Boric acid and tetraborates

BAT (2014) **not established**
Sampling time: difference between the boron concentration in the pre-shift urine and post-shift urine

	Boric acid	Disodium tetraborate	Disodium tetraborate pentahydrate	Disodium tetraborate decahydrate
CAS No.	10043-35-3	1330-43-4	12179-04-3	1303-96-4
Formula	$B(OH)_3$	$B_4Na_20_7$	$Na_2B_40_7 \cdot 5(H_20)$	$Na_2B_40_7 \cdot 10(H_20)$
Molecular weight	61.83 g/mol	201.22 g/mol	291.35 g/mol	381.37 g/mol
Melting point	171°C	742°C	no data	75°C
Boiling point	100–130°C (decomposes when heated)	1 575°C	no data	320°C
Vapour pressure at 20°C	2.7 hPa	no data	no data	0.213 hPa
Density at 20°C	1.44 g/cm³	2.37 g/cm³ at 25°C	1.82 g/cm³	1.72 g/cm³

MAK value (2010)	**Boric acid:** **10 mg/m³ I (1.8 mg as boron/m³)** **Disodium tetraborate pentahydrate:** **5 mg/m³ I (0.75 mg as boron/m³)** **Other tetraborates and hydrates:** **0.75 mg as boron/m³** when boric acid and borates are present at the same time, 0.75 mg boron/m³ applies
Peak limitation (2010)	Category I, excursion factor 1
Absorption through the skin	–
Carcinogenicity	–
Prenatal toxicity (2010)	Boric acid: Pregnancy Risk Group B Tetraborates: Pregnancy Risk Group C
Germ cell mutagenicity	–

Boric acid and tetraborates occur at workplaces in the form of dust/aerosol and cause acute irritation to the respiratory tract. The MAK values established on the basis of this irritation by means of studies in test persons are 10 mg boric acid/m^3 I (1.8 mg boron/m^3) or 5 mg disodium tetraborate pentahydrate/m^3 I (0.75 mg boron/m^3). The MAK value of 0.75 mg boron/m^3 I also applies for other tetraborates and their hydrates. A potentially relevant systemic effect is a possible reproductive damage, in particular an effect on male fertility and embryotoxicity. From animal studies such effects are, however, only to be expected at concentrations above about 30 mg boron/m^3 (Hartwig 2011, translated). Exposures at such high levels have not been described for the workplace collectives documented in the literature even under worst case occupational hygienic conditions (Başaran et al. 2012; Bolt et al. 2012; Duydu et al. 2012 a).

As the local irritant effect is the main effect for the derivation of a threshold value in the workplace air, and no systemic effects below this concentration are to be expected, biological threshold values can only be derived from a correlation with the air concentration. Appropriate data from more extensive field studies have been published.

Boric acid is a weak acid with a pK_a of 9.2. After the uptake of boric acid or boric acid salts, boric acid is practically quantitatively available (98.4%) in the organism in non-dissociated form (Woods 1994). In the literature, the data for boric acid/borate concentrations in biological materials exclusively relate to elemental boron. As regards the methods of biological monitoring, therefore, boric acid and borates can be treated in the same way.

1 Metabolism and Toxicokinetics

The toxicokinetics of boric acid have been investigated in animal studies and in humans. There is practically no absorption through the intact skin. After ingestion, boric acid is rapidly and completely absorbed. The exact amount of uptake via the respiratory tract is not clear; a systemic uptake of dust deposited in the respiratory tract via swallowing is thereby possible (Hartwig 2011, translated). Boric acid is eliminated from the blood in unchanged form (non-dissociated boric acid) almost completely via the kidneys; there are slight differences between species with regard to velocity which are explained by differences in the glomerular filtration rate (Murray 1995). In humans, the plasma half-life of boric acid is about 21 hours (Jansen et al. 1984). Sampling of biological materials (blood, urine) to determine the boron concentration related to exposure at the workplace can therefore be carried out at the end of any shift as required.

2 Critical Toxicity

The critical toxicity of boric acid/borates is the local irritant effect. This local effect occurs primarily in the nasal mucosa and is explained by a locally increased osmolality from a deposition of boric acid/borate (for a more detailed explanation, see Hartwig 2011, translated).

3 Exposure and Effects

In the literature, studies on the relationship between internal exposure and effects in the form of effects on male fertility have been published. These yielded no significant results as, apparently, even under worst case conditions, the level of possible exposures at the workplace for the induction of such effects is too low (Duydu et al. 2011, 2012 a, 2012 b; Robbins et al. 2010).

The relationship between external and internal exposure can be derived from the following published field studies in collectives exposed to boric acid/borate.

In California, 14 workers exposed to borax were examined (Culver et al. 1994). By using the IOM (Institute of Occupational Medicine Edinburgh) sampler, the inhalable fraction in the air at the workplaces (I-dust) was determined during a working week. The "total dust" according to the ACGIH definition (ACGIH 1999) was determined simultaneously. Because the MAK value for boric acid/borates is related to the I-dust, and due to the generally better correlation with the biological parameters, the data obtained using the IOM method are listed below. In addition, during the test week and two days before, the boron levels of ingested foods in solid and liquid form were determined. The analysis of the materials for boron takes place via ICP (inductively coupled argon plasma spectroscopy) according to the method by Hunt and Shuler (1989). The averaged exposure values (I-dust) were as follows:

- exposure category **"low"**: 0.470 ± 0.169 mg boron/m^3
- exposure category **"medium"**: 1.618 ± 1.164 mg boron/m^3 and
- exposure category **"high"**: 2.477 ± 1.535 mg boron/m^3

(mean value ± standard deviation)

For estimation of the internal inhalation exposure, a respiratory volume of 10 m^3 per shift and a complete pulmonary absorption was assumed. The inspired exposure levels corresponding to the three exposure categories were thus 4.70 mg boron/day, 16.18 mg boron/day and 24.77 mg boron/day, respectively. On the other hand, the mean daily dietary boron intake in all groups was 1.35 ± 0.72 mg/day. Between the levels of exposure by inhalation determined with the IOM method and the biological values in blood and urine found at the end of the respective shift, the following relationships were obtained:

boron in blood [µg boron/g blood]
= 0.07 [baseline value from food intake] + 0.008 · [mg inhaled boron/shift]

and

boron in urine [µg boron/mg creatinine] = 0.6 + 0.46 · [mg inhaled boron/shift].

From 2003 on, studies were carried out with workers exposed to boron in Northern China; their primary aim was to investigate possible effects of boron on male fertility.

In 2003, 60 workers employed in boron mining and processing and 9 occupationally non-exposed persons from a district in the same province with a low level of exposure to boron from the environment were investigated. In 2004, the same authors examined 74 workers exposed to boron and 61 persons from the same region not exposed at the workplace. Close relationships between the calculated daily boron intake, the concentration of boron in blood and the urinary boron excretion (post-shift urine) were obtained (Xing et al. 2008). This resulted in the following function between the total boron intake and the post-shift boron excretion in the urine:

log [boron intake in mg/day] = 1.03912 + log 0.908 [mg boron/g creatinine]

For biological monitoring, the determination of boron in the post-shift urine was recommended.

In another study, the level of boron intake was given. The mean daily intake in 75 workers exposed to boron was 31.3 mg boron; this was 125 mg boron in a subgroup of 16 workers with the highest exposure (Scialli et al. 2010). Estimates of mean daily boron intake in a local community and remote background controls were 4.25 mg boron/day and 1.40 mg/day, respectively.

For 66 workers exposed to boron, 59 controls from the same region and 67 remote background controls (Robbins et al. 2010), the boron concentrations in blood, urine and seminal fluid (average value ± standard deviation) listed in Table 1 were obtained.

Table 1 Boron concentrations in exposed workers and control persons (Robbins et al. 2010)

	Workers exposed to boron	**Control persons**	
		from the same region	**from a remote region**
	Workers exposed to boron	**Control persons**	
Boron in blood [µg/l]	499.2 ± 790.6	96.1 ± 92.1	47.9 ± 24.1
Boron in urine [mg/l]*	16.7 ± 31.4	5.5 ± 15.6	2.0 ± 0.9
Boron in seminal fluid [µg/l]	785.6 ± 605.7	310.6 ± 245.3	214.0 ± 113.9

* post-shift

Table 2 Boron concentrations in exposed workers and control persons (average value ± standard deviation) (Duydu et al. 2011)

	Workers exposed to boron	Control persons
Boron in blood [ng/g]	139.8 ± 80.7	62.1 ± 44.0
Boron in urine [mg/g creatinine]	6.6 ± 4.2	5.0 ± 3.1
Boron in seminal fluid [ng/g]	1 718.1 ± 1 997.8	1 023.9 ± 1 630.9

In Turkey, 102 male workers exposed to boric acid or borax and 102 not occupationally exposed workers as controls were examined (Duydu et al. 2011). The results of the boron concentrations in blood, urine and seminal fluid are shown in Table 2.

During the study, a previously not known additional boron exposure due to a considerable contamination of the drinking water (about 9.5 mg boron/l) in the central canteen of the company was found which meant that, in addition to inhalation by exposed persons, a quantitatively important exposure to boron via the drinking water and the canteen meals was also present. Thus, due to the high additional exposure from the drinking water, this study cannot be used for the evaluation.

4 Selection of Indicators

Suitable biological indicators are principally boron in whole blood or in urine. Both parameters correlate closely with each other. For reasons of practicability, non-invasive determination via the urine is to be preferred. Both for toxicokinetic reasons and due to the published field data, the post-shift urine is highly suitable for the determination of internal exposure to boron at the workplace.

5 Test Methods

The boric acid or borate levels in biological materials are generally related to elemental boron (B). As analytical methods, ICP-MS (inductively coupled plasma mass spectrometry) (Xing et al. 2008) and ICP-OES (inductively coupled plasma optical emission spectrometry) (Duydu et al. 2011) have been described. The detection limit for the determination of boron in urine using ICP-OES was given as 0.1 mg/l, the quantitation limit as 0.4 mg/l (Duydu et al. 2011, Electronic Supplementary Material).

6 Background Exposure

Traces of boron are essential for plant growth and therefore found ubiquitously in food. The level of background exposure to boron depends, however, for the most part on the boron content in drinking water and is thus subject to marked geographical differences. Economically exploitable boron deposits are found in regions with former or present volcanic or hydrothermal activity, for example in Western Anatolia, California, Northern China and the Andes. Extremely high drinking water exposures have been described for narrowly localized regions in Turkey (Şaylı et al. 1998). This means that, for not occupationally exposed persons, markedly different background concentrations in biological materials between 0.01 and 0.36 mg boron/l blood and between 0.04 and 7.80 mg boron/l urine are given in the references of different authors (Culver et al. 1994).

7 Evaluation

Owing to the differences in the local irritant effects of boric acid and sodium tetraborate (borax), different MAK values for boric acid (1.8 mg boron/m^3 I) and borates (0.75 mg boron/m^3 I) were established. Biological monitoring to determine internal exposure at the workplace is best carried out by measuring the boron concentration in the post-shift urine (see Section 4).

The available data from field studies (see Section 3) indicate quantitatively comparable relationships between the total boron intake and its urinary excretion. From the study on the connection between external and internal exposure to boron at the workplace, the following relationship was derived for the urinary excretion of boron (post-shift urine) (Culver et al. 1994; see Section 3):

$$\text{Boron in urine [mg boron/g creatinine]} = 0.6 + 0.46 \cdot \text{[mg inhaled boron/shift]}$$

In this equation, the axis intercept of the function (0.6 mg boron/g creatinine) gives the boron excretion caused by background exposure (see Section 6). As this is subject to considerable variations, it is expedient to establish the individual boron background exposure on a personal basis by analyzing the pre-shift urine (for practical purposes at the beginning of a working week).

The occupational exposure is then obtained from the difference in boron excretion between post-shift and pre-shift urine. According to Culver et al. (1994), this increment is

$$\text{Boron in urine [mg boron/g creatinine]} = 0.46 \cdot \text{[mg inhaled boron/shift]}$$

This derivation by Culver et al. (1994) was based on a respiratory volume of 10 m^3 per shift and the determination of boron in I-dust (IOM procedure) (see Section 3).

Accordingly, a shift increment of 8.28 mg boron/g creatinine in urinary excretion is obtained for an 8-hour exposure to boric acid at the level of the MAK value (1.8 mg boron/m³ I), and a shift increment of 3.45 mg boron/g creatinine for an 8-hour exposure to borates at the level of their MAK value (0.75 mg boron/m³ I).

The factor of 0.46 used by Culver et al. (1994) in the relationship given above results from the half-life of boron in blood/plasma of 10 hours and the fact that the elimination of boron almost exclusively takes place via the kidneys (see Section 1).

From this, for an exposure at the level of the MAK values, 8.5 mg boron/g creatinine is obtained as shift increment for urinary boron excretion in the case of boric acid and 4 mg boron/g creatinine in the case of borates. These values refer to the individually determined difference between the boron concentration in post-shift and pre-shift urine.

Owing to the fact that local irritation is the main effect and that there is no systemic toxicity at this concentration, the evaluation of a biological tolerance value (BAT value) derived on this basis is not meaningful.

8 Interpretation of Results

In Section 6, attention has been drawn to the importance of determining the background concentration of boron in urine.

The above-mentioned values relate to normally concentrated urine, in which the creatinine concentration should be in the range of 0.3–3.0 g/l. In addition to this, the Commission considers it useful, for further improving the validity of the analyses, to select a narrower target range of 0.5–2.5 g/l for urine samples. As a rule, where urine samples are outside the above limits, a repetition the measurement in normally hydrated test persons is recommended (see BAT Documentation 2010, translated).

9 References

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