Australian Government
Department of Health and Aged Care
Australian Industrial Chemicals Introduction Scheme

Alkyl borate esters

Evaluation Statement (EVA00161)

31 March 2025

Draft

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AICIS evaluation statement (EVA00161)

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Reason for the evaluation

Evaluation Selection Analysis indicated a potential human health risk.

Parameters of evaluation

All chemicals in this group are structurally related esters of boric acid listed on the Australian Inventory of Industrial Chemicals (the Inventory). This evaluation is a human health risk assessment for all identified uses.

These chemicals have been assessed as a group because they have similar use patterns and reactivity (hydrolysis to boric acid).

Summary of evaluation

Summary of introduction, use and end use

There is currently no specific information about the introduction, use and end use for the chemicals in this group in Australia. Based on international information, the chemicals in this group are expected to have mostly site-limited functional use as intermediates and commercial uses, primarily in:

- metal working,
- adhesive and sealants
- lubricants and greases
- paints and coatings.

Low concentrations (<1%) of tributyl borate were only identified in:

- paints and coatings
- lubricants and greases.

Human health

Summary of health hazards

Alkyl borate esters such as those included in this evaluation are organoboron esters with 3 linear alkoxy chains. These esters are known to hydrolyse rapidly into boric acid and the respective alcohols. These alcohols include: methanol (CAS 67-56-1), ethanol (CAS 64-17-5), propanol (CAS 71-23-8) and butanol (CAS 71-36-3). Limited data are available for the chemicals in this evaluation. Data on the metabolites has been used to infer the health hazards.

Based on the available data the chemicals:

- are not expected to be skin irritants or sensitisers
- are not expected to have genotoxic potential
- are not expected to be carcinogenic.

Based on the available data for the boric acid and alcohol metabolites, the driver of the systemic effects of the chemicals will be the boric acid metabolite. The alcohol metabolites generally only produced transient effects or effects at very high doses.

These chemicals are expected to cause specific adverse effects on fertility and development. Boric acid, along with other boron containing compounds have been shown to negatively impact animal species such as mice, rats and rabbits. Reprotoxic effects of boric acid include:

- atrophy and impacts on the development of the testis and the associated structures
- decreased foetal weight
- increased prenatal mortality
- malformations and variations of the eyes central nervous system (CNS), cardiovascular system and axial skeleton.

A no observed adverse effect level (NOAEL) for fertility was determined to be 100 mg/kg bw/day boric acid and a NOAEL for developmental effects was established as 55mg/kg bw/day boric acid in rats in various studies. Studies have not adequately shown reproductive effects in humans.

In addition to reprotoxic effects, repeated oral exposure to boric acid in mice, rats and rabbits were reported to have:

- haematological effects such as decreased red blood cell volume
- desquamation of tails, ears and paws
- inflammation of eyes
- decreased body weights.

Most reported NOAELs range from 100–150mg/kg bw/day boric acid in mice and rats.

Based on the available animal data, these chemicals have low acute toxicity. However, human data for methanol (one of the metabolites of trimethyl borate) indicate that humans may be more susceptible to the effects of methanol at comparatively lower doses (NICNAS 2013a). Therefore, acute effects cannot be ruled out for trimethyl borate. This chemical is classified for effects following contact with skin based on available LD50 value (1820 mg/kg bw/day).

Based on the limited information available for trimethyl borate chemicals in this group may cause serious eye damage. Irreversible damage to the cornea was observed in available studies.

Hazard classifications relevant for worker health and safety

The chemicals satisfy the criteria for classification according to the Globally Harmonized System of Classification and Labelling of Chemicals (GHS) (UNECE 2017) for hazard classes relevant for work health and safety as follows. This does not consider classification of physical hazards and environmental hazards.

Some of these recommended classifications are based on read across principles (see **Supporting Information - Rationale** section). If empirical data become available for any member of the group indicating that a lower (or higher) classification is appropriate for a specific chemical, this data may be used to amend the default classification for that chemical.

The acute toxicity classification applies to trimethyl borate only.

Health hazards	Hazard category	Hazard statement
Reproductive Toxicity	Repr.1B	H360FD May damage fertility; May damage the unborn child
Acute Toxicity	Acute Tox. 4	H312 Harmful in contact with skin
Serious Eye Damage/Eye irritation	Eye Damage 1	H318 Causes serious eye damage

Summary of health risk

Public

Based on available information, the public is unlikely to be significantly exposed to these chemicals. Although tributyl borate has been identified in some consumer products, given the intermittent exposure and the low concentration of the chemical, these uses are not expected to significantly increase exposure of the public to boric acid. Therefore, there are no identified risks that require management.

Workers

During product formulation and packaging, ocular, dermal and inhalation exposure might occur, particularly where manual or open processes are used. These could include transfer and blending activities, quality control analysis, and cleaning and maintaining equipment. Worker exposure to these chemicals at lower concentrations could also occur while using formulated products containing these chemicals. The level and route of exposure will vary depending on the method of application and work practices employed. Good hygiene practices to minimise incidental oral exposure are expected to be in place.

Given the critical systemic and local health effects, exposure to these chemicals could pose a risk to workers.

Control measures to minimise ocular, dermal and inhalation exposure are needed to manage the risk to workers (see **Proposed means for managing risks** section).

Control measures implemented due to the reproductive toxicity classification are expected to be sufficient to protect workers from any potential acute toxicity effects.

Proposed means for managing risk

Workers

Recommendation to Safe Work Australia

It is recommended that Safe Work Australia (SWA) update the Hazardous Chemical Information System (HCIS) to include classifications relevant to work health and safety.

Information relating to safe introduction and use

The information in this statement including recommended hazard classifications, should be used by a person conducting a business or undertaking at a workplace (such as an employer) to determine the appropriate controls under the relevant jurisdiction Work Health and Safety laws.

Control measures that could be implemented to manage the risk arising from ocular, dermal and inhalation exposure to the chemicals include, but are not limited to:

- using closed systems or isolating operations
- using local exhaust ventilation to prevent these chemicals from entering the breathing zone of any worker
- minimising manual processes and work tasks through automating processes
- adopting work procedures that minimise splashes and spills
- cleaning equipment and work areas regularly
- using protective equipment that is designed, constructed, and operated to ensure that the worker does not come into contact with these chemicals.

Measures required to eliminate or manage risk arising from storing, handling and using these hazardous chemicals depend on the physical form and how these chemicals is used.

These control measures may need to be supplemented with health monitoring conducted for any worker who is at significant risk of exposure to these chemicals if valid techniques are available to monitor the effect on the worker's health.

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.

Model codes of practice, available from the Safe Work Australia website, provide information on how to manage risks of hazardous chemicals in the workplace, prepare an SDS and label containers of hazardous chemicals. Your Work Health and Safety regulator should be contacted for information on Work Health and Safety laws and relevant Codes of Practice in your jurisdiction.

Conclusions

The Executive Director proposes to be satisfied that the identified risks to human health from the introduction and use of the industrial chemicals can be managed.

Note:

1. Obligations to report additional information about hazards under *Section 100* of the *Industrial Chemicals Act 2019* apply.
2. You should be aware of your obligations under environmental, workplace health and safety and poisons legislation as adopted by the relevant state or territory.

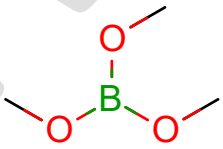
Supporting information

Grouping rationale

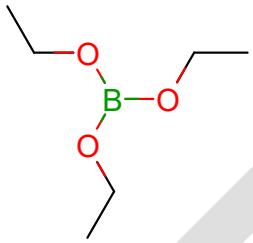
These chemicals have been assessed as a group because they are structurally similar and have similar physicochemical properties and reactivity. The chemicals are all esters of boric acid. The chemicals are expected to readily hydrolyse into the corresponding alcohols and boric acid.

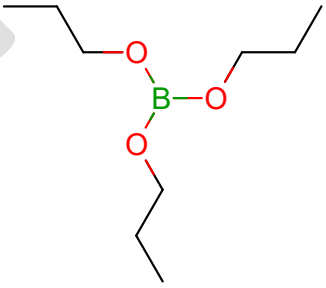
The chemicals have similar use patterns.

Chemical identity

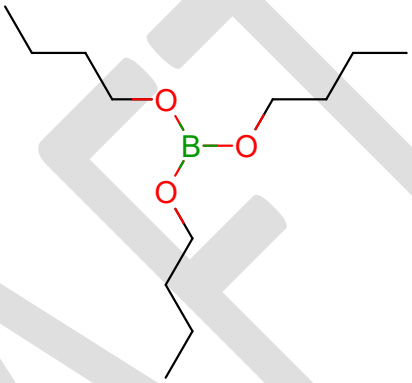
CAS number	121-43-7
CAS name	Boric acid (H_3BO_3), trimethyl ester
Molecular formula	$C_3H_9BO_3$
Associated names	Trimethyl Borate
	Trimethylborate
	Trimethoxyborane
Molecular weight (g/mol)	103.91
SMILES (canonical)	O(B(OC)OC)C
Structural formula	

CAS number	150-46-9
CAS name	Boric acid (H_3BO_3), triethyl ester
Molecular formula	$C_6H_{15}BO_3$
Associated names	Triethyl borate
	Boron ethoxide

	Triethoxyborane
Molecular weight (g/mol)	145.99
SMILES (canonical)	O(B(OCC)OCC)CC
Structural formula	

CAS number	688-71-1
CAS name	Boric acid (H_3BO_3), tripropyl ester
Molecular formula	$C_9H_{21}BO_3$
Associated names	Tripropyl borate
	Boron propoxide
	Tripropoxyborane
Molecular weight (g/mol)	188.07
SMILES (canonical)	O(B(OCCC)OCCC)CCC
Structural formula	

CAS number	688-74-4
CAS name	Boric acid (H_3BO_3), tributyl ester

Molecular formula	$C_{12}H_{27}BO_3$
Associated names	Tributyl borate
	Butyl borate
	Boron tributoxide
	Tributoxyborane
Molecular weight (g/mol)	230.15
SMILES (canonical)	O(B(OCCCC)OCCCC)CCCC
Structural formula	

Relevant physical and chemical properties

These chemicals are liquids at room temperature and standard atmospheric pressure, with boiling points that increase with increasing chain length (approx. 68–230°C). Trimethyl borate and triethyl borate have reported vapour pressures (measured and calculated) of 23–30 KPa 30°C. Tributyl borate has a calculated vapour pressure of 0.38 KPa at 25°C based on measured values at higher temperatures. Information on water solubility and partition coefficient are not available due to the rapid hydrolysis of the chemicals in contact with water.

Introduction and use

Australia

No specific information is available on the introduction, use and end use of these chemicals in Australia.

International

The following international uses have been identified through the:

- European Union (EU) Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH n.d.-b, REACH n.d.-c, REACH n.d.-d) dossiers
- the Substances in Preparations in Nordic Countries (SPIN n.d.) database
- Galleria Chemica (Chemwatch n.d.)
- United States Environmental Protection Agency Chemical Data Reporting (CDR) (US EPA 2012; US EPA 2016; US EPA 2020).

Available data for these chemicals indicate that the use is primarily site-limited or commercial.

Site-limited uses include use:

- as a viscosity adjuster in oil and gas drilling, extraction and support activities (trimethyl borate) (US EPA 2012; US EPA 2016; US EPA 2020)
- intermediate petroleum products, in the manufacture of rubber and synthetic rubber products (tributyl borate) (US EPA 2012; US EPA 2016; US EPA 2020)
- as intermediates in the manufacture of other chemicals.

Commercial uses include:

- in metal working
- additives in lubricants and greases
- adhesives and sealants (triethyl borate)
- paints, coatings and inks (tributyl borate).

No information indicating cosmetic use could be identified. Some of the commercial uses such as paints and coatings may also be used in domestic applications. Consumer uses were only identified for tributyl borate. Tributyl borate was reported to be used in lubricant

and greases and paints and coating products available to consumers. The reported concentration is < 1% (REACH n.d.-d; US EPA 2012; US EPA 2016).

Reported non- industrial uses include in pesticides and disinfectants.

Existing Australian regulatory controls

AICIS

No specific controls are currently available for these chemicals.

Public

These chemicals are a derivative of boric acid and are, therefore, captured by the entry for boric acid in the *Poisons Standard—Standard for the Uniform Scheduling of Medicines and Poisons* (SUSMP).

Schedule 5

BORIC ACID **except**:

(a) when included in Schedule 4; or

(b) in cosmetic hand cleaning preparations when labelled with a warning to the following effect:

NOT TO BE USED FOR CHILDREN UNDER 3 YEARS OF AGE; and

if the concentration of free soluble borates exceeds 1.5% (as boric acid), with the words:

NOT TO BE USED ON PEELING OR IRRITATED SKIN; or

(c) in cosmetic talc preparations containing 5% or less calculated as boric acid when labelled with a warning to the following effect:

NOT TO BE USED FOR CHILDREN UNDER 3 YEARS OF AGE; and

if the concentration of free soluble borates exceeds 1.5% (as boric acid), with the words:

NOT TO BE USED ON PEELING OR IRRITATED SKIN; or

(d) in cosmetic oral hygiene preparations containing 0.1% or less calculated as boric acid when labelled with a warning to the following effect:

NOT TO BE SWALLOWED. NOT TO BE USED FOR CHILDREN UNDER 3 YEARS OF AGE; or

(e) in other cosmetic preparations containing 3% or less calculated as boric acid when labelled with a warning to the following effect:

NOT TO BE USED FOR CHILDREN UNDER 3 YEARS OF AGE; and

if the concentration of free soluble borates exceeds 1.5% (as boric acid), with the words:

NOT TO BE USED ON PEELING OR IRRITATED SKIN; or

(f) in preparations, other than insect baits, containing 6% or less calculated as boric acid.

Workers

Trimethyl borate (CAS No. 121-43-7) is listed on the HCIS with the following hazard category and statement for human health: Acute toxicity – category 4 (H312 – Harmful in contact with skin) (SWA n.d.).

No exposure standards are available for chemicals in this group in Australia (SWA n.d.)

International regulatory status

Exposure standards

A Time Weighted Averages (TWAs) for borates of 0.5mg/m^3 is reported for Finland.

The following Protective Action Criteria (PAC) (formerly known as Temporary Emergency Exposure Limits (TEELs) have been recommended by the United States Department of Energy (Chemwatch n.d) for trimethyl borate:

- 290 mg/m^3 (PAC-3)
- 48 mg/m^3 (PAC-2)
- 4.3 mg/m^3 (PAC-1)

The following PAC have been recommended by the United States Department of Energy (Chemwatch n.d) for tributyl borate:

- 25 mg/m^3 (PAC-3)
- 4.1 mg/m^3 (PAC-2)
- 0.37 mg/m^3 (PAC-1)

Health hazard information

These chemicals readily hydrolyse into boric acid and the corresponding alcohol when they come in contact with water. Although there are no studies available under physiological conditions, it is plausible that the chemicals hydrolyse to boric acid and alcohols under such conditions. Therefore, data on the metabolites has been used to infer the systemic health hazards. As limited data are available for trimethyl borate this information has been used to infer the local toxicity of the chemicals.

Toxicokinetics

No toxicokinetic data are available for this chemical group. These chemicals are expected to be rapidly metabolised to boric acid and the corresponding alcohols if absorbed. Based on the molecular weight (<250) it is expected that these chemicals will be absorbed easily.

Toxicokinetics of the metabolite 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 3 times faster in rats than in humans.

Boric acid is readily and completely absorbed in humans and animals following oral administration.

Dermal absorption through intact skin is very low in all species evaluated including rats, rabbits, new-born infants and adult humans, although dermal absorption may occur through damaged or abraded skin.

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. Boric acid is the main species present in the blood and is not further metabolised. Boric acid is excreted rapidly, mostly in the urine with a half-life of <24 hours), regardless of the route of administration (ECHA 2022; NICNAS 2018).

The alcohol metabolites are rapidly absorbed, metabolised and excreted (NICNAS 2013a; NICNAS 2013b; NICNAS 2013c; NICNAS 2014).

Acute toxicity

Oral

Based on the available animal data, the chemicals have low acute oral toxicity. The median lethal dose (LD50) values for trimethyl borate (CAS No. 121-43-7) are >2000 mg/kg bodyweight (bw) (REACH n.d.-b). However human data for methanol, one of the metabolites of trimethyl borate, indicated that humans may be more susceptible to the effects of methanol at comparatively lower doses (NICNAS 2013a). Therefore, acute oral effects cannot be ruled out for trimethyl borate.

Limited data are available for the other chemicals in this evaluation. Cchemicals in this group all have reported median lethal dose (LD50) values >2000 mg/kg bw/day in mice (US EPA n.d.). Data available for the metabolites of boric acid, ethanol and propanol (NICNAS 2013b, NICNAS 2014, NICNAS 2018) support the conclusion that triethyl borate and tripropyl borate will have low acute toxicity. Although butanol is classified as harmful if swallowed, a range of LD50s indicating moderate to low acute toxicity have been reported (NICNAS 2013b)

In a non-guideline study, 4–5 week old male Carworth-Wistar rats (5/dose) were administered a single dose of trimethyl borate via gastric intubation. Doses were a logarithmic series differing by a factor of 2. A fiducial range of 4500–7280mg/kg bw was calculated and an LD50 of 5551 mg/kg bw was determined from 14 day mortality rates (REACH n.d.-b).

In a study following OECD TG 425, female Sprague Dawley (SD) rats (n=5) were administered an oral dose of 2000mg/kg bw trimethyl borate. No mortality was observed - within 14 days. Therefore, the LD50 was determined as greater than 2000 mg/kg bw (REACH n.d. -b).

Dermal

Trimethyl borate (CAS No. 121-43-7) is listed on the HCIS with the following hazard category and statement for human health: Acute toxicity — category 4. (H312 – Harmful in contact with skin) (SWA n.d.). The available data support this classification.

In a non-guideline study, New Zealand White (NZW) rabbits (4/sex/dose) were treated with trimethyl borate under occlusion for 24 hours. An LD50 of 1820mg/kg bw and fiducial range of 1365–2457mg/kg bw was calculated after the 14 day observation period (REACH n.d.-b).

No data are available for the other chemicals in this evaluation.

Inhalation

No data are available for the chemicals. Based on data on the metabolite methanol, inhalation exposure to trimethyl borate may cause adverse effects. Visual disturbances have been reported in workers who experienced methanol air levels of about 1.5 mg/L (NICNAS 2013a).

Corrosion/Irritation

Skin irritation

Based on the limited available information for trimethyl borate, these chemicals are not likely to be skin irritants.

In a non-guideline study, NZW rabbits (3/sex) were treated with trimethyl borate on intact and abraded skin (3 each) for 24 hours under occlusive conditions. Observations continued for 72 hours after removal of application. Individual scores were not provided although a mean score for erythema and oedema based on observations at 24 and 72 hours was 0.5 (REACH n.d.-b)

In a non-guideline study, 5 albino rabbits were treated with trimethyl borate. The substance was applied to intact skin (uncovered) for a period of 24 hours. Observations during the 24 hours determined that trimethyl borate is not irritating to the skin (REACH n.d.-b).

Eye irritation

The limited information available indicates that trimethyl borate causes serious eye damage, warranting classification (see **Hazard classifications relevant to worker health and safety** section). Data are not available for the other chemicals, although the severity of effects may vary across the group, in the absence of data, read across is considered appropriate.

In a non-guideline study, NSW rabbits (5 male, 4 female) were administered with 0.1 ml of undiluted trimethyl borate solution with 3 of the 9 animals receiving a washout after 30 seconds exposure. Results were reviewed on a reversible effect scale for 19 days

(unwashed) and 35 days (rinsed eyes). Effects on the iris, conjunctivae and cornea were observed in all animals. The scoring system used does not enable comparison with the classification criteria. The effects on conjunctivae and cornea were not fully reversible in one animal (rinsed eyes) (REACH n.d.-b).

In a non-guideline study in rabbits with limited study detail available, undiluted trimethyl borate, was reported to produce severe damage to the cornea of the rabbit eye when treated with 0.5 ml and moderate injury in 0.1 ml dose. Corneal injury in rabbits was recorded to be Grade 3. No further details were provided (REACH n.d.-b).

Sensitisation

No data are available to evaluate skin or respiratory sensitisation. The boric acid and alcohol metabolites are not considered to be sensitisers (NICNAS 2013a; NICNAS2013b; NICNAS 2013c; NICNAS 2014; NICNAS 2018).

Repeat dose toxicity

No data are available for the chemicals in this group. Based on the available data for the boric acid and alcohol metabolites, the driver of the systemic effects of the chemicals will be the boric acid metabolite. The alcohol metabolites generally only produced transient effects or effects at very high doses (NICNAS 2013a; NICNAS2013b; NICNAS 2013c; NICNAS 2014).

Oral

A number of repeated dose oral toxicity studies in animals have indicated that the main target organ for boron toxicity is testes, leading to reproductive and developmental adverse effects. In a number of studies, atrophied seminiferous epithelium and decreased tubular size in testes were observed. Adverse haematological effects indicative of increased red blood cell destruction has 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 2 year study of boric acid in rats for effects on 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) (NICNAS 2018).

Dermal

No data are available.

Inhalation

Limited inhalation data are available for boron compounds.

In a non-guideline study, rats that were exposed to 470 mg/m^3 boron oxide (CAS 1303-86-2) 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. A NOAEC of 470 mg/m^3 for systemic toxicity in rats is established based on the study results. A NOAEC of 175 mg/m^3 is appropriate for local effects due to irritation of noses of rats .The NOAEC of 57 mg/m^3 for dogs is based on the absence of any toxic effect (NICNAS 2018; REACH n.d.).

Genotoxicity

No data are available for these chemicals. Based on available information on the metabolites, these chemicals in this group are not expected to have mutagenic or genotoxic potential. The boric acid and the alcohol metabolites were negative in a number of in vitro and in vivo genotoxicity studies (NICNAS 2013a; NICNAS2013b; NICNAS 2013c; NICNAS 2014; NICNAS 2018).

Carcinogenicity

No data are available for the chemicals. The available carcinogenicity information on the metabolites indicate that the chemicals in this group are not likely to be carcinogenic. There was no evidence of carcinogenicity in available studies for boric acid and methanol (NICNAS 2013a, NICNAS 2018). While ethanol in alcoholic beverages is linked to cancer, animal studies using very high oral doses may not be relevant for assessing risks associated with occupational exposure or using consumer products containing the chemical. Therefore, classification for ethanol was not considered appropriate (NICNAS 2014). No data were available for propanol and butanol. It is also noted above that the metabolites are not considered to have mutagenic or genotoxic potential (see **Genotoxicity** section).

Reproductive and development toxicity

No data are available for the chemicals. Based on the available data for the boric acid and alcohol metabolites the driver of the reproductive and developmental effects of the chemicals will be the boric acid metabolite. Specific reproductive or developmental effects were not observed in studies with the alcohol metabolites (ECHA 2022; NICNAS 2013a; NICNAS2013b; NICNAS 2013c; NICNAS 2014).

Boric acid is classified as hazardous for reproductive and developmental toxicity—category 1B; H360FD (May damage fertility. May damage the unborn child) in the HCIS (SWA n.d.). Based on the expected rapid metabolism to boric acid, this classification is considered warranted for all chemicals in this group.

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
- reduced fertility.

The developmental effects that have been reported included:

- high prenatal mortality and reduced foetal body weight
- 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 2 and 3 year 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 (ECHA 2022; NICNAS 2018).

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 (ECHA 2022; NICNAS 2018).

The above epidemiological studies have been considered as part of the opinion on harmonised classification and labelling of trimethyl borate 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. The exposure levels were reported to be 15–135 times lower than the animal LOAEL for human fertility effects and 7–66 times lower for humans than the animal LOAEL for developmental toxicity. At those exposure levels in epidemiological studies, assuming a similar sensitivity of humans as in the 4 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 showed no clear evidence of reproductive toxicity and do not contradict the animal data (ECHA 2022; NICNAS 2018). The opinion concluded that the classification of boric acid should apply to trimethyl borate and that the toxicity of methanol would not mask the reproductive and developmental effects of boric acid after exposure to trimethyl borate (ECHA 2022).

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