boric acid, five infants became lethargic, developed vomiting and diarrhoea, and died within three days of exposure (estimated dose of 4.5–14 g boric acid). Deaths have also occurred in a 77-year-old man following ingestion of 30 g of boric acid and in a 45-year-old man following ingestion of approximately 280 g of boric acid. In both instances, clinical signs were similar—vomiting, diarrhoea, erythema, cyanotic extremities, acute renal failure, cardiopulmonary hypertension and death from cardiac insufficiency (WHO, 1998; US EPA, 2004; EU RAR, 2009; ATSDR, 2010; REACH).

Corrosion / Irritation

Skin Irritation

The chemical is reported to either not irritate the skin or slightly irritate the skin in animal studies. The effects were not sufficient to warrant a hazard classification.

The chemical did not cause skin irritation when applied at a dose of 0.5 g and only caused very mild irritation when applied as 10 mL of 5 % borax in water in rabbit studies. The chemical has been reported to be a mild skin irritant in guinea pigs (WHO, 1998; HERA, 2005; EU RAR, 2009).

Eye Irritation

Although slight eye irritant effects were reported in animal studies, effects were not sufficient to warrant a hazard classification for the chemical.

The chemical was found to induce reversible conjunctival redness and chemosis, and has effects on the cornea and iris in rabbits. Irritation was possibly due to the crystalline nature of the compound (HERA, 2005; EU RAR, 2009).

Observation in humans

Acute respiratory effects have been extensively documented in workers following inhalation of boric acid, boron oxide, and other borates (including borax) as dusts in a number of studies. Effects include nasal and eye irritation, throat irritation, cough and breathlessness. No effects on lung function were observed and the effects identified by workers were 'chemesthetic' (physical presence of dusts on the sensory system of workers). These effects were regarded as sensory irritant effects that would typically be seen in normal populations in the absence of respiratory hypersensitivity.

It was also concluded that these effects are most likely due to the physical exposure to the dust of these chemicals rather than a specific irritant chemical effect. As these effects were not considered a 'serious irritation to the respiratory tract' and were most likely due to a physical effect, a hazard classification for respiratory system irritation is not warranted (EU RAR, 2009).

Sensitisation

Skin Sensitisation

The available information indicates that the chemical is not likely to be a skin sensitiser.

In a skin sensitisation test (Buehler) conducted in guinea pigs (male/female) according to the OECD Test Guideline (TG) 406, borax did not cause skin sensitisation following application with concentration of 95 %, moistened with distilled water to enhance skin contact, during both the induction and challenge phases (EU RAR, 2009).

Observation in humans

No evidence of skin or respiratory sensitisation in humans exposed occupationally to borates has been reported (European Commission, 2009; EU RAR, 2009).

Repeated Dose Toxicity

Oral

A number of repeated dose oral toxicity studies in animals have indicated that the main target organ for boron toxicity is the testis, leading to reproductive and developmental adverse effects. Adverse haematological effects indicative of increased red blood cell destruction have also been commonly noted.

An overall no observed adverse effect level (NOAEL) of 17.5 mg boron/kg bw/day (equivalent to 155 mg borax/kg bw/day) has been determined, from a two-year study of borax in rats, for clinical effects and the testicular atrophy observed at the highest dose. The lowest observed adverse effect level (LOAEL) was stated to be 58.5 mg boron/kg bw/day (equivalent to 516 mg borax/kg bw/day) (WHO, 1998; US EPA, 2004; EU, 2009; EU RAR, 2009; ATSDR, 2010; REACH).

In a repeated dose toxicity study, Sprague Dawley (SD) rats (10/sex/group) were fed borax or boric acid in the diet at doses of 0, 52.5, 175, 525, 1750, and 5250 ppm boron mg/kg bw/day for 13 weeks (equivalent to 0, 2.6, 8.8, 26, 88, and 260 mg boron/kg bw/day). Similar effects were observed with both borax and boric acid. The chemical produced a 100 % mortality at the highest dose. Rapid respiration, eye inflammation, swelling of the paws, and desquamation of the skin on paws and tails were observed in animals at the top two doses. Microscopic examination revealed complete testicular atrophy at 1750 ppm in all males and partial testicular atrophy at 525 ppm boron in four males fed the chemical. A 90-day NOAEL of 175 ppm boron (equivalent to 8.8 mg boron/kg bw/day) was established in this study, based on clinical signs of toxicity and testicular atrophy (WHO, 1998; US EPA, 2004; EU RAR, 2009; REACH).

In another repeated dose toxicity study, SD rats (35/sex/group) were fed borax (CAS No. 1303-96-4) in the diet at doses of 0, 117, 350, or 1170 ppm boron, or as 0, 52, 155, 516 mg borax/kg bw/day (equivalent to 0, 5.9, 17.5, 58.5 mg boron/kg bw/day) for two years. Treatment-related effects were not observed in rats receiving borax at doses of 52 and 155 mg/kg bw/day. Reduction in body weight was observed in males and females in the highest dose group, accompanied by decreased food consumption. Animals of the highest dose groups had swelling and desquamation of the paws, scaly tails, inflammation of the eyelids, and bloody discharge from the eyes. Testicular atrophy and atrophied seminiferous epithelium were seen in the highest dose males at 6, 12, and 24 months. Testes weights and testes body weight ratios were also significantly ($p < 0.05$) decreased. A NOAEL of 155 mg/kg bw/day of borax (equivalent to 17.5 mg boron/kg bw/day) was determined following 24 months of exposure; based on clinical effects and the testicular atrophy observed at the highest dose (WHO, 1998; US EPA, 2004; ATSDR, 2010; REACH).

Dermal

No data are available.

Inhalation

No data are available.

Observation in humans

In addition to numerous acute poisoning incidents with boric acid (see **Acute toxicity: Observation in humans**), some data are available on effects from repeated doses of boric acid or borax as treatments for medical conditions. Multiple exposures from

oral and dermal routes have resulted in a variety of symptoms including dermatitis, alopecia, loss of appetite, nausea, vomiting, diarrhoea, and focal or generalised CNS effects or convulsions (WHO, 1988; European Commission, 2009; ATSDR, 2010).

Exposures ranging from 4 to 30 g (estimated average daily ingestion of 0.143–0.429 g) of borax have been reported in seven infants (aged 6–16 weeks) following the use of pacifiers coated with a borax and honey mixture for 4–10 weeks. Toxicity was manifested by generalised or alternating focal seizure disorders, irritability, and gastrointestinal disturbances (O'Sullivan & Taylor, 1983).

Genotoxicity

Although the relevant data are not available for the chemical, the available information on boric acid indicates that the chemical is not likely to have mutagenic or genotoxic potential (US EPA, 2004; EU RAR, 2009; ATSDR, 2010; REACH).

Boric acid (CAS No. 10043-35-3) tested negative in several in vitro tests such as:

- bacterial reverse mutation tests with *Salmonella typhimurium* strains;
- in vitro mammalian cell gene mutation tests with mouse lymphoma L5178Y cells;
- in vitro mammalian chromosome aberration (chromosome aberration) tests using Chinese hamster ovary (CHO) cells and human peripheral lymphocytes;
- sister chromatid exchange assays in mammalian cells (DNA damage and/or repair) in CHO cells and human peripheral lymphocytes; and
- unscheduled DNA synthesis (DNA damage and/or repair) in mammalian cells in vitro using rat hepatocytes.

In an in vivo mouse bone marrow micronucleus test with boric acid (CAS No. 10043-35-3), the chemical did not induce chromosome aberrations.

Carcinogenicity

Limited data available on the chemical and on other inorganic borates indicate that the chemical is not likely to have carcinogenic potential. The chemical is also not considered to have mutagenic or genotoxic potential (see **Genotoxicity**).

In a chronic toxicity study, SD rats (35/sex/group) were fed borax (CAS No. 1303-96-4) in the diet at doses of 0, 117, 350, or 1170 ppm boron or as 0, 52, 155, 516 mg borax/kg bw/day (equivalent to 0, 5.9, 17.5, 58.5 mg boron/kg bw/day) for two years (see **Repeat dose toxicity: Oral**). No signs of carcinogenicity were reported in the study. It was reported that less than one third of treated animals (10 animals/sex) of the control and high dose group in the rat study were used for macroscopic and histopathological examination. Animals in the low and mid-dose groups were not examined. A NOAEL of 155 mg/kg bw/day of borax (equivalent to 17.5 mg boron/kg bw/day) was determined following 24 months of exposure; based on clinical effects and the testicular atrophy observed at the highest dose (WHO, 1998; US EPA, 2004; ATSDR, 2010; REACH).

In a carcinogenicity study, boric acid (CAS No. 10043-35-3) was administered to B6C3F1 mice (50/sex/group) in the diet at 0, 2500, 5000 ppm (equivalent to 0, 446, 1150 mg boric acid/kg bw/day) for two years (see **Reproductive and developmental toxicity**). Male mice showed an increase in testicular atrophy (3/49 control, 6/50 low dose and 27/47 high dose) and interstitial cell hyperplasia in the testis (0/49 control, 0/50 low dose, 7/47 high dose) at the high dose. There was no evidence of carcinogenicity in the study. The testicular effects noted related to reproductive and developmental toxicity. The NOAEL for carcinogenicity was equivalent to 1150 mg boric acid/kg bw/day (201 mg boron/kg bw/day), the highest tested dose.

Data were not available regarding cancer in humans or animals following inhalation exposure to boron compounds in the group (US EPA, 2004; EU RAR, 2009; ATSDR, 2010; REACH).

Reproductive and Developmental Toxicity

The chemical is classified as hazardous—Category 2 substance toxic to reproduction—with the risk phrases ‘May impair fertility’ (T; R60) and ‘May cause harm to the unborn child’ (T; R61) in HSIS (Safe Work Australia). The available data support this classification.

The testes and the developing foetus have been identified as the most sensitive targets of boron toxicity in animal studies, with the rat being the most sensitive species. The reported testicular effects included reduced organ weight and organ:body weight ratio; atrophy and degeneration of the spermatogenic epithelium; impaired spermatogenesis; and reduced fertility. The reported developmental effects included high prenatal mortality; reduced foetal body weight; and malformations and variations of the eyes, CNS, cardiovascular system, and axial skeleton. The NOAEL for fertility of 100 mg/kg bw/day of boric acid (equivalent to 17.5 mg boron/kg bw/day) has been determined, from two-year and three-generational studies in rats, based on testicular effects. The critical endpoint NOAEL for developmental effects has been determined as 55 mg/kg bw/day of boric acid (equivalent to 9.6 mg boron/kg bw/day) in rats (WHO, 1998; US EPA, 2004; EU RAR, 2009; ATSDR, 2010; REACH).

In a combined repeated/reproductive toxicity study, SD rats (35/sex/group) were fed borax (CAS No. 1303-96-4) in the diet at doses of 0, 117, 350, or 1170 ppm boron or 0, 52, 155, 516 mg borax/kg bw/day (equivalent to 0, 5.9, 17.5, 58.5 mg boron/kg bw/day) for two years (see **Repeat dose toxicity: Oral**). Testicular atrophy, degeneration of seminiferous epithelium, reduced sperm count, and a reduction in fertility were seen in the highest dose males. Testes weights and testes:body weight ratios were also significantly ($p < 0.05$) decreased. A NOAEL for fertility of 155 mg/kg bw/day of borax (equivalent to 17.5 mg boron/kg bw/day) was determined following 24 months of exposure; based on clinical effects and the testicular atrophy observed at the highest dose (WHO, 1998; US EPA, 2004; ATSDR, 2010; REACH).

Limited data are available for developmental effects of borax although developmental effects have been reported for boric acid (CAS No. 10043-35-3). In a developmental toxicity study, boric acid was fed in the diet to pregnant SD rats (60/group) for gestation days (GD) 0–20. The calculated average dose of boric acid consumed was 19, 36, 55, 76, and 143 mg/kg bw/day (3.3, 6.3, 9.6, 13.3, and 25 mg boron/kg bw/day). There was little evidence of maternal toxicity at any of the doses tested. Reduction in mean foetal body weights and an increased percentage of foetuses with skeletal malformations (wavy ribs, short rib XIII) per litter were noted on GD 20 at the highest two doses. The NOAEL for developmental toxicity was determined as 9.6 mg boron/kg bw/day and the LOAEL was 13.3 mg boron/kg bw/day, based on decreased foetal body weight (US EPA, 2004; EU RAR, 2009; ATSDR, 2010; REACH).

In another developmental toxicity study, boric acid was fed to pregnant SD rats in the diet at doses (calculated average) of 0, 78, 163, or 330 mg boric acid/kg bw/day (equivalent to 0, 13.6, 28.5, or 57.7 mg boron/kg bw/day) on GD 0–20. A maternal NOAEL of 13.6 mg boron/kg bw/day and LOAEL of 28.5 mg boron/kg bw/day was established, based on the changes in organ weights. Foetal body weight per litter decreased at the lowest dose of 13.6 mg boron/kg bw/day and above, and the NOAEL for developmental toxicity was determined to be < 13.7 mg boron/kg bw/day. Increased incidence of foetal skeletal abnormalities occurred at 28.4 mg boron/kg bw/day (US EPA, 2004; EU RAR, 2009; ATSDR, 2010; REACH).

In a developmental toxicity study, New Zealand White rabbits were administered (by gavage) boric acid at doses of 0, 62.5, 125, 250 mg/kg bw/day (equivalent to 0, 10.9, 21.9 and 43.8 mg boron/kg bw/day) during the major organogenesis period on GD 6–19. Decreased food intake during treatment, vaginal bleeding, and increased prenatal mortality (90 % post-implantation resorption compared with 6 % in controls) were noted in dams at the highest dose (43.8 mg boron/kg bw/day). The number of pregnant females with no live foetuses was greatly increased (73 % compared with 0 % in controls) and the number of live foetuses per litter on day 30 was significantly reduced (2.3/litter compared with 8.8/litter in controls). The percentage of foetuses with cardiovascular variations (defects) was significantly increased from 11 % in controls to 64 % in the highest dose group. Primarily due to the incidence of foetuses with cardiovascular defects in this group, malformed live foetuses per litter increased significantly. A maternal NOAEL for boric acid of 125 mg/kg bw/day (21.8 mg boron/kg bw/day) was determined, based on reduced food intake at the next higher dose. The NOAEL for developmental toxicity was also 125 mg/kg bw/day (21.8 mg boron/kg bw/day), based on resorptions and cardiovascular malformations at the next higher dose. The observed maternal effects were minor and the observed severe developmental effects were not secondary to the maternal toxicity (WHO, 1998; US EPA, 2004; EU RAR, 2009; ATSDR, 2010; REACH).

Observation in humans:

Correlations between boron levels and reproductive or developmental effects were investigated in several epidemiological studies in Chinese and Turkish workers and in populations living in areas with high environmental levels of boron. Three groups were compared in Chinese study: boron mining and processing workers; men living in local village, not in boron industry (high soil boron); and men living in distant village (normal soil boron content). In Turkish study, reproductive effects of boron exposure in workers employed in a boric acid production plant were investigated. As semen analysis is the most sensitive indicator for testicular toxicity in humans, semen parameters were evaluated in both studies. Even though a mean boron intake of up to 125

mg boron/day of over 100 times greater than the average daily exposure of the general population was determined for the highest exposed Chinese group, adverse testicular effects were not seen. Turkish workers also did not show any adverse testicular effects despite a high mean calculated daily boron exposure (14.45 ± 6.57 mg boron/day) in the highly exposed group.

Other epidemiological studies of exposure to workers and the general population with high environmental boron showed no reproductive or developmental effects. The absence of reproductive and developmental effects in humans has been postulated to be due to the presence of higher levels of zinc in the soft tissue of humans (compared with rodents), which reduced the toxicity of boron containing compounds by interacting with boron (Bureau for Chemical Substances, 2013; REACH).

The above epidemiological studies have been considered recently as part of the opinion on harmonised classification and labelling of boric acid (CAS No. 10043-35-3) at EU level. The highest occupational exposure levels of boron in the two occupational cohorts and in the environmental exposed cohorts were much lower than the animal studies; 15-135 times lower than the animal LOAEL for fertility effects and 7-66 times lower than the animal LOAEL for developmental toxicity. At those exposure levels in epidemiological studies, assuming a similar sensitivity of humans as in the four laboratory species studies, it is unlikely that any adverse effects on human male fertility would have been noted. It was also noted that effects on female fertility and prenatal developmental were not investigated as part of the epidemiological studies. Therefore, the stated epidemiological studies do not sufficiently address the relevance of the animal toxicity data to humans at similar dose levels as causing toxicity in experimental animals. It was concluded that human data showing no clear evidence of reproductive toxicity do not contradict the animal data (ECHA, 2014).

Other Health Effects

Neurotoxicity

Although CNS depression was observed in humans poisoned with boric acid (CAS No. 10043-35-3) at very high doses, there was no indication that the chemical has neurotoxic properties (EU RAR, 2009).

In a study to evaluate potential neurotoxicity, SD rats (10/sex/dose) were administered boric acid (CAS No. 10043-35-3) as a single gavage dose of 2000 mg/kg bw followed by a 14-day observation period. Although there were no mortalities and no clinical signs of toxicity, a 16 % decrease in total body weight gain was noted in the treatment group, compared with the control group at the end of the study. Functional observation battery and motor activity evaluations did not show any evidence of neurotoxicity and neurohistopathological findings were also negative. It was concluded that a single oral (gavage) dose of boric acid (CAS No. 10043-35-3) at a dose of 2000 mg/kg bw administered to rats was not neurotoxic (REACH).

Rats exposed to boron oxide (aerosol) at concentrations of 470 mg boron oxide/m³ (73 mg boron/m³) for 10 weeks, 175 mg boron oxide/m³ (27 mg boron/m³) for 12 weeks, or 77 mg boron oxide/m³ (12 mg boron/m³) for 24 weeks did not show any gross or microscopic effects on the brain (ATSDR, 2010).

Risk Characterisation

Critical Health Effects

The critical health effects for risk characterisation include reproductive and developmental toxicity.

Public Risk Characterisation

Although the use of the chemical in cosmetic products in Australia is not known, the chemical has reported cosmetic use overseas as a buffering agent (see **Import, manufacture and use**). Considering the stated use concentrations for cosmetics and the low dermal absorption through intact skin, the chemical is unlikely to be present in final cosmetic products at a sufficiently high concentration to cause any significant human health concerns.

The chemical also has reported domestic uses in Australia and overseas. As the chemical will also be used for formulation of other products such as consumer cleaning products, the risks associated with these uses were assessed by the (former) National Drugs and Poisons Schedule Committee (NDPSC) for boric acid (CAS No. 10043-35-3). The concentrations in these final products were not considered to be sufficiently high to cause any significant human health concern. A quantitative risk assessment of consumer cleaning products containing boric acid at 1 % (laundry products) and 2 % (dishwashing liquids), concluded that these products are not of any significant human health concerns. This assessment was based on worst case exposure estimates of absorption in relation to hand laundry washing and dish washing of 0.0001 µg/kg/day and 0.00015 ug/kg/day, respectively, compared with the ADI for exposure to boron of around 20 mg/day (Australian Government Department of Health, 2008). It is noted that absorption through the intact skin is negligible (see **Toxicokinetics**).

Therefore, the risk to public health is not considered to be unreasonable and further risk management is not considered necessary for public safety.

Occupational Risk Characterisation

Dermal, ocular, and inhalation exposure of workers to the chemical can occur during product formulation, particularly where manual or open processes are used. These might include transfer and blending activities, quality control analysis, and cleaning and maintaining equipment. Worker exposure to the chemical at lower concentrations could also occur while using formulated products containing the chemical. The level and route of exposure will vary depending on the method of application and work practices employed.

Given the critical health effects, the chemical could pose an unreasonable risk to workers unless adequate control measures to minimise dermal, ocular and inhalation exposure to the chemical are implemented. The chemical should be appropriately classified and labelled to ensure that a person conducting a business or undertaking (PCBU) at a workplace (such as an employer) has adequate information to determine appropriate controls.

Based on the available data, the hazard classification in HSIS is considered appropriate.

NICNAS Recommendation

Current risk management measures are considered adequate to protect public and workers' health and safety, provided that all requirements are met under workplace health and safety and poisons legislation as adopted by the relevant state or territory.

Should additional use becomes available that may pose a risk to workers and/or the public, a Tier III assessment will be undertaken to characterise the exposure and potential risk from this use scenario.

Regulatory Control

Work Health and Safety

The chemical is recommended for classification and labelling under the current approved criteria and adopted GHS as below. This assessment does not consider classification of physical hazards and environmental hazards.

Hazard	Approved Criteria (HSIS) ^a	GHS Classification (HCIS) ^b
Reproductive and Developmental Toxicity	Repro. Cat 2 - May impair fertility (T; R60)* Repro. Cat 2 - May cause harm to the unborn child (T; R61)*	May damage fertility. May damage the unborn child - Cat. 1B (H360FD)

^a Approved Criteria for Classifying Hazardous Substances [NOHSC:1008(2004)].

^b Globally Harmonized System of Classification and Labelling of Chemicals (GHS) United Nations, 2009. Third Edition.

* Existing Hazard Classification. No change recommended to this classification

Advice for consumers

Products containing the chemical should be used according to the instruction on the label.

Advice for industry

Control measures

Control measures to minimise the risk from dermal, ocular, and inhalation exposure to the chemical should be implemented in accordance with the hierarchy of controls. Approaches to minimise risk include substitution, isolation and engineering controls. Measures required to eliminate or minimise risk arising from storing, handling and using a hazardous chemical depend on the physical form and the manner in which the chemical is used. Examples of control measures which may minimise the risk include, but are not limited to:

- using closed systems or isolating operations;
- health monitoring for any worker who is at risk of exposure to the chemical if valid techniques are available to monitor the effect on the worker's health;
- air monitoring to ensure control measures in place are working effectively and continue to do so;
- minimising manual processes and work tasks through automating processes;
- work procedures that minimise splashes and spills;
- regularly cleaning equipment and work areas; and
- using protective equipment that is designed, constructed, and operated to ensure that the worker does not come into contact with the chemical.

Guidance on managing risks from hazardous chemicals are provided in the *Managing risks of hazardous chemicals in the workplace—Code of practice* available on the Safe Work Australia website.

Personal protective equipment should not solely be relied upon to control risk and should only be used when all other reasonably practicable control measures do not eliminate or sufficiently minimise risk. Guidance in selecting personal protective equipment can be obtained from Australian, Australian/New Zealand or other approved standards.

Obligations under workplace health and safety legislation

Information in this report should be taken into account to assist with meeting obligations under workplace health and safety legislation as adopted by the relevant state or territory. This includes, but is not limited to:

- ensuring that hazardous chemicals are correctly classified and labelled;
- ensuring that (material) safety data sheets ((m)SDS) containing accurate information about the hazards (relating to both health hazards and physicochemical (physical) hazards) of the chemical are prepared; and
- managing risks arising from storing, handling and using a hazardous chemical.

Your work health and safety regulator should be contacted for information on the work health and safety laws in your jurisdiction.

Information on how to prepare an (m)SDS and how to label containers of hazardous chemicals are provided in relevant codes of practice such as the *Preparation of safety data sheets for hazardous chemicals—Code of practice* and *Labelling of workplace hazardous chemicals—Code of practice*, respectively. These codes of practice are available from the Safe Work Australia website.

A review of the physical hazards of the chemical has not been undertaken as part of this assessment.

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