Bromine

General Information

Key Points

**Fire**
- Non flammable
- Vaporises rapidly at room temperature. Reacts violently with reducing agents, metals, ammonia, alcohols and organic materials causing fire and explosion hazard.
- Emits toxic and corrosive fumes when heated to decomposition.
- In the event of a fire involving bromine, use fine water spray and liquid tight fire kit with breathing apparatus

**Health**
- Toxic by all routes of exposure
- Very toxic and corrosive
- Inhalation may cause irritation of respiratory tract, cough, chest tightness, headache, lack of coordination, confusion and delayed wheeze and fluid accumulation in the lungs
- Ingestion causes immediate burning of the mouth and throat, drooling, difficulty swallowing, abdominal pain and heart and circulation problems
- Skin exposure may cause burns
- Eye exposure may result in irritation, tearing, pain, involuntary muscle contraction around the eyes and sensitivity to light

**Environment**
- Dangerous for the environment
- Inform Environment Agency of substantial incidents

Prepared by the Toxicology Department
CRCE, PHE
2009
Version 1
Background

Bromine is found naturally occurring in the earth’s crust and seawater, principally in the form of inorganic bromides. The three major producers of bromine are the United States of America (USA), Israel and the United Kingdom (UK).

Bromine is used in the production of fire retardants, water sanitiser and in agriculture as insecticides. Bromine was used industrially to make compounds such as antiknocking agents for leaded gasoline, but due to environmental considerations this has been phased out. Other uses include fumigants, dyes, agents for photography, bleaching silks and fibres, in brominated vegetable oil, as emulsifiers in soft drinks and in chemical warfare agents.

Skin exposure to bromine will most likely result in local effects, such as blister formation, skin discolouration and slow healing ulcers. Eye exposure to low and high levels of bromine may produce eye irritation and sensitivity to light, respectively.

Exposure may also occur through ingestion of food contaminated with bromine. Seafood has relatively high levels of bromine. Eating food that has been fumigated with bromine may also be a source of oral exposure to bromine through food. Ingestion of pure bromine is likely to result in burns to the mouth, throat and stomach followed by severe stomach irritation. Prolonged exposure may result in bromine being stored in the body and damage to the brain may be observed if levels reach sufficient levels, possibly resulting in coma.

Exposure to bromine is usually as a result of accidental spills or leaks during transportation or manufacturing. Workers producing or using bromine are the most at risk of exposure to bromine, although safe levels of exposure are enforced to protect workers. Such levels are below those that are thought to cause harmful effects.

Exposure to bromine may occur by breathing it in or by skin or eye contact. If exposed to bromine, the harmful effects largely depend on the way people are exposed. Breathing air with levels of bromine can cause shortness of breath, coughing, choking and wheezing, which may lead to death in severe cases.
Frequently Asked Questions

What is bromine?
Bromine is found naturally occurring in the earth's crust and seawater in various chemical forms.

How does bromine get into the environment?
Bromine is a naturally occurring element; however its release into the environment is attributed to human use. Bromine enters the environment principally through its use in industry as a fire retardant, in water sanitation, insecticides, and an antiknocking agent for leaded gasoline. Other uses of bromine include fumigants, dyes, agents for photography, bleaching silks and fibres, in brominated vegetable oil and in chemical warfare gas.

How will I be exposed to bromine?
People can be exposed to bromine by breathing it in, eating food that has been contaminated with bromine, such as seafood or food that has been fumigated with bromine, or absorption through skin or the eyes. Usually exposure to bromine occurs as a result of accidental spill or leak during transportation or manufacturing.

If there is bromine in the environment will I have any adverse health effects?
The presence of bromine in the environment does not always lead to exposure. Clearly, in order for it to cause any adverse health effects you must come into contact with it. You may be exposed by breathing, eating, or drinking the substance or by skin contact. Following exposure to any chemical, the adverse health effects you may encounter depend on several factors, including the amount to which you are exposed (dose), the way you are exposed, the duration of exposure, the form of the chemical and if you were exposed to any other chemicals.

Breathing high levels of bromine can damage the lungs, which may lead to death in severe cases. The immediate effects of ingestion of pure liquid bromine are burns to the mouth, throat and stomach. This may be followed by severe stomach irritation. Prolonged exposure results in storage of bromine in the body and when sufficient levels are reached damage to the brain occurs, possibly resulting in coma. Skin exposure is likely to result in blister formation, skin discoloration and long-term exposure may result in slow healing ulcers. Eye exposure to bromine may result in eye irritation and photophobia.

Can bromine cause cancer?
There is no evidence to suggest that exposure to bromine would cause cancer in humans.

Does bromine affect children or damage the unborn child?
Children will be affected by bromine in the same way as adults. Infants may be exposed to bromine through the placenta.

What should I do if I am exposed to bromine?
It is very unlikely that the general population will be exposed to a level of bromine high enough to cause adverse health effects.
Bromine

Incident management

Key Points

Fire
- Non flammable
- Vaporizes rapidly at room temperature. Reacts violently with reducing agents, metals, ammonia, alcohols and organic materials causing fire and explosion hazard.
- Emits toxic and corrosive fumes when heated to decomposition.
- In the event of a fire involving bromine, use fine water spray and liquid tight fire kit with breathing apparatus.

Health
- Toxic by all routes of exposure
- Inhalation may cause irritation of respiratory tract irritation, cough, chest tightness, wheeze, dyspnoea, tachycardia, headache, confusion, and pulmonary oedema.
- Ingestion causes immediate burning of the mouth and throat and stomach followed by abdominal pain, vomiting, haematemesis and dyspnoea.
- Dermal exposure can cause burns, deep ulcers and scars. Burns may initially cause no pain or visible effects and may develop 1 to 5 days after exposure.
- Ocular exposure to the vapour or liquid can cause severe burns to the eye. Lower concentrations cause inflammation of the eyelids, lacrimation, conjunctivitis and irritation.

Environment
- Acute hazard to the aquatic environment
- Inform Environment Agency of substantial incidents

Prepared by the Toxicology Department
CRCE, PHE
02/2013
Version 2
Hazard Identification

*Standard (UK) Dangerous Goods Emergency Action Codes*<sup>a</sup>

<table>
<thead>
<tr>
<th>UN</th>
<th>1744</th>
<th>Bromine or bromine solution</th>
</tr>
</thead>
<tbody>
<tr>
<td>EAC</td>
<td>2XE</td>
<td>Use fine water spray. Wear liquid-tight chemical protective clothing in combination with breathing apparatus*. Spillages and decontamination run-off should be prevented from entering drains and watercourses. There may be a public safety hazard outside the immediate area of the incident**.</td>
</tr>
<tr>
<td>APP</td>
<td>B</td>
<td>Gas-tight chemical protective suit with breathing apparatus.</td>
</tr>
</tbody>
</table>

### Hazards

<table>
<thead>
<tr>
<th>Class</th>
<th>8</th>
<th>Corrosive substances</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subrisks</td>
<td>6.1</td>
<td>Toxic substances</td>
</tr>
</tbody>
</table>

| HIN   | 886 | Highly corrosive substance, toxic |

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UN – United Nations number; EAC – Emergency Action Code; APP – Additional Personal Protection; HIN - Hazard Identification Number

*Liquid-tight chemical protective clothing (BS 8428) in combination with self-contained open circuit positive pressure compressed air breathing apparatus (BS EN 137).** People should stay indoors with windows and doors closed, ignition sources should be eliminated and ventilation stopped. Non-essential personnel should move at least 250 m away from the incident.

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### Chemical Hazard Information and Packaging for Supply Classification\(^{(a)}\)

<table>
<thead>
<tr>
<th>Classification</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>T+</td>
<td>Very toxic</td>
</tr>
<tr>
<td>C</td>
<td>Corrosive</td>
</tr>
<tr>
<td>N</td>
<td>Dangerous for the environment</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Risk phrases</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>R26</td>
<td>Very toxic by inhalation</td>
</tr>
<tr>
<td>R35</td>
<td>Causes severe burns</td>
</tr>
<tr>
<td>R50</td>
<td>Very toxic to aquatic organisms</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Safety phrases</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>S1/2</td>
<td>Keep locked up and out of the reach of children</td>
</tr>
<tr>
<td>S7/9</td>
<td>Keep container tightly closed and in a well-ventilated place</td>
</tr>
<tr>
<td>S26</td>
<td>In case of contact with eyes, rinse immediately with plenty of water and seek medical advice</td>
</tr>
<tr>
<td>S45</td>
<td>In case of accident or if you feel unwell seek medical advice immediately (show the label where possible)</td>
</tr>
<tr>
<td>S61</td>
<td>Avoid release to the environment. Refer to special instructions/safety data sheet</td>
</tr>
</tbody>
</table>

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### Globally Harmonised System of Classification and Labelling of Chemicals (GHS)\(^{(a)}\)*

<table>
<thead>
<tr>
<th>Hazard Class and Category</th>
<th>Hazard Statement</th>
<th>Signal Words</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute Tox. 2</td>
<td>Acute toxicity (inhalation), category 2</td>
<td>DANGER</td>
</tr>
<tr>
<td>Skin Corr. 1A</td>
<td>Skin corrosive, category 1A</td>
<td></td>
</tr>
<tr>
<td>Aquatic Acute 1</td>
<td>Acute hazard to the aquatic environment, category 1</td>
<td></td>
</tr>
<tr>
<td>H330</td>
<td>Fatal if inhaled</td>
<td></td>
</tr>
<tr>
<td>H314</td>
<td>Causes severe skin burns and eye damage.</td>
<td></td>
</tr>
<tr>
<td>H400</td>
<td>Very toxic to aquatic life.</td>
<td></td>
</tr>
</tbody>
</table>

* * Implemented in the EU on 20 January 2009.

## Physicochemical Properties

<table>
<thead>
<tr>
<th>Property</th>
<th>Value/Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAS number</td>
<td>7726-95-6</td>
</tr>
<tr>
<td>Molecular weight</td>
<td>159.82</td>
</tr>
<tr>
<td>Empirical formula</td>
<td>Br₂</td>
</tr>
<tr>
<td>Common synonyms</td>
<td>-</td>
</tr>
<tr>
<td>State at room temperature</td>
<td>Dark red-brown fuming liquid</td>
</tr>
<tr>
<td>Volatility</td>
<td>Vapour pressure = 175 mm Hg (at 21 °C)</td>
</tr>
<tr>
<td>Specific gravity</td>
<td>5.51 (air = 1)</td>
</tr>
<tr>
<td>Flammability</td>
<td>Non-flammable. Bromine itself does not burn but may decompose upon heating to produce corrosive and/or toxic fumes. Containers may explode when heated.</td>
</tr>
<tr>
<td>Lower explosive limit</td>
<td>Data not available</td>
</tr>
<tr>
<td>Upper explosive limit</td>
<td>Data not available</td>
</tr>
<tr>
<td>Water solubility</td>
<td>Slightly soluble; 3.58 g100 mL⁻¹ water (at 20 °C ). Soluble in common organic solvents</td>
</tr>
<tr>
<td>Reactivity</td>
<td>Bromine vaporizes rapidly at room temperature. Not combustible but enhances combustion of other substances. A strong oxidant and reacts violently with reducing agents, combustible materials, alkali metals, powdered metals, steel, iron, copper, organic materials, aqueous ammonia and phosphorus causing a fire and explosion hazard. It forms a vigorous reaction with methanol and other alcohols. It corrodes iron, steel, stainless steel and copper and attacks some forms of plastic rubber and coatings.</td>
</tr>
<tr>
<td>Reaction or degradation products</td>
<td>Emits highly toxic fumes when heated to decomposition.</td>
</tr>
<tr>
<td>Odour</td>
<td>Choking, irritating odour resembling chlorine</td>
</tr>
<tr>
<td>Structure</td>
<td>Br —— Br</td>
</tr>
</tbody>
</table>

Table references [a,b,c]

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Threshold Toxicity Values

<table>
<thead>
<tr>
<th>ppm</th>
<th>mg m⁻³</th>
<th>SIGNS AND SYMPTOMS</th>
<th>REFERENCES</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.05 – 3.5</td>
<td>0.3 - 23</td>
<td>Odour threshold</td>
<td>a</td>
</tr>
<tr>
<td>&gt; 1.0</td>
<td>&gt; 6.5</td>
<td>Irritation level</td>
<td>a</td>
</tr>
<tr>
<td>40 – 60</td>
<td>260 - 390</td>
<td>Toxic pneumonitis and pulmonary oedema</td>
<td>a</td>
</tr>
<tr>
<td>1000</td>
<td>6500</td>
<td>Fatal within a few minutes</td>
<td>a</td>
</tr>
</tbody>
</table>

Published Emergency Response Guidelines

Emergency Response Planning Guideline (ERPG) Values

<table>
<thead>
<tr>
<th>Listed value (ppm)</th>
<th>Calculated value (mg m⁻³)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ERPG-1*</td>
<td>0.1</td>
</tr>
<tr>
<td>ERPG-2**</td>
<td>0.5</td>
</tr>
<tr>
<td>ERPG-3***</td>
<td>5</td>
</tr>
</tbody>
</table>

* Maximum airborne concentration below which it is believed that nearly all individuals could be exposed for up to 1 hr without experiencing other than mild transient adverse health effects or perceiving a clearly defined, objectionable odour.

** Maximum airborne concentration below which it is believed that nearly all individuals could be exposed for up to 1 hr without experiencing or developing irreversible or other serious health effects or symptoms which could impair an individual's ability to take protective action.

*** Maximum airborne concentration below which it is believed that nearly all individuals could be exposed for up to 1 hr without experiencing or developing life-threatening health effects.

Acute Exposure Guideline Levels (AEGLs)

<table>
<thead>
<tr>
<th>ppm</th>
<th>10 min</th>
<th>30 min</th>
<th>60 min</th>
<th>4 hr</th>
<th>8 hr</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AEGL-1†</td>
<td>0.033</td>
<td>0.033</td>
<td>0.033</td>
<td>0.033</td>
<td>0.033</td>
</tr>
<tr>
<td>AEGL-2††</td>
<td>0.55</td>
<td>0.33</td>
<td>0.24</td>
<td>0.13</td>
<td>0.095</td>
</tr>
<tr>
<td>AEGL-3†††</td>
<td>19</td>
<td>12</td>
<td>8.5</td>
<td>4.5</td>
<td>3.3</td>
</tr>
</tbody>
</table>

† The level of the chemical in air at or above which the general population could experience notable discomfort.

†† The level of the chemical in air at or above which there may be irreversible or other serious long-lasting effects or impaired ability to escape.

††† The level of the chemical in air at or above which the general population could experience life-threatening health effects or death.
### Exposure Standards, Guidelines or Regulations

#### Occupational Standards

<table>
<thead>
<tr>
<th>WEL(^{(a)})</th>
<th>LTEL (8 hour reference period): 0.1 ppm (0.66 mg m(^{-3}))</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>STEL (15 min reference period): 0.2 ppm (1.3 mg m(^{-3}))</td>
</tr>
</tbody>
</table>

#### Public Health Guidelines

<table>
<thead>
<tr>
<th>DRINKING WATER QUALITY GUIDELINE</th>
<th>Data not available</th>
</tr>
</thead>
<tbody>
<tr>
<td>AIR QUALITY GUIDELINE</td>
<td>Data not available</td>
</tr>
<tr>
<td>SOIL GUIDELINE VALUE AND HEALTH CRITERIA VALUES</td>
<td>Data not available</td>
</tr>
</tbody>
</table>

WEL – Workplace exposure limit; LTEL - Long-term exposure limit; STEL – Short-term exposure limit

Health Effects

Major Route of Exposure

- Toxic by all routes of exposure

Immediate Signs or Symptoms of Acute Exposure

- Inhalation may cause irritation of eyes and nose with sore throat, cough, chest tightness and wheeze. It can also cause headache, fever, tachycardia and confusion. Chemical pneumonitis, tachypnoea, dyspnoea and stridor due to laryngeal oedema can occur. Pulmonary oedema with increasing breathlessness, wheeze, hypoxia and cyanosis may take up to 36 hours to develop.
- Ingestion will cause immediate pain with burning in the mouth, throat and stomach, followed by abdominal pain, vomiting, haematemesis and dyspnoea. The lips, tongue and mucous membranes may become stained a brown colour. Pain and oedema may make swallowing difficult. Haemorrhagic or hypovolaemic shock and airway obstruction from laryngeal and/or epiglottic oedema are features of severe cases. Stridor and respiratory complications can develop following aspiration of corrosive materials.
- Skin contact with either liquid or fumes can cause burns which take a long time to heal and which can become deeply ulcerated if not decontaminated. Liquid spilt on the skin causes a cooling sensation on first contact followed by a burning sensation. Burns may initially cause no pain or visible effects and may develop 1 to 5 days after exposure. Burns initially appear as brown discoloration of the skin; subsequently blisters, vesicles and pustules develop. Third degree burns, deep ulcers, and scars can develop, depending on the severity of exposure.
- Skin exposure to lower concentrations of bromine e.g. diluted in swimming pools can cause pruritic, blotchy, measles-like rashes in the face, trunk and extremities lasting up to two weeks.
- Patients dermally exposed to lower concentrations of bromine tend to seek medical attention late. However, they can still sustain severe injury if treatment is delayed.
- Ocular exposure to the vapour or liquid can cause severe burns to the eye. Lower concentrations cause inflammation of the eyelids, lacrimation, conjunctivitis and irritation. High concentrations can cause blepharospasm, palpebral oedema and photophobia.

TOXBASE - http://www.toxbase.org (accessed 01/2013)

* TOXBASE: Bromine, 2011.
Decontamination and First Aid

**Important Notes**

- Ambulance staff, paramedics and emergency department staff treating chemically-contaminated casualties should be equipped with Department of Health approved, gas-tight (Respirex) decontamination suits based on EN466:1995, EN12941:1998 and prEN943-1:2001, where appropriate.
- Decontamination should be performed using local protocols in designated areas such as a decontamination cubicle with adequate ventilation.

**Dermal Exposure**

- Do **NOT** apply neutralising chemicals as heat produced during neutralisation reactions may cause thermal burns and increase injury.
- Contaminated clothing should be removed, double bagged, sealed and stored safely.
- Decontaminate open wounds first and avoid contamination of unexposed skin.
- Any particulate matter adherent to skin should be removed and the patient washed with copious amounts of water under low pressure for at least 10 – 15 minutes or until pH of the skin is normal (pH of the skin is 4.5 – 6 although it may be closer to 7 in children, or after irrigation.
- **The earlier the irrigation begins, the greater the benefit.**
- Pay particular attention to mucous membranes, moist areas such as skin folds, fingernails and ears.
- Recheck pH of affected areas after a period of 15-20 minutes and repeat irrigation if abnormal. Burns with strong solutions may require irrigation for several hours or more.
- Once the pH is normal and stabilised, treat as per a thermal injury.
- Burns totalling more than 15% of body surface area in adults (more than 10% in children) will require standard fluid resuscitation as for thermal burns.
- Moderate/severe chemical burns should be reviewed by a burns specialist.
- Other measures as indicated by the patient’s clinical condition

**Ocular Exposure**

- Remove patient from exposure.
- Remove contact lenses if present and immediately irrigate the affected eye thoroughly with water or 0.9% saline for at least 10 – 15 minutes. Continue until the conjunctival sca pH is normal (7.5 – 8.0). Retest after 20 minutes and use further irrigation if necessary.
- Any particles lodged in the conjunctival recesses should be removed.
- Patients with corneal damage and those whose symptoms do not resolve rapidly should be referred for **urgent** ophthalmological assessment.

**Inhalation**

- Maintain a clear airway and ensure adequate ventilation.
- Remove from exposure if appropriate and give oxygen
- All patients with abnormal vital signs, chest pain, respiratory symptoms or hypoxia should have a 12 lead ECG performed.

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TOXBASE - [http://www.toxbase.org](http://www.toxbase.org) (accessed 01/2013)

* TOXBASE: Bromine, 2011

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Incident Management: Page 10 of 11
• If the patient has clinical features of bronchospasm treat conventionally with nebulised bronchodilators and steroids.
• Endotracheal intubation, or rarely, tracheostomy may be required for life-threatening laryngeal oedema.
• Apply other supportive measures as indicated by the patient’s clinical condition.

**Ingestion (a)**

• **MAINTAIN AIRWAY AND ESTABLISH HAEMODYNAMIC STABILITY**
• In severely affected patients critical care input is essential. Urgent assessment of the airway is required. A supraglottic-epiglottic burn with erythema and oedema is usually a sign that further oedema will occur that may lead to airway obstruction. It is an indication for consideration of early intubation or tracheotomy.
• Do **NOT** attempt gastric lavage.
• Do **NOT** give neutralising chemicals as heat produced during neutralization reactions may increase injury.
• Monitor BP, pulse and oxygen saturation.
• Treat haemorrhagic or hypovolaemic shock by replacing lost fluids and blood intravenously.
• Apply other supportive measures as indicated by the patient’s condition.
Bromine
Toxicological Overview

Key Points

Kinetics and metabolism

- Bromine is rapidly absorbed by the lungs.
- Ingestion of liquid bromine results in rapid and complete absorption from the intestine.
- Bromine is distributed widely into tissues. Majority of bromine is distributed into the extracellular fluid of the body.
- Bromine is not metabolised by the body.

Health effects of acute exposure

- The major route of exposure is by inhalation.
- Acute inhalation exposure to bromine vapour may cause upper respiratory effects, cough, headache, CNS effects and lacrimation.
- Acute oral exposure to bromine results in central nervous system effects.
- Deep partial skin loss and skin discoloration have been reported following acute dermal exposure to bromine.
- Ocular exposure to bromine causes lacrimation, photophobia and blepharospasm.

Health effects of chronic exposure

- Inhalation exposure to bromine vapour causes disturbances of the respiratory, nervous and endocrine systems.
- Chronic oral exposure to liquid bromine results in dermal effects, changes in conditioned reflexes and blood indexes.
Toxicological Overview

**Summary of Health Effects**

Following acute inhalation exposure to bromine in humans, irritation of the eyes, nose and throat and lacrimation of the eyes may occur in a concentration-dependent manner [1]. Exposure to lower doses may result in irritation of the eyes, nose and throat, while exposure to higher doses may result in upper respiratory symptoms, cough and headache. These effects are likely to last for up to 3 days. Some individuals may experience gastrointestinal effects, which may include diarrhoea, nausea, vomiting and abdominal pain [2].

Following acute inhalation exposure to low levels of bromine, irritation of the upper respiratory tract was the most observed effect in experimental animals. At high levels of bromine exposure disturbances to central nervous system (CNS) function was noted [1-3].

Acute oral exposure to high doses of bromine in humans may result in adverse effects in the kidneys [2]. However, in the majority of cases, except for a rise in blood plasma levels, no other effects were observed [4, 5].

Bromine is of low acute oral toxicity in experimental animals [4, 5].

Acute dermal exposure to bromine in humans results in a cooling sensation on the skin followed by deep partial skin loss injuries and skin discolouration [1]. Acute ocular exposure to bromine may result in lacrimation at low doses and, at higher doses photophobia and blepharospasm may occur [6]. Acute dermal exposure to bromine may cause irritation of the skin and, may be highly corrosive and cause severe burns [5].

No data could be located on the human health effects following chronic inhalation, dermal or ocular exposure to bromine.

In experimental animals chronic inhalation exposure to bromine results in disturbances of the respiratory, nervous and endocrine systems [5].

Chronic oral exposure to bromine results in the replacement of 50% of the chloride in plasma, brain, kidneys and liver in experimental rats [4]. Other effects of chronic ingestion of bromine at high doses include decreased body weight gain and decreased thymus weight in males and females, respectively. Increases in thyroid weight were observed in females at high doses. Decreased grooming, motor in-coordination of the hind limbs and effects on the gonadotropic hormones were seen in rats.

Liquid bromine is mutagenic in the Ames test employing *Salmonella typhimurium* [7]. No other data could be located on the genotoxicity of bromine.

Bromine is not listed as a carcinogen by the International Agency for Research on Cancer (IARC) [8].
Kinetics and Metabolism

Bromine is a gas and, therefore, inhalation exposure is the most relevant route of exposure to humans [6]. Other routes of exposure are minimal.

Following inhalation, bromine is absorbed by the lungs and the physical characteristics of bromine determine the depth and site of penetration into the lung tissue and therefore the rate of absorption. Bromine deposition in the lungs is primarily determined by the water solubility of bromine. Bromine is relatively more water soluble than chlorine and thus tends to produce effects on the upper respiratory tract. However, inhalation of high concentrations, e.g. in confined spaces, may also cause marked irritant effects on the lower airways [6].

No data could be located regarding the absorption of bromine vapours via the ocular or dermal routes of exposure.

Following ingestion, bromine liquid is rapidly and completely absorbed from the intestine by passive, paracellular transport. Bromine crosses blood cell membranes in an electrically neutral form [1].

Bromine is distributed widely into various tissues and mainly into the extracellular fluid of the body [1].

There are no data regarding the metabolism of inhaled bromine, however bromine has been known to quickly form bromide in living tissue [6]. Bromide is partitioned in the body similarly to chloride and acts by replacing chloride. Bromide ion is a CNS depressant and its adverse effects are as a result of overdoses, however due to the extreme irritant nature of bromine, the duration of exposure is generally severely limited, reducing any likely body burden of bromide [1].

No data could be located regarding the biological half-life of inhaled bromine. The biological half-life of ingested bromine has been reported to be between 12 and 30 days in humans [6]. The biological half-life in rats is markedly shorter, being approximately 3 days.

Bromine reacts with water resulting in the formation of hydrobromous acid, which slowly decomposes to hydrogen bromide and O$_2$ [7]. The mechanism of action of bromine is by liberation of nascent oxygen or oxygen free radicals from the water present in mucous membranes. It is the nascent oxygen, a potent oxidiser, which is responsible for bromine-induced tissue damage [2, 6].

No data could be located regarding the excretion of bromine from the body.

Sources and Route of Human Exposure

Bromine is a halogen element found naturally occurring in the earth’s crust and seawater in various chemical forms [6].

Exposure to bromine usually occurs as a result of accidental spill or leak during transportation or manufacturing. One of the major routes of exposure in humans is through inhalation of bromine vapour, with other routes of exposure being minimal [6].

Exposure to bromine may occur via inhalation, oral, dermal or ocular routes [6]. Bromine is a gas and therefore, inhalation exposure is the most relevant route to humans.
A small number of the population may also be exposed to bromine through their occupation in industry involved in the manufacture and use of bromine [9].

In the UK, the long-term exposure limit (LTEL) for bromine is 0.66 mg/m$^3$ (8-hour time weighted average (TWA) exposure reference period). The short-term exposure limit (STEL) is 1.3 mg/m$^3$ (15-minute reference period) [10]. In the EU, the Scientific Committee on Occupational Exposure Limits (SCOEL) has set an Indicative Occupational Exposure Limit Value (IOEL) of 0.7 mg/m$^3$ [11].

In the UK, the Expert Panel on Air Quality Standards has recommended that a concentration of bromine gas or mass equivalent to aerosol not exceeding 0.07 mg/m$^3$ (equivalent to 0.01 ppm) over a 1-hour averaging period should protect against irritant and inflammatory responses to the skin, eyes and breathing airways [12].

The Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment (COT) has set a Tolerable Daily Intake (TDI) of 1 mg/kg bw/day [13]. This TDI was based on a short-term toxicity study in rats and a human study [4].
Health Effects of Acute / Single Exposure

**Human Data**

**Inhalation**

Initial irritant symptoms of inhalation of bromine vapour include shortage of breath, cough, choking and wheezing, bronchoconstriction, inflammation of the oesophagus, and laryngeal spasm. Such respiratory distress can lead to hypoxaemia, metabolic acidosis and death [12].

Low concentrations of bromine vapour have also caused inflammation of the eyelids, lacrimation, nosebleeds, a feeling of oppression, dizziness and headache [7]. Inhalation may also cause gastrointestinal effects including diarrhoea, nausea, vomiting and abdominal pain, and dermal effects such as a measles–like eruption on the trunk and extremities and dermatitis [2, 7].

Inhalation of high concentrations of bromine vapour have resulted in brown colouration of the eyes, tongue, and mucous membranes of the mouth as well as catarrh, salivation, coughing, feeling of suffocation, glottis cramps, hoarseness, bronchitis and bronchial asthma [7].

A worker was exposed to bromine vapour (unknown concentration) during an industrial incident. Bromine burns to 20% of the body, extensive pulmonary and tracheal damage, and effects on the kidneys and liver were found at autopsy. In a separate incident, several workers were exposed to bromine vapour (unknown concentration) and developed bronchopneumonia, one developed blepharospasm, and the remainder developed laryngitis. One worker died as a result of circulatory failure associated with bronchopneumonia [7].

Table 1 – Calculated LC$_{50}$S for humans exposed to bromine vapour [7].

<table>
<thead>
<tr>
<th>Population</th>
<th>10-minute LC$_{50}$</th>
<th>30-minute LC$_{50}$</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>mg/m$^3$</td>
<td>ppm</td>
</tr>
<tr>
<td>Regular</td>
<td>2124</td>
<td>325</td>
</tr>
<tr>
<td>Vulnerable</td>
<td>850</td>
<td>130</td>
</tr>
<tr>
<td>Average (regular + vulnerable)</td>
<td>1359</td>
<td>208</td>
</tr>
</tbody>
</table>

A group of healthy volunteers were exposed to bromine concentrations of 0.07-6.7 mg/m$^3$ (0.01-1.0 ppm) for 0.5 h. A concentration-dependent increase in the number affected and severity of irritation was observed in the subjects. Bromine caused irritation of the eyes, nose and throat at a concentration of 1.3 mg/m$^3$ (0.2 ppm), while levels of 3.3 mg/m$^3$ (0.5 ppm) and above were not tolerable. The most common symptoms of exposure to bromine at concentrations of 1.3-3.3 mg/m$^3$ (0.2-0.5 ppm) for 4 hours were upper respiratory symptoms, cough and headache, with symptoms lasting for up to 3 days in some individuals [1, 12].

Exposure to high levels of bromine vapour (actual concentration unknown) generated from a widely used water disinfectant employed in hot tubs was implicated in the development of reactive airways dysfunction syndrome in two exposed patients [1]. No further details were available. Table 2 outlines the health effects in humans following exposure to bromine vapour.
Table 2 - Human health effects of bromine vapour at various concentrations [6].

<table>
<thead>
<tr>
<th>Bromine</th>
<th>Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mg/m³</td>
<td>ppm</td>
</tr>
<tr>
<td>0.04</td>
<td>0.006</td>
</tr>
<tr>
<td>1.3 – 3.3</td>
<td>0.2 – 0.5</td>
</tr>
<tr>
<td>&gt;3.33</td>
<td>&gt;0.5</td>
</tr>
<tr>
<td>261 - 392</td>
<td>40 - 60</td>
</tr>
<tr>
<td>6536</td>
<td>1000</td>
</tr>
</tbody>
</table>

**Ingestion**

Haemorrhagic nephritis, with oliguria or anuria, may develop within 1 to 2 days following ingestion of liquid bromine (concentration not stated) [2]. No further data were available.

**Dermal / ocular exposure**

The initial effect of dermal exposure to bromine is a cooling sensation on the skin. Signs of dermal exposure to bromine are deep partial skin loss injuries and skin discolouration [1].

Exposure to bromine vapour at 3 mg/m³ (0.5 ppm) has been reported to cause a stinging and burning sensation of the conjunctiva [7].

Irritation of the eye, with lacrimation were seen following exposure to low levels of bromine and at higher levels (concentrations not stated) photophobia and blepharospasm were observed [6].

**Delayed effects following an acute exposure**

A feature of dermal exposure to bromine is the delay in the appearance of injury [1]. The delayed effects include upper respiratory effects as well as dermal effects, since bromine vapour is capable of causing skin lesions/blisters.

**Animal and In-Vitro Data**

**Inhalation**

An LC<sub>50</sub> of 1569 mg/m³ (240 ppm) has been reported in mice (strain and sex not specified) exposed to bromine for 2 hours [2].

Rats (strain and sex not specified) were exposed to 0.8-503 mg/m³ (approximately 0.12-77 ppm) bromine vapour for 4 hours. Decreased respiratory frequency was noted at a concentration of 10 mg/m³ (1.5 ppm). Olfactory sharpness was decreased and the number of ‘free cells’ in the upper respiratory pathways was increased. At a concentration of 50
mg/m³ (8 ppm) respiratory, cardiac, vascular, neural and endocrine systems were affected. Spermatogenesis was affected at 100 mg/m³ (15 ppm) [7].

Inhalation LC₅₀s of 2.7 mg/l (equivalent to 17.65 mg/m³ or 2.7 ppm) for an unspecified exposure time has been reported in rats (strain and sex not specified). In mice (strain and sex not specified), LC₅₀s of 4902 mg/m³ (750 ppm) and 1569-4902 mg/m³ (240-750 ppm) for 9 and 270 minutes, respectively, have been reported [5].

Mice exposed via inhalation to bromine concentrations of >147 mg/m³ resulted in mortality. The majority of animals died within the first 4 days and the remainder died between 8 and 10 days when exposed to 1158 mg/m³ (174 ppm). Death was caused by either bronchospasm or oedema of the lungs and by peribronchitis, with abscess formation. Exposure to bromine at 33 and 67 mg/m³ (5 and 10 ppm) for 8 hours/day for 3 days did not cause mortality, but body weights were decreased, thought to be due to irritation of the upper respiratory tract. A Lowest Observed Adverse Effect Level (LOAEL) of 147 mg/m³ (5 ppm) was identified from this study [1].

Cats, rabbits and guinea pigs (strain and sex not specified) exposed to 150 mg/m³ (approximately 23 ppm) bromine for 7 hours provoked a slight irritation of the respiratory tract, while 1176 mg/m³ (180 ppm) caused CNS function disturbances [2, 3]. A LOAEL of 150 mg/m³ was identified.

**Ingestion**

Oral LD₅₀s of 2600-3500 mg/kg bw/day in rats; 3100-7000 mg/kg bw/day in mice, 4160 mg/kg bw/day in rabbits and 5500 mg/kg bw/day in guinea pigs have been reported [4, 5]. Strain and sex of animals were not specified for these studies.

Oral Lowest Lethal Concentrations (LCLo) have been reported as 5.4 mg/kg bw/day for 6.5 hours, 7 mg/kg bw/day for 7 hours and 5.6 mg/kg bw/day for 7 hours in rabbits, cats and guinea pigs, respectively [5].

**Dermal / ocular exposure**

Bromine is a skin irritant in rats, no further information was available. It is also reported to be highly corrosive to the skin and causes severe burns, no further information available [5].
Health Effects of Chronic / Repeated Exposure

**Human Data**

**Inhalation**

No data could be located regarding effects in humans following chronic inhalation exposure to bromine.

**Ingestion**

No data could be located regarding effects in humans following chronic oral exposure to bromine.

**Dermal / ocular exposure**

No data could be located regarding dermal/ocular effects in humans following chronic exposure to bromine.

**Genotoxicity**

No data could be located regarding genotoxicity in humans following chronic exposure to bromine.

**Carcinogenicity**

Bromine is not listed as a carcinogen by the International Agency for Research on Cancer (IARC) [8]. No data are available to assess the carcinogenicity of bromine in humans.

**Reproductive and developmental toxicity**

No data could be located regarding reproductive and developmental effects in humans following exposure to bromine.

**Animal and In-Vitro Data**

**Inhalation**

Rats (strain and sex not specified) were exposed continually to bromine vapour via inhalation for 4 months at a dose of 12.4 mg/m³ (1.9 ppm). Disturbances of the respiratory, nervous and endocrine systems were observed in the animals [5].

Rats, mice and rabbits (strain and sex not specified) were exposed via inhalation to bromine vapour continually for 4 months at doses of 0.13-1.31 mg/m³ (approximately 0.02-0.2 ppm). At the highest dose, animals developed disturbances in respiratory, nervous and endocrine functions. No adverse effects were observed at the lowest dose employed. A no observed adverse effect level (NOAEL) of 0.13 mg/m³ could be identified from this study [5].

**Ingestion**

Rats (strain and sex not specified) were fed liquid bromine at 20 mg/kg bw/day in a 28 day feeding study. Clinical signs of salivation and decreased activity were observed, with
increased red blood cell count, haemoglobin and packed cell volume, increased serum glucose and increased urinary volume with protein also being reported [7].

Rats (strain and sex not specified) received oral 0.01 mg/kg bw continually for 6 months. Changes in conditioned reflexes and several blood indexes were observed in the animals. No further details about this study were available [5].

**Genotoxicity**

Liquid bromine was mutagenic in the Ames test employing *Salmonella typhimurium* strains TA1537 and TA100 in the absence of a metabolic activation system, and with TA1537 in the presence of a metabolic activation system [7].

**Carcinogenicity**

Male and female Fischer 344 rats were fed bromine in their diet continually for 2 years at doses of 0, 80, 200 and 500 mg/kg bw (equivalent to 0, 80, 200 or 500 ppm). The No Observed Effect Level (NOEL) in this study was stated to be 6.77 mg/kg bw/day (200 ppm) in males and the maximum NOEL could not be determined for females [5].

There was no evidence to suggest that bromine was carcinogenic in experimental animals [5].

**Reproductive and developmental toxicity**

No data could be located regarding reproductive and developmental effects of bromine in experimental animals.
References


This document from the PHE Centre for Radiation, Chemical and Environmental Hazards reflects understanding and evaluation of the current scientific evidence as presented and referenced in this document.