Bromine

(CAS No: 7726-95-6)

Health-based Reassessment of Administrative Occupational Exposure Limits

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

No. 2000/15OSH/143 The Hague, October 27, 2005

Preferred citation:
Health Council of the Netherlands: Committee on Updating of Occupational Exposure Limits. Bromine; Health-based Reassessment of Administrative Occupational Exposure Limits. The Hague: Health Council of the Netherlands, 2005; 2000/15OSH/143.

1 Introduction

The present document contains the assessment of the health hazard of bromine by the Committee on Updating of Occupational Exposure Limits, a committee of the Health Council of the Netherlands. The first draft of this document was prepared by AAE Wibowo, Ph.D. (Coronel Institute, Academic Medical Centre, Amsterdam, the Netherlands).

In October 1997, literature was searched in the databases Medline, Toxline, Chemical Abstracts, Embase (starting from 1966, 1967, 1970, and 1988, respectively), and HSELINE, CISDOC, MHIDAS, and NIOSHTIC (from 1997 backwards), databases available from CD-ROM, and using the following keywords: bromine and 7726-95-6.

In February 1999, the President of the Health Council released a draft of the document for public review. Comments were received from the following individuals and organisations: A Aalto (Ministry of Social Affairs and Health, Tampere, Finland), P Wardenbach, Ph.D. (Bundesanstalt für Arbeitsschutz und Arbeitsmedizin, Dortmund, Germany).

An additional literature search was performed in Toxline and Medline in October 2004.

In December 2004, the President of the Health Council released a revised draft of the document for public review. Comments were received from the following individuals and organisations: E Ball (Health and Safety Executive, London, UK) and E González-Fernández, Ph.D. (Instituto Nacional de Seguridad e Hygiene en el Trabajo, Madrid, Spain). These comments were taken into account in deciding on the final version of the document.

2 Identity

name	: bromine
molecular formula	: Br_2
CAS number	: 7726-95-6

3 Physical and chemical properties

molecular weight	: 159.8
boiling point	: 58.8°C
melting point	: -7.3°C
flash point	: not found
vapour pressure	: 23 kPa
solubility in water	: slightly soluble (at 25°C: 3.4 g/100 mL)
log $P_{octanol/water}$	: 1.03 (estimated)
conversion factors	: at 20°C, 101.3 kPa: 1 mg/m^3 = 0.15 ppm 1 ppm = 6.66 mg/m^3

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

Bromine is a fuming reddish-brown liquid, with a pungent odour. The vapour is heavier than air. The odour threshold was reported to be about 0.33 mg/m^3 (0.051 ppm) (Amo83, Rut86), although an experiment with 20 volunteers suggested that it could be below 0.07 mg/m^3 (0.01 ppm) (Rup67).

4 Uses

Bromine is used in the manufacture of ethylene dibromide (an antiknock compound in gasoline), fire-extinguishing fluids, and fire retardants for plastics; in organic synthesis, bleaching, dyes, pharmaceuticals, photographic chemicals, and shrink-proofing wool; for water purification; as an intermediate for fumigants; and as an analytical reagent (ACG02).

5 Biotransformation and kinetics

The committee did not find data on the biotransformation and kinetics following exposure to bromine vapours.

Occupational exposure usually occurs by inhalation of its vapour, or probably by accidental contact of the liquid with the skin. In the latter case, bromine can cause burns depending on the concentration. It is not known whether absorption through the skin takes place.

Absorption, distribution, and excretion of bromide (ion) are closely analogous to chloride. Bromide is completely absorbed from the gastrointestinal tract by passive, paracellular transport. It is distributed throughout the body nearly exclusively into extracellular fluids. Exceptions are the erythrocytes and the acinar cells of the gastric wall. The volume of distribution of bromide is

about 0.3 L/kg bw. Bromide is more readily transported than chloride leading to larger bromide/chloride ratios in saliva and gastric acid than in plasma and to lower ratios in urine. Transport into the extracellular fluid of the central nervous system is by an active transport system via the choroid plexus, which has a preference for chloride. Since the elimination rate from the cerebrospinal fluid flow is similar for both ions, bromide never reaches the same cerebrospinal fluid/plasma ratio as chloride and reaches plateau levels in the central nervous system later than in plasma. Bromide is excreted mainly by the kidneys and small quantities in sweat, tears, and other body excretions. Tubular reabsorption of bromide is faster than that of chloride, which plays a role in the accumulation of bromide. Biological half-lives of bromide reported are 12 and 10.5 days with an average clearance of 0.68 mL/min. This half-life may be increased by a salt-deficient diet while it can be decreased by administering an excess of chloride ions. Bromide crosses the placental barrier easily and replaces chloride in the fetal body fluids. Experimental animal distribution studies in fetuses on gestational day 20 suggested that the fetus might be more accessible to bromide than, for instance, the mother's brain and that elimination from the fetus is much slower than from the mother's plasma and brain, which may lead to considerable accumulation of bromine in the fetus. Bromide is excreted in maternal milk as well (Rau83, Sti88). Generally, therapeutic use of bromide is associated with serum bromide levels of 5-50 mg/L, toxic levels range from 700-4100 mg/L, and levels >2000 mg/L may be fatal. Levels of 1500 mg/L are generally regarded as necessary to produce symptoms of intoxication, although cases of bromism have been reported at levels as low as 40 mg/L (Eld96, Ste83).

Krari et al. determined the concentrations of bromide in various tissues of unexposed male rats. The highest average concentration was found in plasma (69 µmol/L), followed by the kidney, liver, heart, and brain (14, 12, 10, and 4 µmol/kg wet weight). Administration of NaBr at a dose of 5 µmol/kg bw/day via the drinking water for 21 days increased the bromine concentration to 188 µmol/L in the plasma and 32, 31, 47, and 8 µmol/kg wet weight in kidney, liver, heart, and brain, respectively (Kra92).

Eldan et al. studied the use of serum bromine concentration as a measure of exposure in a group of 670 male and 150 female workers employed at a bromine compounds-producing company. About 66% of the men and 31% of the women worked directly with chemicals. The average levels in men and women were higher than in the general population: 24.7 and 14.5 mg/L, respectively (range: 8.3-428.6 mg/L) vs. 3-5 mg/L. Levels were related to work site, department type, chemical handling, and occupation (Eld96).

6 Effects

Human data

The irritation threshold concentration was reported to be 2.1 mg/m^3 (0.32 ppm) (Rut86).

According to Rupp and Henschler, Flury and Zernike erroneously cited data on bromine from the thesis of Matt (published in 1889) in their monograph (published in 1931). Reviewing the original thesis, Rupp and Henschler stated that Matt had exposed himself to chlorine concentrations of 1.3, 2.5, 3.5, and 4 ppm and bromine concentrations of 1, 3, and 4 ppm*, for 9-22 minutes, and had concluded that the irritating properties of chlorine and bromine were similar. According to Matt, bromine (or chlorine) concentrations of 1-2 ppm were tolerable, of 2-3 ppm tolerable but annoying, and concentrations of 4 ppm intolerable (Rup67).

Rupp and Henschler investigated the odour intensity and irritation of bromine vapours by exposing groups of healthy students to nominal concentrations of 0.01-1.0 ppm (0.07-6.7 mg/m^3)** for 0.5 h. In all experiments, all subjects noticed the presence of the test compound although only a few could identify it as bromine. The intensity score increased with increasing dose ranging from minimal to moderate at 0.01 ppm to strong to very strong at 1.0 ppm. A concentration-related increase in the number and severity of symptoms of irritation was noticed. The irritating properties of bromine were investigated further by exposing 3 volunteers to concentrations gradually increasing from 0 to 0.9 ppm (6 mg/m^3) over 50 minutes. At 0.006 ppm (0.04 mg/m^3), some irritation of the eyes was reported. At 0.2 ppm (1.3 mg/m^3), clear irritation of eyes, nose, and throat occurred, while levels of 0.5 ppm (3.3 mg/m^3) and above became hardly tolerable (Rup67).

Eldan et al. examined the performance of 820 workers (670 males; 150 females) employed in a bromine compounds-producing company (see Section ‘Biotransformation and kinetics’) in 10 tests from the Neurobehavioural Evaluation System (NES) battery. The relationship between serum bromide levels and test results were analysed by ordinary least squares regression analysis and by logistic regression analysis. The analyses suggested subtle, but distinct

* Except for the lowest bromine concentration of 1 ppm, all levels could be determined by analytical methods.
** The average analytical concentrations ranged from 0.007-0.55 ppm (0.05-3.7 mg/m^3).

associations between serum bromide levels and impaired performance in certain tests. The strongest association was found with functions measured by the Symbol-Digit Coding test (odds ratio: 2.34; $p<0.01$). When serum bromide levels were considered as a categorical variable, a dose-response relationship was found; odds ratios ranged from 1.16 for the lowest serum levels to 2.71 for the highest (reported in an abstract; no more data presented) (Eld95).

Morabia et al. reported an accidental release of bromine from chemical plant in Geneva, Switzerland, in 1984, resulting in exposure to concentrations of ca. 0.2-0.5 ppm (1.3-3.3 mg/m^3) lasting for maximum 4 hours. In the outpatient and casualty departments of the cantonal hospital, 91 patients with symptoms of bromine exposure were seen, but the clinical course was described as mild and self-limiting in nearly all cases. One patient was admitted for 24 hours. The most common symptoms were upper respiratory tract symptoms, cough, and headache. In 20 to 30% of the cases, the symptoms persisted for more than 3 days, and sometimes up to one month (Mor86). [In view of the analytical method used (Dräger tubes that are developed to detect chlorine and uses very short sampling times of ca. 20 seconds), the committee questions the reliability of these exposure values].

Krasniuk et al. studied the health status of workers engaged in the manufacture of bromine and its derivative. Chronic bronchitis was the most common disorder among the workers. Pathological changes in the respiratory tract, contact and allergic dermatitis, and arterial hypertension were observed. Exposure levels were not reported (Kra87).

During the years 1976-1985, there were 173 admissions to a department of the University hospital in Beer-Sheva, Israel, due to chemical burns. The most common cause was bromine (42 admissions) and bromine compounds (22 admissions) due to the proximity of the department to the bromine industry. The common features of bromine injury were the delayed appearance of signs of injury, resulting sometimes in deep partial skin loss injuries, and skin discolouration. The upper and lower extremities were most commonly affected despite the use of protective clothes such as sleeves, gloves, and boots (Sag85, Sin92).

Kim and Seo described 4 cases of delayedly appearing blisters. All patients had worn protective clothing during work and may have been exposed due to leakage into protected areas or residual bromine on clothes (Kim99).

Lossos et al. reported a case after accidental exposure to bromine. On admission, the patient was coughing and choking. Grade I-II chemical burns were present on the anterior chest and face. Immediate chest films showed no abnormality. A few hours later, the patient still experienced severe cough, and a

chest X-ray film showed pneumomediastinum. No evidence of subcutaneous emphysema or chemical pneumonitis was present. Progressive improvement and resolution of mediastinal air occurred (Los90).

Kraut and Lilis reported a chemical pneumonitis in a 60-year-old laboratory technician following accidental exposure to bromine compounds (a mixture of hydrogen bromide and phosphorus tribromide). The exposure duration was estimated at 5-10 minutes; the concentration was not known. The patient complained of dry cough, light-headedness and slight congestion in her throat. During the next 2 weeks, the subject experienced increasing shortness of breath. A protracted clinical course ensued consistent with bronchiolitis obliterans. After about 10 months, no other respiratory symptoms were present except shortness of breath on climbing 2 flights of stairs. Chest X-ray was normal and pulmonary function tests showed normal flows and decreased TLC and diffusing capacity (Kra88).

Recently Burns and Linden described the clinical course of 2 patients who developed acute pneumonitis followed by reactive airways dysfunction syndrome (RADS) after bathing in a hot tub. Additional findings suggested exposure to a corrosive agent. Bromine and hydrobromic acid generated from a widely used water disinfectant were implicated as the underlying cause. However, the concentrations of these agents were unknown. One patient developed chemical pneumonitis and a restrictive pattern of pulmonary dysfunction. Both patients described fulfil the criteria for RADS. The abrupt onset of irritant symptoms within minutes of a single bath suggested high exposure concentrations (Bur97).

Lyubchenko and Alekseeva reported a worker accidentally exposed to bromine vapour with unknown concentration for about 30 minutes. The compound caused skin lesions and cough. The patient was immediately treated and with success. After approximately 3 weeks, the worker experienced toxic bronchitis with haemorrhage, myocardial dystrophy, and increased γ-glutamyl transferase and bilirubin blood concentrations (Lyu91).

Carel et al. evaluated the health effects in 2 passing drivers and 7 rescuers who were exposed for 45 to 240 minutes to bromine gas released from broken and exploded bottles when trying to extricate a driver from the cabin of his overturned truck. The driver died of bromine intoxication during these activities. Six out of the 9 subjects, 21- to 35-years old, participated in the evaluations. During exposure, all had some respiratory symptoms and skin burns. When examined in the hospital, eye irritation (in 6/6), shortness of breath (in 5/6), 1st-2nd degree burning of feet, legs, and wrists (in 5/6), cough (in 4/6), nausea (in 4/6), and chest pain/tightness (in 4/6) were seen. No eye injuries were identified.

Auscultation, chest roentgenograms, electrocardiograms, blood chemistry and haematology evaluations, and blood pressure measurements did not reveal bromine exposure-induced changes. All subjects were released within 1 to 4 days. At follow-up examinations, 6 to 8 weeks later, they still experienced chest pain/tightness (in 4/6), cough (in 3/6), eye irritation (in 3/6), and shortness of breath (in 2/6), but also complained of dizziness (in 4/6), chronic fatigue (in 4/6), itching of skin (in 4/6), constipation/diarrhoea (in 4/6), memory disturbances (in 4/6), headache (in 3/6), and sex disturbances (in 3/6), but no objective laboratory or clinical evidence of effects were found (Car92).

Potashnik et al. evaluated the reproductive performance of 8 of these men, and their spouses, 9 to 40 weeks after the accident. Semen analysis showed normal semen volumes in all men. An extremely low sperm density with low motility and low percentage of normal forms was seen in 1 subject. He and his wife appeared to have sought medical assistance about 2.5 years prior to the accident because of failure to conceive, and oligo-terato-asthenozospermia (OTA) was then detected in this patient. In 2 other subjects, sperm density, motility (in one of them), and percentage normal values were lower than normal. However, their fertility was not impaired as confirmed by spontaneous pregnancies in their spouses prior to and after the accident. Plasma levels of follicle-stimulating (FSH) and luteinising hormone (LH) were normal in all men. Testosterone levels were lower in the subject diagnosed with the long-standing OTA as well as in 2 other subjects who showed normal levels 3 months later. Among the 5 spontaneous pregnancies in 5 families within 2 to 15 weeks after the accident, 2 went to term uneventfully, one was interrupted at the request of the couple, and one first-trimester abortion and one late abortion (due to chorioamnionitis) occurred. The results suggested a mild degree of spermatogenic suppression and impaired reproductive performance following paternal exposure to bromine vapour. However, Potashnik et al. stated that due to the small size of the study cohort, a cause-effect relationship could not be established (Pot92).

Animal data

The 30-minute LC_{50} of bromine in female (NMRI) mice was reported to be 174 ppm (1158 mg/m^3) (observation period: 10 days). Generally, mortality occurred in 2 distinct periods, viz., within the first 4 days (the majority) and between day 8 and 10. The cause of death was reported to be either bronchospasm or lung oedema in the early deaths and peribronchitis with abscess formation in the animals dying during days 8 to10. Exposure to 22 and 40 ppm (147 and 266

mg/m^3) for 3 hours caused mortality in 0/10 and 3/10 mice while 7/10 and 8/10 animals, respectively, died within 10 days following a 6-hour exposure. Exposure to 5 or 10 ppm (33 and 67 mg/m^3), 8 hours/day, for 3 days did not induce mortality but decreased body weights by ca. 18 and 23%, respectively, which was thought to be an expression of the irritation of the upper respiratory tract (Sch67).

Bitron and Aharonson studied the delayed mortality (observation time: 30-45 days) following single inhalation of bromine, in comparison with formaldehyde, sulphur dioxide, and chlorine. Mice were exposed to bromine concentrations of 240 ppm (ca. 1600 mg/m^3) for 15-270 minutes or to 750 ppm (ca. 5000 mg/m^3) for 5-30 minutes. They found that the mean time of death at a constant bromine concentration decreased with increasing exposure duration. A figure presenting cumulative mortality as a function of exposure time indicated that exposures for 100 minutes to 240 ppm or for 9 minutes to 750 ppm would induce 50% mortality (Bit78).

Disturbances of respiratory, nervous, and endocrine system functions were seen in rats exposed to bromine concentrations of 12.4 mg/m^3 (1.9 ppm) for 4 months, but not at exposure to 0.16 mg/m^3 (0.02ppm) (Iva76). Due to limited reporting, the committee considers that this study is not appropriate for use in standard setting.

The committee did not find (other) data on long-term toxicity, carcinogenicity, mutagenicity, genotoxicity, and reproduction toxicity of bromine.

7 Existing guidelines

The current administrative occupational exposure limit (MAC) for bromine in the Netherlands is 0.7 mg/m^3 (0.1 ppm), 8-hour TWA.

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

8 Assessment on health hazard

The committee did not find data on the biotransformation and kinetics following exposure to bromine vapours. Bromide (ion) is absorbed, distributed, and excreted closely analogously to chloride. It is completely absorbed from the gastrointestinal tract and distributed throughout the body nearly exclusively into extracellular fluids (including that of the central nervous system), erythrocytes and acinar cells of the gastric walls being exceptions. Bromide is excreted mainly

by the kidneys and in small quantities in sweat, tears, and other body excretions. Biological half-lives are about 11 days with an average clearance of ca. 0.7 mL/min. Because tubular reabsorption of bromide is faster than that of chloride, excretion of bromide can be increased or decreased by administering a salt-deficient diet or an excess of chloride ions, respectively. Bromide can accumulate in the fetus. It is excreted in maternal milk.

Bromine is a severely irritating compound. Several cases of severe, sometimes delayed, skin injury and of respiratory tract effects following occupational exposure to bromine have been reported. Studies in young, healthy volunteers (n=3) exposed to concentrations gradually increasing from 0 to 0.9 ppm (6 mg/m^3) over 50 minutes showed some eye irritation at 0.006 ppm (0.04 mg/m^3) and clear irritation of eyes, nose, and throat at 0.2 ppm (1.3 mg/m^3); concentrations of 0.5 ppm (3.3 mg/m^3) were hardly tolerable. Limited information concerning the performance of a group of 820 workers, employed in a bromine compounds-producing company, in Neurobehavioural Evaluation System battery tests indicated that bromine at relatively high serum levels might have some subtle effects on the nervous system.

In mice, a 30-minute LC_{50} of 174 ppm (1158 mg/m^3) was found. Mortality occurred in 2 distinct periods, viz., within the first 4 days and between day 8 and 10, the cause of death being bronchospasm or lung oedema and peribronchitis with abscess formation, respectively. Exposure to 22 ppm (147 mg/m^3) for 3 or 6 hours caused mortality in 0/10 and 7/10 mice, respectively. All mice survived exposure to 5 or 10 ppm (33 and 67 mg/m^3), 8 hours/day, for 3 days, but showed body weight decreases (by ca. 18-23%), which was thought to be an expression of upper respiratory tract irritation.

The committee did not find valid data on long-term toxicity, carcinogenicity, mutagenicity, genotoxicity, and reproduction toxicity of bromine.

The committee considers irritation of the eyes, nose, and throat as reported at 1.3 mg/m^3 (0.2 ppm) in a small group of volunteers exposed to gradually increasing bromine levels (Rup67) as the critical effect. Taking this LOAEL of 1.3 mg/m^3 (0.2 ppm) as a starting point for deriving a health-based occupational exposure limit (HBROEL), the committee considers a concentration of 0.2 mg/m^3 (0.03 ppm) sufficiently low to prevent significant irritation from exposure to bromine. In order to prevent peak exposures, this should be a 15-minute time-weighted average value.

The committee recommends a health-based occupational exposure limit for bromine of 0.2 mg/m^3 (0.03 ppm), as a 15-minute time-weighted average.

References

ACG02 American Conference of Governmental Industrial Hygienists (ACGIH). Bromine. In: Documentation of the TLVs® and BEIs® with other worldwide occupational exposure values. CD-ROM - 2002. Cincinnati OH, USA; ACGIH®, 2002.

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: 15.

Amo83 Amoore JF, Hautala E. Odor as an aid to chemical safety: thresholds compared with threshold limit values and volatilities for 214 industrial chemicals in air and water dilution. J Appl Toxicol 1983; 3: 272-90.

Arb02 Arbejdstilsynet. Grænseværdier for stoffer og materialer. Copenhagen, Denmark: Arbejdstilsynet, 2002: 18 (At-vejledning C.0.1).

Bit78 Bitron MD, Aharonson EF. Delayed mortality of mice following inhalation of acute doses of CH_2O, SO_2, Cl_2 and Br_2. Am Ind Hyg Assoc J 1978; 39: 129-38.

Bur97 Burns MJ, Linden CH. Another hot tub hazard. Toxicity secondary to bromine and hydrobromic acid exposure. Chest 1997; 111: 816-9.

Car92 Carel RS, Belmaker I, Potashnik G, et al. Delayed health sequelae of accidental exposure to bromine gas. J Toxicol Environ Health 1992; 36: 273-7.

DFG05 Deutsche Forschungsgemeinschaft (DFG): Commisson for the Investigation of Health Hazards of Chemical Compounds in the Work Area. List of MAK and BAT values 2005. Maximum concentrations and biological tolerance values at the workplace. Weinheim, FRG: Wiley-VCH Verlag & Co. KGaA, 2005: 30 (rep no 41).

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.

Eld95 Eldan M, Carel R, Weitzman S, et al. Assessment of the relationship between chronic exposure of workers to bromine and neuropsychological manifestations. Am J Epidemiol 1995; 141 (11 suppl): S7.

Eld96 Eldan M, Carel RS, Factor-Litvak P, et al. Biological monitoring of workers exposure to bromine. J Occup Environ Med 1996; 38: 1026-31.

HSE02 Health and Safety Executive (HSE). EH40/2002. Occupational Exposure Limits 2002. Sudbury (Suffolk), England: HSE Books, 2002: 13.

Iva76 Ivanov NG, Klyachkina AM, Germanova AL. [Experimental materials for hygienic standardization of bromine and hydrogen bromine in the air of the production area]. In Russian with English abstract. Gig Tr Prof Zabol 1976; (3): 36-9 (cited from Chemical Abstracts 85: 129771m).

Kim99 Kim IH, Seo SH. Occupational chemical burns caused by bromine. Contact Dermatitis 1999; 41: 43.

Kra87 Krasnyuk EP, Timofeeva NT, Beznisko TG, et al. [Influence of labor conditions on the health status of workers engaged in manufacture of bromine and its derivatives]. In Russian. Gig Sanit 1987; (7): 81-2 (cited from Chemical Abstracts 107:182619/20).

Kra88 Kraut A, Lilis, R. Chemical pneumonitis due to exposure to bromine compounds. Chest 1988; 94: 208-10.

Kra92 Krari N, Berre S, Allain P. Effects of thyroparathyroidectomy on the distribution of bromine and iodine in rat tissues. Biol Trace Element Res 1992; 32: 275-9.

Los90 Lossos IS, Abolnik I, Breuer R. Pneumomediastinum: a complication of exposure to bromine. Br J Ind Med 1990; 47: 784.

Lyu91 Lyubchenko PN, Alekseeva, GA. [Acute poisening with bromine vapors of an operator at a chemical-pharmaceutical plant]. In Russian. Gig Tr Prof Zabol 1991; (9): 32-4.

Mor86 Morabia A, Selleger Ch, Conne P, et al. Nuage de brome à Genève. Schweiz Med Wochenschr 1986; 116: 11-8.

NLM04 US National Library of Medicine (NLM), ed. Bromine. In: The Hazardous Substances Data Bank (HSDB) (last revision data bromine file: November 2002; last review date: May 1999); http://toxnet.nlm.nih.gov.

Per94 Perry WG, Smith FA, Kent MB. Bromine. In: Patty's industrial hygiene and toxicology, fourth ed. Clayton GD, Clayton FE, eds. New York: John Wiley & Sons, 1994: 4505-8.

Pot92 Potashnik G, Carel R, Belmaker I, et al. Spermatogenesis and reproductive performance following human accidental exposure to bromine vapor. Reprod Toxicol 1992; 6: 171-4.

Rau83 Rauws AG. Pharmacokinetics of bromide ion - an overview. Food Chem Toxicol 1983; 21: 379-82.

Rup67 Rupp H, Henschler D. Wirkungen geringer Chlor- und Bromkonzentrationen auf den Menschen. Int Arch Gewerbepathol Gewerbehyg 1967; 23: 79-90.

Rut86 Ruth JH. Odor thresholds and irritation levels of several chemical substances: a review. Am Ind Hyg Assoc J 1986; 47: A142-51.

Sag85 Sagi A, Baruchin AM, Ben-Yakar Y, et al. Burns caused by bromine and some of its compounds. Burns 1985; 11: 343-50.

Sch67 Schlagbauer M, Henschler D. Toxizität von Chlor und Brom bei einmaliger und wiederholter Inhalation. Int Arch Gewerbepathol Gewerbehyg 1967; 23: 91-8.

Sin92 Singer A, Sagi A, Ben Meir P, et al. Chemical burns: our 10-year experience. Burns 1992; 18: 250-2.

Ste83 Stead AH, Moffat AC. A collection of therapeutic, toxic and fatal blood drug concentration in man. Hum Toxicol 1983; 3: 437-64.

Sti88 Sticht G, Käferstein H. Bromine. In: Seiler H, Sigel H, Sigel A, eds. Handbook on toxicity of inorganic compounds. New York, USA: Marcel Dekker, Inc, 1988: 143-54 (Chapter 13).

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: 22 (Ordinance AFS 2000:3).

SZW05 Ministerie van Sociale Zaken en Werkgelegenheid (SZW). Nationale MAC-lijst 2005. The Hague, the Netherlands: Sdu Uitgevers, 2005: 18.

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

Annex

Occupational exposure limits for bromine 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	0.1	0.7	8 h	administrative		SZW05
Germany						
- AGS	0.1	0.66	8 h			TRG04
	0.1	0.66	15 min			
- DFG MAK-Kommission	-[c]	-[c]				DFG05
Great-Britain						
- HSE	0.1	0.66	8 h	OES		HSE02
	0.3	2.0	15 min	STEL		
Sweden	0.1	0.7	8 h			Arb02
	0.3	2	15 min			
Denmark	0.1	0.7	8 h			Swe00
USA						
- ACGIH	0.1	-	8 h	TLV		ACG05
	0.2	-	15 min	STEL		
- OSHA	0.1	0.7	8 h	PEL		ACG04
- NIOSH	0.1	0.7	10 h	REL		ACG04
	0.3	2	15 min	STEL		
European Union						
- SCOEL	0.1	0.7	8 h	IOELV		EC05

[a] S = skin notation; which means 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 animals have yielded insufficient information for the establishment of MAK values.