Diboron trioxide

(CAS No: 1303-86-2)

Health-based Reassessment of Administrative Occupational Exposure Limits

Committee on Updating of Occupational Exposure Limits,
a committee of the Health Council of the Netherlands

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1 Introduction

The present document contains the assessment of the health hazard of diboron trioxide by the Committee Updating of Occupational Exposure Limits, a committee of the Health Council of the Netherlands. The first draft of this document was prepared by MA Maclaine Pont, M.Sc. (Wageningen University and Research Centre, Wageningen, the Netherlands).

In February 1998, literature was searched in the databases Medline, Toxline, and Chemical Abstracts, starting from 1966, 1981, and 1947, respectively, and using the following key words: boron oxide, boria, or 1303-86-2. The final search in Toxline and Medline was carried out in October 2004.

In December 2004, the President of the Health Council released a draft of he document for public review. No comments were received.

2 Identity

name	: diboron trioxide
synonyms	: boron oxide; boron trioxide; boria; boric anhydride; boron sesquioxide; fused boric acid
molecular formula	: B_2O_3
CAS number	: 1303-86-2

3 Physical and chemical properties

molecular weight	: 69.64
melting point	: 450°C
boiling point	: ca. 1860°C
flash point	: -
vapour pressure	: at 20°C: negligible
solubility in water	: slightly soluble (at 20°C: 3 g/100 mL)
log $P_{octanol/water}$	: -0.22 (estimated)
conversion factors	: not applicable

Data from ACG02, NLM04, http://www.syrres.com/esc/est_kowdemo.htm.

Diboron trioxide occurs as an odourless, white powder or granular solid, with a bitter taste. It is quite hygroscopic and it reacts exothermally with water to form boric acid (ACG02, NLM04).

4 Uses

Diboron trioxide is used in the production of boron, heat resistant glass, fire retardants for paints and cellulose insulation, boron carbide, and also in electronics (ACG02).

5 Biotransformation and kinetics

The committee did not find data on the biotransformation and kinetics of diboron trioxide.

In rats exposed to aerosol concentrations of diboron trioxide of 77 mg/m^3 for 24 weeks, increased urinary boron levels (average: 11.9 mg/kg bw/day; range: 1.9-23.2 mg/kg bw/day) when compared to controls (average: 0.2 mg/kg bw; range: 0.1-0.7 mg/kg bw). After exposure, levels of both groups were similar (Wil59).

Diboron trioxide reacts with water to form boric acid. Boric acid is well absorbed through the gastrointestinal tract, open wounds, and serous cavities (Bur92).

6 Effects and mechanism of action

Human data

Workers (n=113) occupationally exposed to dusts containing diboron trioxide and boric acid reported statistically significantly more symptoms of local irritation compared with an unexposed control group (n = 214): eye irritation ($p<0.001$), dryness of the mouth, nose, or throat ($p<0.001$), sore throat ($p=0.004$), and productive cough ($p=0.002$). The concentration of total particulate matter, measured during full shifts, ranged from 1.2 to 8.5 mg/m^3, with a mean of 4.1 mg/m^3 (n=8) (Gar84). The committee notes that the proportion of diboron trioxide of the total dust measured is not known and that the effects reported cannot be ascribed to diboron trioxide exposure alone. Because of the limited number of measurements and incomplete reporting, the level of exposure remains rather uncertain.

Boron might be a nutritional beneficial, if not essential, element for humans (Cou96, Nie96), who may have a boron requirement between 0.5 and 1 mg/day (Nie96).

Application of diboron trioxide dust (1 g/25 cm^2) to the clipped, wetted skin of rabbits (n=4) caused erythema that lasted for 2 to 3 days. Instillation of 50 mg into the (left) eyes of rabbits (n=4) almost immediately produced conjunctivitis. Wilding et al. ascribed these effects to exothermic hydration to boric acid (Wil59).

The oral and intraperitoneal LD_{50} values in mice were 3163 and 1868 mg/kg bw, respectively (Izm82).

In mice, daily inhalation exposure to 150-230 mg/m^3, 2 hours/day, for 15 days, caused irritation of the mucous membranes of the upper respiratory tract. Changes were observed in rheobase and chronaxie*. Histologically, there was interstitial inflammation in the lungs (Kas67).

Groups of rats (n=70, 4, and 20, respectively) were exposed to concentrations of diboron trioxide aerosols (particle size: mass median aerodynamic diameter - MMAD: 2.5, 1.9, and 2.4 µm, respectively) of 77, 175, or 470 mg/m^3, 6 hours/day, 5 days/week, for 24, 12, and 10 weeks, respectively. The animals of the high-concentration group were covered with dust. They grew somewhat less fast than the control rats (by ca. 9%). Some of them had a slight reddish exudate from the nose. No changes were observed in urinalysis or haematology values or upon macroscopic or microscopic examination of all organs. Apart from some unclear effects on urinalysis values, which might have been the result of formation of boric acid, there were no effects in animals exposed to 77 mg/m^3. Wilding et al. did not present results regarding the animals exposed to 175 mg/m^3 (Wil59).

In dogs (n=3) exposed to 57 mg/m^3 (MMAD: 2.4 µm), 6 hours/day, 5 days/week, for 23 weeks, no significant compound-related effects were observed (Wil59).

No toxic signs or effects on body weight were seen in rats (n=10) daily given a 10% slurry of diboron trioxide (ca. 500 mg/kg) by gavage for 3 weeks. When rats were given doses of B_2O_3 of 0.25, 0.5, 1.0, or 1.5% in the drinking water, the animals of the 2 higher dose groups rapidly lost weight within 10 days because of refusing to drink the water. Animals given 0.5% lost weight to 73% of control values in 19 days, while animals given 0.25% showed a small initial loss followed by a slow recovery (Wil59).

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* Rheobase is the minimal strength of an electrical stimulus of indefinite duration that is able to cause excitation of a tissue, e.g. muscle or nerve; chronaxie is the shortest duration of an effective electrical stimulus having a strength equal to twice the minimum strength required for excitation (rheobase) (from: http://cancerweb.ncl.ac.uk/omd).

The committee did not find data from long-term toxicity, including carcinogenicity, studies on diboron trioxide. In a long-term study in which boric acid was administered via the diet to mice, there was no evidence of a carcinogenic potential (study by the NTP, cited in ECE95).

Mutagenicity and genotoxicity

The committee did not find data from mutagenicity/genotoxicity studies on diboron trioxide.

The European Centre for Ecotoxicology and Toxicology of Chemicals (ECETOC) summarised data from studies on boric acid. Boric acid was negative when tested in the presence and absence of metabolic activating systems in various strains of *S. typhimurium*. It was negative in *E. coli* strain sd 4-73 but produced positive results, which were inconsistent and showed great variability, in another test in strain sd-4. Negative results were obtained in mouse lymphoma cells. Boric acid did not increase the incidence of chromosomal aberrations and SCEs when tested with and without metabolic activation in Chinese hamster ovary cells. A UDS test in rat hepatocytes was negative. *In vivo*, oral (drinking water) administration of doses of 900-3500 mg/kg bw/day, for 2 days did not induce an increase in the incidence of micronuclei in bone marrow of mice.

Reproduction toxicity

The committee did not find data from reproduction toxicity studies on diboron trioxide.

Many reproduction toxicity studies have been performed with boric acid. They have been summarised by the Committee on Compounds Toxic to Reproduction, a committee of the Health Council of the Netherlands (Hea98), and by ECETOC (ECE95). In a 2-year and a 3-generation study in rats, daily dietary doses of 58.5 mg B/kg bw caused fertility effects such as testicular atrophy, decreased testis weights, decreased ovulation, and infertility in rats; the NOAEL was 17.5 mg B/kg bw. In rats, mice, and rabbits, orally (diet or gavage) treated with boric acid during gestation or organogenesis, developmental effects such as increased numbers of resorptions and fetal abnormalities were observed in the presence of maternal toxicity. In rats, doses of 13.3 mg B/kg bw induced slightly decreased fetal weights (by 6%). This dose level was close to the maternally toxic dose of 25 mg B/kg bw. No maternal or developmental toxicity was seen in rats at 9.6 mg B/kg bw.

7 Existing guidelines

The current administrative occupational exposure limit (MAC) for diboron trioxide in the Netherlands is 10 mg/m^3, 8-hour TWA.

Existing occupational exposure limits for boron oxide in some European countries and in the USA are summarised in the annex.

8 Assessment of health hazard

Workers occupationally exposed to mean levels of diboron trioxide and boric acid of 4.1 mg/m^3 reported statistically significantly more symptoms of eye and respiratory tract irritation as unexposed controls.

In experimental animals, diboron trioxide was found irritating to the skin and eyes of rabbits.

In mice, the oral LD_{50} was 3163 mg/kg bw. Exposure to 150-230 mg/m^3, 2 hours/day for 15 days, caused irritation of the upper respiratory tract in mice. No effects were seen in rats exposed to diboron trioxide levels of 77 mg/m^3, for 24 weeks, while there were signs of nose irritation and some unclear effects on urinalysis values at exposure to 470 mg/m^3, for 10 weeks. The committee did not find data from long-term toxicity, including carcinogenicity, mutagenicity/ genotoxicity, and reproduction studies on diboron trioxide.

The committee takes the study of Garabrant et al. (Gar84), in which local irritation was observed in workers, as a starting point for deriving a health-based recommended occupational exposure limit (HBROEL). The committee cannot determine which diboron trioxide concentration induced irritation because exposure was to both diboron trioxide and boric acid. However, since this situation is representative for normal working conditions, the committee takes the mean diboron trioxide/boric acid level of 4.1 mg/m^3 as a starting point. For the extrapolation to an HBROEL, the committee establishes an overall assessment factor of 4. This factor covers the following aspects: the absence of a NOAEL and the uncertainties in the study (the composition of the dust, the limited number of measurements, the lack of a dose-response relationship). The committee considered an intraspecies factor not necessary because the population under study consisted of 100 persons. Applying this factor of 4, a health-based occupational exposure limit of 1 mg/m^3, 8-hour TWA, is recommended for diboron trioxide. In order to prevent local irritation from diboron trioxide, the committee recommends a short-term exposure limit (STEL) of 3 mg/m^3, 15-minute TWA.

The committee recommends a health-based occupational exposure limit for diboron trioxide of 1 mg/m^3, as an 8-hour time-weighted average (TWA), and of 3 mg/m^3, as a 15-minute time-weighted average (TWA), both as inhalable dust.

NOTE: In the presence of water, diboron trioxide is readily converted into boric acid. Boric acid did not induce mutations in bacteria and mouse lymphoma cells, SCEs or chromosomal aberrations in Chinese hamster ovary cells, UDS in rat hepatocytes, or micronuclei in bone marrow obtained from orally treated mice. Boric acid did not show a carcinogenic potential in mice. The critical effects of boric acid were fertility and developmental effects in rats with NOAELs of 13.3 and 9.6 mg B/kg day.

The committee considers the HBROEL for diboron trioxide of 1 mg/m^3 to be sufficient to protect workers from reproduction toxicity. Assuming a 60-70-kg person inhales 10 mg/m^3 during an 8-hour working day and a retention of 100%, exposure to the HBROEL of 1 mg/m^3 or 0.3 mg B/m^3 results in a daily uptake of 0.04-0.05 mg B/kg bw which is a factor of about 200 or more lower than the NOAELs for reproduction toxicity in rats.

References

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ACG04 American Conference of Governmental Industrial Hygienists (ACGIH). Guide to occupational exposure values - 2004. Cincinnati OH, USA: ACGIH®, 2004: 16.

ACG05 American Conference of Governmental Industrial Hygienists (ACGIH). 2005 TLVs® and BEIs® based on the documentation of the Threshold Limit Values for chemical substances and physical agents & Biological Exposure Indices. Cincinnati OH, USA: ACGIH®, 2005: 14.

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EC05 European Commission: Directorate General for Employment, Social Affairs and Equal Opportunities. Indicative occupational exposure limit values. http://europe.eu.int/comm/employment_social/health_safety/docs/oels_en.pdf.

ECE95 European Centre for Ecotoxicology and Toxicology of Chemicals (ECETOC). Reproductive and general toxicology of some inorganic borates and risks assessment for human beings. Brussels, Belgium: ECETOC, 1995; Technical Report No 63.

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HSE02 Health and Safety Executive (HSE). EH40/2002. Occupational Exposure Limits 2002. Sudbury (Suffolk), UK: HSE Books, 2002: 16.

Hea98 Health Council of the Netherlands: Committee on Compounds Toxic to Reproduction. Boric acid. The Hague, the Netherlands: Health Council of the Netherlands, 1998; publ no 1998/19.

Izm82 Izmerov NF, Sanotsky IV, Sidorov KK. Boron oxide. In: Toxicometric parameters of industrial toxic chemicals under single exposure. Moscow, Russia: Centre of International Projects, GKNT, 1982: 27.

Kas67 Kasparov AA. [Toxic effects of boron and boric anhydride in mice.] In Russian. Nov Dannye Toksikol Redk Metal Ikh Soedin 1967, 126-42 (cited from Chemical Abstracts 71:68976u).

Nie96 Nielsen FH. Evidence for the nutritional essentiality of boron. J Trace Elem Exp Med 1996; 9: 215-29.

NLM04 US National Library of Medicine (NLM), ed. Boron oxide. In: The Hazardous Substances Data Bank (HSDB) (last revision date boron oxide file: March 2003; last review date: August 1989); http://toxnet.nlm.nih.gov.

Swe00 Swedish National Board of Occupational Safety and Health. Occupational exposure limit values and measures against air contaminants. Solna, Sweden: National Board of Occupational Safety and Health, 2000; Ordinance AFS 2000:3.

SZW05 Ministerie van Sociale Zaken en Werkgelegenheid (SZW). Nationale MAC-lijst 2005. The Hague, the Netherlands: Sdu Uitgevers, 2005: 23.

TRG04 TRGS 900. Technische Regeln für Gefahrstoffe. Grenzwerte in der Luft am Arbeitsplatz. BArbBl 2004; (7/8).

Wil59 Wilding JL, Smith WJ II, Yevich P, et al. The toxicity of boron oxide. Am Ind Hyg Assoc J 1959; 20: 284-9.

Annex

Occupational exposure limits for diboron trioxide in various countries.

country - organisation	occupational exposure limit		time-weighted average	type of exposure limit	note[a]	reference[b]
	ppm	mg/m^3				
the Netherlands						
- Ministry of Social Affairs and Employment	-	10	8 h	administrative		SZW05
Germany						
- AGS	-	-				TRG04
- DFG MAK-Kommission	-	-[c]				DFG05
Great Britain						
- HSE	-	10	8h	OES		HSE02
	-	20	15 min			
Sweden	-	-				Swe00
Denmark	-	10	8h			Arb02
USA						
- ACGIH	-	10	8 h	TLV		ACG05
- OSHA	-	15[d]	8h	PEL		ACG04
- NIOSH	-	10	10 h	REL		ACG04
European Union						
- SCOEL	-	-				EC05

[a] S = skin notation, which mean that skin absorption may contribute considerably to body burden; sens = substance can cause sensitisation.

[b] Reference to the most recent official publication of occupational exposure limits.

[c] Listed among compounds for which studies of the effects in man or in experimental animals have yielded insufficient information for the establishment of MAK values.

[d] Total dust.