Boric acid: Human health tier II assessment

29 June 2018

Chemicals in this assessment

Chemical Name in the Inventory	CAS Number
Boron oxide (B2O3)	1303-86-2
Boric acid (H3BO3)	10043-35-3
Boric acid	11113-50-1
Boric acid (H3B3O6)	13460-51-0

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.

For more detail on this program please visit:**www.nicnas.gov.au**

Disclaimer

ACRONYMS & ABBREVIATIONS

Grouping Rationale

The chemicals in this group are boron-containing compounds and their toxicity is driven predominantly by boron. Boron is a naturally-occurring element found in the environment; it forms strong covalent bonds with oxygen in a range of borate oxyanions. The broader borate category includes salts and esters of boric acid and has also been defined (in industrial usage) to include any substance with significant borate oxyanion content. Borax, ulexite, and colemanite are three important mineral sources of borates. Boric acid, borax and boron oxide are among the main commodity borate compounds. Following ingestion, borate anions, whether single (BO_3^{3-}) or condensed ($B_4O_7^{3-}$), react readily with hydrochloric acid in the stomach to form boric acid.

Boric acid is a very weak acid with a pKa of 9.2 and exists primarily as the undissociated acid (H_3BO_3) in aqueous solutions at physiological pH and acidic pH at low concentrations, regardless of whether the source of boron is boric acid or other simple inorganic borates, including boron oxide (B_2O_3). Boron oxide, being an anhydride of boric acid and oxyanions, reacts exothermically with water in the body to form boric acid.

Therefore, the toxicokinetics and the toxicity of the borate salts and acids, including the chemicals in this group, will be similar on a boron-equivalent basis, particularly following ingestion, and read across can be applied for the assessment of borate substances. Read across among borate substances is further supported by the fact that the systemic effects and some local effects have been attributed to the production of boric acid (WHO, 1998; US EPA, 2004; EU RAR, 2009; ATDSR, 2010; REACHb).

It is noted that boric acid (CAS No. 11113-50-1) is described as 'crude natural, containing not more than 85 % of (H_3BO_3), calculated on a dry weight basis' (Hazardous Substances Information System—HSIS) (Safe Work Australia).

Import, Manufacture and Use

Australian

The following Australian industrial uses were reported under previous mandatory and/or voluntary calls for information. Information on domestic uses of boric acid (CAS No. 10043-35-3) has been accessed at **http://www.boricacid.net.au/uses-of-boric-acid**.

Boric acid (CAS No. 10043-35-3) has reported domestic use including:

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

Chemicals (CAS No. 1303-86-2, 10043-35-3, 1113-50-1) in this group have reported commercial use including:

- as construction materials additives;
- as flame retardants and fire-preventing agents including in heat-resistant glassware;
- as a fire-resistant additive for paints and dyes, and in electronics;
- as tanning agents;
- in nickel-plating baths;
- in hardening steel, welding flux, and copper brazing; and
- for weatherproofing and fireproofing fabrics.

Chemicals in this group have reported site-limited uses, including:

- as intermediates; and
- in manufacture of articles including crockery, porcelain, enamels, glass, leather, carpets, hats, and artificial gems.

The following non-industrial uses have been identified in Australia for chemicals in this group:

- in pharmaceutical preparations (mild antiseptic/ointments/eye washes);
- as an insecticide and herbicide; and
- for mould protection and for dry rot prevention of wood.

Boric acid (CAS No. 10043-35-3) is listed on the 2006 High Volume Industrial Chemicals List (HVICL) with a total reported volume of between 1000 and 9999 tonnes.

The National Pollutant Inventory (NPI) holds data for all sources of environmental release of the chemicals 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;
- 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).

Chemicals in this group have reported cosmetic uses, including as:

- antimicrobial agents;
- buffering agents; and
- denaturants.

The US Cosmetic Ingredient Review (CIR) Expert Panel stated that there were 77 uses of boric acid (CAS No. 10043-35-3) in cosmetic products in 2002 with a range of use concentrations of 0.1 to 2 % (CIR, 2006). Boric acid (CAS No. 10043-35-3) is reported to be present in three personal care products at concentrations up to 3 % (Household Products Database, US Department of Health and Human Services).

Chemicals in this group have reported domestic uses, including in:

- adhesives (binding agents);
- colouring agents;
- cleaning/washing agents;
- fillers;
- fertilisers; and
- surface treatment.

Boric acid (CAS No. 10043-35-3) is reported to be present in a range of domestic products including various home maintenance products (including landscape/yard) up to a concentration of 50 % (Household Products Database, US Department of Health and Human Services).

Chemicals in this group have reported commercial uses, including:

- as conductive agents;
- in construction materials;
- in cutting fluids;
- in corrosion inhibitors;
- in electromechanical components;
- in fixing agents;
- in hydraulic fluids and as additives ;
- in impregnation materials;
- in flame retardants and extinguishing agents including in heat-resistant glassware and as a fire-resistant additive for paints;

- in 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;
- in metal treatment (plating, passivation, galvanising etc.);
- as photochemicals;
- as pH−regulation agents;
- in process regulators;
- in reprographic agents; and
- in welding and soldering agents.

Chemicals in this group have reported site-limited uses, including:

- as intermediates;
- in electroplating agents; and
- in producing glass wool.

The following non-industrial uses have been identified internationally for chemicals in this group:

- pharmaceutical preparations (antiseptic/astringent);
- non-agricultural pesticides and preservatives;
- agricultural pesticides; and
- food/feedstuff flavourings and nutrients.

Restrictions

Australian

Boric acid is listed in the *Poisons Standard* (Standard for the Uniform Scheduling of Medicines and Poisons) (SUSMP, 2017) 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 its 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

The chemicals (CAS Nos. 10043-35-3, 11113-50-1) are listed on the following (Galleria Chemica):

- The Association of Southeast Asian Nations (ASEAN) Cosmetic Directive Annex III – Part 1, EU Regulation (EC) No 1223/2009 of the European Parliament and of the Council of 30 November 2009 on cosmetic products—Annex III;
- 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; and
- Health Canada List of prohibited and restricted cosmetic ingredients (The Cosmetic Ingredient "Hotlist").

The US CIR Expert Panel did not express any concern for the use of the chemical (CAS No. 10043-35-3) in cosmetic products with the stated use concentrations of 0.1 to 2 %, considering the low dermal absorption through intact skin. However, the use of the chemical on damaged skin, in which the barrier function of the skin has been compromised, was not recommended (CIR, 2006).

Existing Worker Health and Safety Controls

Hazard Classification

The chemicals (CAS No. 1303-86-2, 10043-35-3, 11113-50-1) are classified as hazardous, with the following hazard categories and hazard statements for human health in the Hazardous Chemical Information System (HCIS) (Safe Work Australia):

- Reproductive toxicity – category 1B; H360FD (May damage fertility. May damage the unborn child).

Metaboric acid (CAS No. 13460-51-0) is not listed on the HCIS (Safe Work Australia).

Exposure Standards

Australian

Boron oxide (CAS No. 1303-86-2) has an exposure standard of 10 mg/m^3 time weighted average (TWA).

International

The following exposure standards are identified (Galleria Chemica).

Boric acid (H_3BO_3) (CAS No: 10043-35-3) has a TWA exposure limit of 2 mg/m^3 in Canada, 10 mg/m^3 in Germany, and 10 mg/m^3 (insoluble particles) in Spain. The chemical also has a short term exposure limit (STEL) of 6 mg/m^3 (borate compounds) in Canada, and 1 mg/m^3 in Germany.

Health Hazard Information

Simple inorganic borates, including the chemicals in this group, will exist predominantly as undissociated boric acid in dilute aqueous solutions at physiological and acidic pH. As a result, undissociated boric acid is the main species present in the blood of mammals following exposure to borates. The toxicokinetics and toxicological effects of the chemicals in this group will therefore be similar on a boron equivalent basis, and the data obtained from studies with different borates can be read across for human health risk assessment of different boron containing compounds (see **Grouping rationale**).

Boron has been postulated 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 human adult (Australian Government Department of Health, 2008).

Toxicokinetics

The toxicokinetics of the chemicals in this group are 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.

The chemicals in this group are readily and completely absorbed in humans and animals following oral administration, as shown by levels of boric acid in urine, blood and tissues. Several studies of boric acid uptake following oral ingestion in human volunteers provide evidence of rapid and complete oral absorption. Reports of human ingestion of boric acid with fatal consequences also support this notion.

Dermal absorption through intact skin is very low in all species evaluated including rats, rabbits, new-born infants and adult humans; although chemicals in this group have been demonstrated to penetrate damaged or abraded skin. A dermal absorption rate of 0.5 % is assumed. Inhalation absorption is 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 soft tissue levels. 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; REACHa, REACHb).

Acute Toxicity

Oral

The chemicals in this group have low acute toxicity in animal tests following oral exposure. The median lethal dose (LD50) in rats is >2000 mg/kg bodyweight (bw) for boron oxide (CAS No. 1303-86-2) and boric acid (CAS No. 10043-35-3). Observed sub-lethal effects included central nervous system (CNS) depression, ataxia and convulsions (WHO, 1998; European Commission, 2009; EU RAR, 2009; ATSDR, 2010; REACHa, REACHb).

Dermal

The chemicals in this group have low acute toxicity in animal tests following dermal exposure. The LD50 in New Zealand White (NZW) rabbits is >2000 mg/kg bw for boric acid (CAS No. 10043-35-3). No mortalities occurred in this study. Local effects including erythema, oedema, atonia, desquamation, necrosis and some

incidences of skin irritation were noted 24 hours after treatment. An LD50 value of >2000 mg/kg bw in rats has also been determined for boron oxide (CAS No. 1303-86-2) (EU RAR, 2009; ATSDR, 2010; REACHa, REACHb).

Inhalation

The chemicals in this group have low acute toxicity in animal tests following inhalation exposure. The reported median lethal concentration (LC50) in rats is >2 mg/L for boric acid (CAS No. 10043-35-3) and for boron oxide (CAS No. 1303-86-2). Ocular discharge, hypoactivity and hunched posture were noted during the first 30 minutes of exposure. Ocular discharge and nasal discharge persisted in most animals after removal from the chamber. All animals recovered by day seven. It was also noted in another study that the highest attainable concentration in these tests was 2 mg/L (EU RAR, 2009; ATSDR, 2010; REACHa, REACHb).

Observation in humans

There is a large database of accidental or intentional poisoning incidents with borates in humans. A review of more than 700 cases of acute boric acid exposures in adults and children found 88.3 % of cases were without symptoms. Although the report provided only limited information on dose response, dose ranges of 0.1–55 g and 0.01–89 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 boric acid have been quoted as 2–3 g for infants, 5–6 g for children, and 15–30 g for adults, the data are largely unsubstantiated. Further difficulty in making appropriate quantitative judgment about lethal dose was also noted due to medical intervention in most cases. 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 after 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 heart failure (WHO, 1998; US EPA, 2004; EU RAR, 2009; ATSDR, 2010; REACHa, b).

Corrosion / Irritation

Respiratory Irritation

Limited data concerning respiratory irritation are available from animal studies.

Nasal and ocular discharge was noted in inhalation studies in rats with boric acid (CAS No. 10043-35-3) (see **Acute toxicity: inhalation**). Ocular discharge and or nasal discharge persisted in most animals after removal from the chamber. All animals recovered by day seven (EU RAR, 2009; REACHb).

An airway sensory irritation respiratory depression study of boric acid conducted in male Swiss-Webster mice concluded that boric acid is unlikely to be a respiratory irritant. Although it was not possible to achieve an aerosol concentration high enough to result in a 50 % respiratory depression (RD50) in mice, the highest concentration of boric acid with acceptable control of the aerosol concentration (1096 mg/m^3) resulted in an RD of 19 %. The RD50 was concluded to be >1096 mg/m^3 for boric acid. A 9 % reduction in respiratory rate was recorded at an exposure concentration of 221 mg/m^3 (Kirkpatrick, 2010). Given that significant respiratory depression is only observed at levels above nuisance dust limit (10 mg/m^3), it is unlikely the chemicals in this group are specific respiratory irritants.

Skin Irritation

The available information indicates that the chemicals in this group are not likely to be skin irritants.

In a skin irritation study, boric acid (CAS No. 10043-35-3) (500 mg) did not cause skin irritation when applied to the intact or abraded skin of NZW rabbits for 24 hours. In another study, 5 mL of a 10 % boric acid (CAS No. 10043-35-3) solution produced no skin irritation following application (time of exposure not indicated) to the intact or abraded skin of NZW rabbits (EU RAR, 2009; REACHb). Although details were not provided, boron oxide (CAS No. 1303-86-2) has also been reported not to be a skin irritant (European Commission, 2009).

Eye Irritation

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

In an eye irritation study conducted using a protocol similar to the Organisation for Economic Co-operation and Development (OECD) Test Guideline (TG) 405, boric acid (CAS No. 10043-35-3) (100 mg) was applied to one eye of each of six NZW rabbits, which were observed up to 21 days after instillation. Conjunctival redness, chemosis, and minor effects on the iris were noted. Iridial lesions were reversed by 48 hours post application, and conjunctival lesions were reversed by day seven (EU RAR, 2009; REACHb). Although details were not provided, boron oxide (CAS No. 1303-86-2) has also been reported not to be an eye irritant (European Commission, 2009).

Observation in humans

Acute respiratory effects have been extensively documented in workers following inhalation of boric acid, boron oxide and other borates as dusts in a number of studies. Effects include nasal and eye irritation, throat irritation, coughing and breathlessness. No effects on lung function were observed and the effects identified

by workers were ‘chemaesthetic’ (caused by the activation of sensory receptors). 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 dust of 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 as irritating to respiratory system is not warranted (EU RAR, 2009).

Sensitisation

Skin Sensitisation

The available information indicates that the chemicals in this group are not likely to be skin sensitisers.

In a skin sensitisation test (Buehler) conducted in guinea pigs (male/female) according to OECD TG 406, boric acid (CAS No. 10043-35-3) did not cause skin sensitisation following application at a concentration of 95 % (moistened with distilled water to enhance skin contact) during both induction and challenge phases (EU RAR, 2009; REACHb). No sensitisation studies with boron oxide (CAS No. 1303-86-2) were available (European Commission, 2009; REACHa).

Observation in humans

No evidence of skin or respiratory sensitisation in humans occupationally exposed 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 are the testes, leading to reproductive and developmental adverse effects. Adverse haematological effects indicative of increased red blood cell destruction have also been commonly noted.

An no observed adverse effect level (NOAEL) of 17.5 mg boron/kg bw/day (equivalent to 100 mg boric acid/kg bw/day) has been determined, from a two-year study of boric acid in rats for effects on the testes and haematology. The lowest observed adverse effect level (LOAEL) was 58.5 mg boron/kg bw/day (equivalent to 334 mg boric acid/kg bw/day) (US EPA, 2004; EU, 2009; EU RAR, 2009; REACHb).

In a repeated dose toxicity study, Sprague Dawley (SD) rats (10/sex/group) were fed boric acid in the diet at doses of 0, 15, 50, 149, 500 or 1490 mg/kg bw/day for 13 weeks (equivalent to 0, 2.6, 8.8, 26, 88 and 260 mg boron/kg bw/day). Rapid respiration, hunched position, bloody nasal discharge, urine stains on the abdomen, inflamed eyes, desquamation and swollen paws and tails were observed in animals at the top two doses. Reduced food consumption and body weight gains were also noted in these animals. All animals at the top dose had died by week six. All the male rats at the top two doses had atrophied testes, histologically complete atrophy of the spermatogenic epithelium, and decreased size of the seminiferous tubules. A 90-day NOAEL of 149 mg/kg bw/day (equivalent to 26 mg boron/kg bw/day) was determined in this study, based on reduction in bodyweights, clinical signs of toxicity and testicular atrophy (US EPA, 2004; EU RAR, 2009; REACHb).

In another repeated dose toxicity study, B6C3F1 mice (10/sex/group) were fed boric acid in the diet at doses of 0, 194/169, 405/560, 811/1120, 1622/2240 or 3246/4480 mg/kg bw/day in males/females, respectively (equivalent to 0, 34/47, 71/98, 142/196, 284/392 and 568/784 mg boron/kg bw/day in males/females). Eight out of the 10 males and six out of 10 females from the highest dose group died before the end of study, with signs of hunched posture, dehydration, foot lesions, and scaly tails. Reductions in mean bodyweights were observed at the three highest doses. As degeneration and atrophy of the seminiferous tubules were noted at ≥142 mg boron/kg bw/day, the NOAEL was established as 71 mg boron/kg bw/day in males (US EPA, 2004; EU RAR, 2009; REACHb).

In a repeated dose toxicity study, SD rats (35/sex/group) were fed boric acid (CAS No. 10043-35-3) in the diet at doses of 0, 33, 100 or 334 mg/kg bw/day for two years (equivalent to 0, 5.9, 17.5 and 58.5 mg boron/kg bw/day). Males of the highest dose group showed hunched posture, inflamed bleeding eyes, desquamation of the tail skins and pads on the paws, and shrunken scrotums. Reduced body weight was noted in males and females in the highest dose group. Significant reduction in red cell volume and haemoglobin was observed mainly in the highest dosed males. Testicular atrophy and seminiferous tubule degeneration was seen in the highest dosed males at six, 12 and 24 months. Microscopic examination of the tissue revealed atrophied seminiferous epithelium and decreased tubular size in the testes. A two-year NOAEL of 100 mg/kg bw/day of boric acid (equivalent to 17.5 mg boron/kg bw/day) was determined based on clinical and haematological effects and the testicular atrophy observed at the highest doses (US EPA, 2004; EU RAR, 2009; REACHb).

Dermal

No data are available.

Inhalation

Limited data are available from animal studies.

Rats exposed to 470 mg/m^3 boron oxide aerosol for 10 weeks, and female dogs exposed to 57 mg/m^3 boron oxide aerosol for 23 weeks, did not show any signs of toxicity or any significant changes in tissues (Wilding et al. 1959; Wilding et al., 1960).

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

Genotoxicity

Based on available information, the chemicals in this group are not considered to have mutagenic or genotoxic potential (US EPA, 2004; EU RAR, 2009; ATSDR, 2010; REACHb).

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 (gene mutation) tests with mouse lymphoma L5178Y cells;
- in vitro mammalian 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

The available information indicate that the chemicals in this group are not likely to be carcinogenic. It is also noted above that the chemicals in this group are not considered to have mutagenic or genotoxic potential (see **Genotoxicity**).

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 or 5000 ppm (equivalent to 0, 446 and 1150 mg boric acid/kg bw/day) for two years. Male mice showed an increase in testicular atrophy (3/49 control, 6/50 low dose and 27/47 highest dose) and interstitial cell hyperplasia in the testes (0/49 control, 0/50 low dose, 7/47 highest dose). There was no evidence of carcinogenicity in the study. The testicular effects noted related to reproductive and developmental toxicity (see **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. It was reported that less than one third of treated animals (10 animals/sex) of the control and the highest dose group in the rat study were used for macroscopic and histopathological examination. Animals in the low and mid-dose groups were not examined.

Evidence of carcinogenicity was absent in two two-year dietary studies in rats exposed to 81 mg boron/kg bw/day as boric acid; and dogs exposed to 6.8 mg boron/kg bw/day as boric acid. Conclusions were limited regarding carcinogenicity in the study in dogs as only 1–2 animals/sex/dose/time were macroscopically and histopathologically examined.

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

Reproductive and Developmental Toxicity

The chemicals (CAS No. 1303-86-2, 10043-35-3, 11113-50-1) are classified as hazardous for reproductive and developmental toxicity—Category 1B; H360FD (May damage fertility. May damage the unborn child) in the HCIS (Safe Work Australia).

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 to bodyweight ratio; atrophy and degeneration of the spermatogenic epithelium; impaired spermatogenesis; and reduced fertility. The developmental effects that have been reported included: high prenatal mortality and reduced foetal body weight as well as 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 (based on testicular effects) from two-year and three-generation studies in rats. The critical NOAEL for developmental effects has been established at 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; ATDSR, 2010; REACHb).

In a repeated dose toxicity study, B6C3F1 mice (10/sex/group) were fed boric acid in the diet at doses of 0, 194/169, 405/560, 811/1120, 1622/2240 or 3246/4480 mg/kg bw/day in males/females, respectively (equivalent to 0, 34/47, 71/98, 142/196, 284/392 and 568/784 mg boron/kg bw/day in males/females) (see **Repeated dose toxicity: oral**). As degeneration and atrophy of the seminiferous tubules were noted at ≥142 mg boron/kg bw/day, the NOAEL was established as 71 mg boron/kg bw/day (equivalent to 405 mg boric acid/kg bw/day) in males (US EPA, 2004; EU RAR, 2009; REACHb).

In another repeated dose toxicity study, SD rats (35/sex/group) were fed boric acid (CAS No. 10043-35-3) in the diet at doses of 0, 33, 100 or 334 mg/kg bw/day for two years (equivalent to 0, 5.9, 17.5 and 58.5 mg boron/kg bw/day) (see **Repeated dose toxicity: oral**). Males of the highest dose group had shrunken scrotums. Testicular atrophy and seminiferous tubule degeneration was seen in the highest dose males at six, 12 and 24 months. Microscopic observations were consistent with these effects. An NOAEL of 100 mg/kg bw/day of boric acid (equivalent to 17.5 mg boron/kg bw/day) was determined, based on the testicular atrophy observed at the highest doses in SD rats (US EPA, 2004; EU RAR, 2009; REACHb).

In a developmental toxicity study, boric acid was fed in the diet to pregnant SD rats (60/group) through gestation days (GD) 0–20. The calculated average dose of boric acid consumed was 19, 36, 55, 76 or 143 mg/kg bw/day (equivalent to 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. A reduction in mean foetal body weights and an increased percentage of foetuses with skeletal malformations per litter were noted on GD 20 at the highest two doses. The NOAEL for developmental toxicity was determined to be 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; REACHb).

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 and 57.7 mg boron/kg bw/day) on GD 0–20. A maternal NOAEL of 13.6 mg boron/kg bw/day was established and the LOAEL was 28.5 mg boron/kg bw/day, 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; REACHb).

In a developmental toxicity study, NZW rabbits were administered (by gavage) boric acid at doses of 0, 62.5, 125 or 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. The percentage of foetuses with cardiovascular 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 highest 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; REACHb).

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 a Chinese study: boron mining and processing workers; men living in local village, not in the boron industry (high soil boron); and men living in a distant village (normal soil boron content). In a 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 (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 exposed group.

Other epidemiological studies of exposure to workers and general populations with high environmental boron showed no reproductive or developmental effects. The higher levels of zinc in the soft tissue of humans have been postulated to have a protective effect against boron toxicity. There was limited evidence of a reduction in reproductive and developmental toxicity for zinc borate compared with boric acid in laboratory studies (SCCS, 2010; Bureau for Chemical Substances, 2013; NICNAS).

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 the 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 chemicals in this group have 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. Animals were observed for a 14-day 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 (REACHb).

Rats exposed to boron oxide (aerosol) at concentrations of 470 mg boron oxide/m^3 (73 mg boron/m^3) for 10 weeks, 175 mg boron oxide/m^3 (27 mg boron/m^3) for 12 weeks, or 77 mg boron oxide/m^3 (12 mg boron/m^3) 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.

Although the available animal data show clear evidence of reproductive and developmental toxicity, epidemiological studies of workers and general populations exposed to boron show no reproductive or developmental effects. However, there are limitations in the human studies (See **Reproductive and Developmental Toxicity Section – Observation in humans**). The available human data are not sufficient to invalidate the animal data.

Public Risk Characterisation

Although the use of chemicals in this group in cosmetic products in Australia is not known, chemicals in this group have reported limited cosmetic uses overseas (see **Import, manufacture and use**). Considering the reported cosmetic uses overseas (as antimicrobial, buffering agents and as denaturants), the concentrations in final cosmetic products are not considered to be sufficiently high to cause any significant human health concerns.

The chemicals in this group have also reported domestic uses in Australia and overseas. As these chemicals will also be used for formulation of other products such as consumer cleaning products, the risks associated with these uses were assessed by the National Drugs and Poisons Schedule Committee (NDPSC). The concentrations in these final products were not considered to be sufficiently high to cause any significant human health concerns. 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 µg/kg/day, respectively, as compared to 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

During product formulation oral, dermal, and inhalation exposure of workers to the chemicals in this group may occur, 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 chemicals at lower concentrations could also occur while using formulated products containing the chemicals. The level and route of exposure will vary depending on the method of application and work practices employed.

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

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 chemicals are recommended for classification and labelling aligned with the Globally Harmonized System of Classification and Labelling of Chemicals (GHS) as below. This does not consider classification of physical hazards and environmental hazards.

From 1 January 2017, under the model Work Health and Safety Regulations, chemicals are no longer to be classified under the Approved Criteria for Classifying Hazardous Substances system

Note:

While the reproductive and developmental toxicity classification (Category 1B; H360FD) is already listed on the HCIS for some members of this group (CAS Nos. 1303-86-2, 10043-35-3, 11113-50-1), this classification should also be applied to the other member of this group (CAS No. 13460-51-0). 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	Not Applicable	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 chemicals in this group should be used according to the instruction on the label.

Advice for industry

Control measures

Control measures to minimise the risk from oral, dermal, and inhalation exposure to the chemicals 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 chemicals are 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 these chemicals has not been undertaken as part of this assessment.

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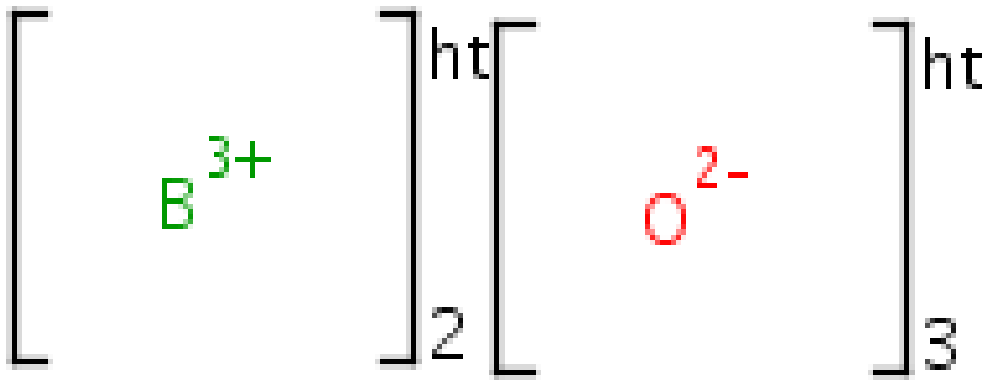
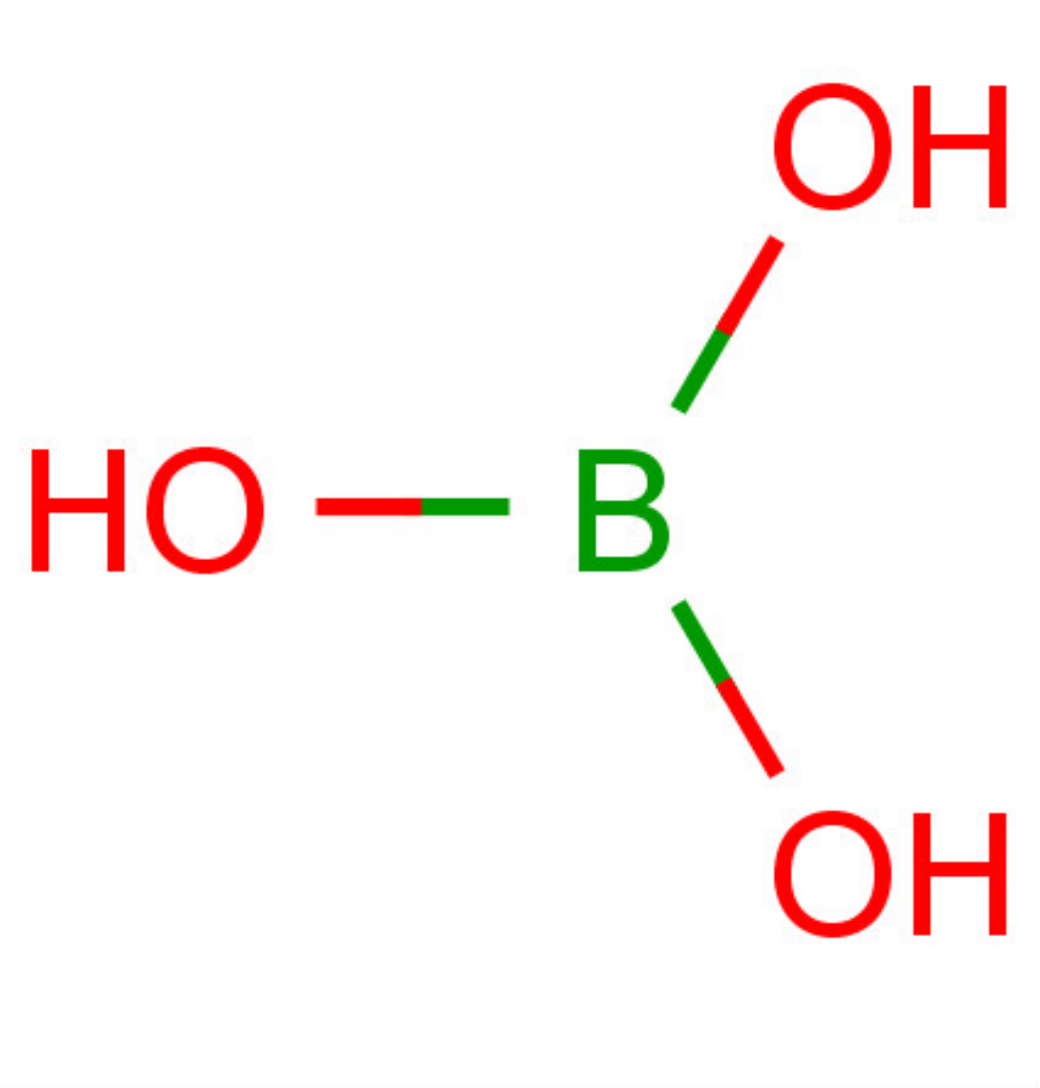
Last Update 29 June 2018

Chemical Identities

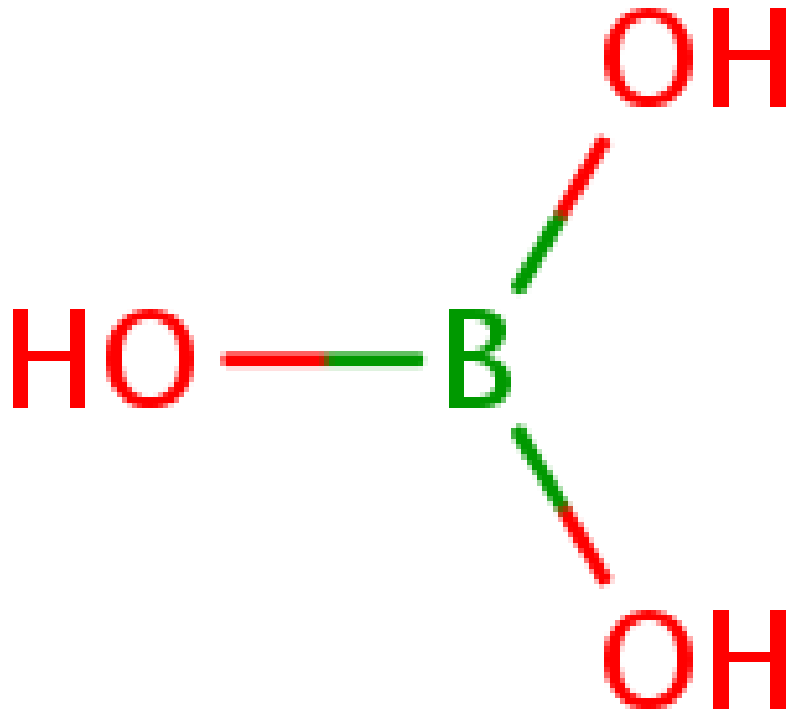
Chemical Name in the Inventory and Synonyms	**Boron oxide (B2O3)** boric oxide diboron trioxide boric anhydride boron trioxide
CAS Number	1303-86-2
Structural Formula	

	
Molecular Formula	B2O3
Molecular Weight	69.62

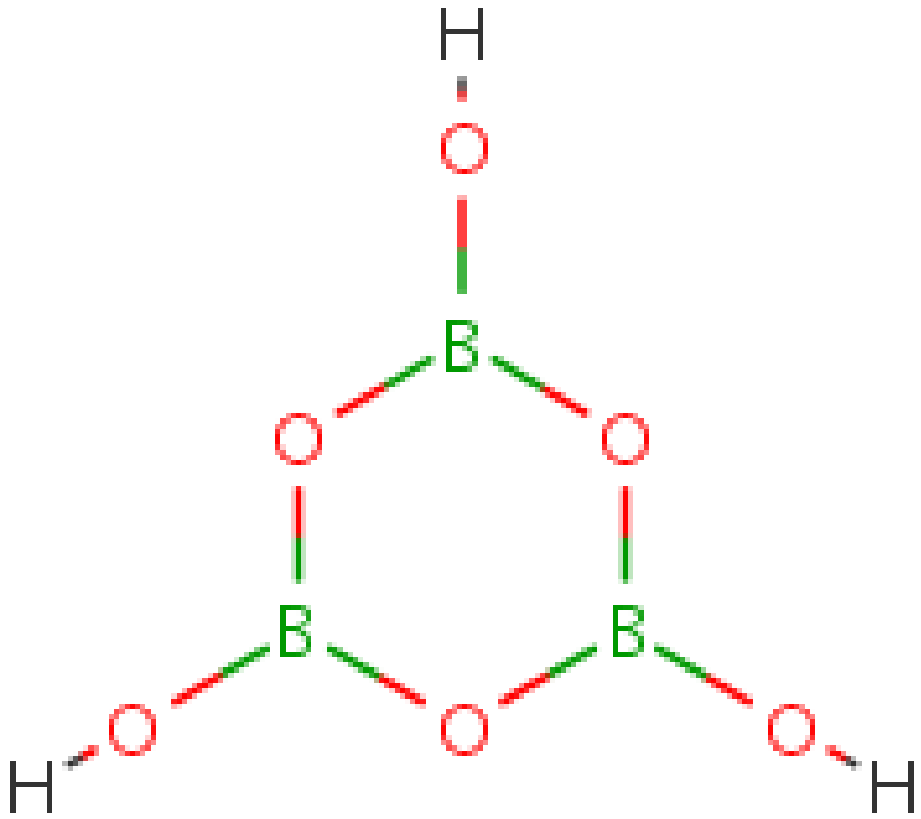
Chemical Name in the Inventory and Synonyms	**Boric acid (H3BO3)** boracic acid boron hydroxide boron trihydroxide orthoboric acid
CAS Number	10043-35-3
Structural Formula	

	
Molecular Formula	BH3O3
Molecular Weight	61.83

Chemical Name in the Inventory and Synonyms	**Boric acid** boric acid, anhydrous
CAS Number	11113-50-1
Structural Formula	

	
Molecular Formula	Unspecified
Molecular Weight	61.83

Chemical Name in the Inventory and Synonyms	**Boric acid (H3B3O6)** metaboric acid (H3B3O6)
CAS Number	13460-51-0
Structural Formula	

	
Molecular Formula	B3H3O6
Molecular Weight	131.45

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