

Health and Safety Guide No. 70

# INORGANIC ARSENIC COMPOUNDS OTHER THAN ARSINE HEALTH AND SAFETY GUIDE



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**IPCS**

Health and Safety Guide No. 70

**INORGANIC ARSENIC  
COMPOUNDS  
OTHER THAN ARSINE  
HEALTH AND SAFETY  
GUIDE**

Published by the World Health Organization for the International Programme on Chemical Safety (a collaborative programme of the United Nations Environment Programme, the International Labour Organisation, and the World Health Organization)

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## INTRODUCTION

This Health and Safety Guide is not based on an existing Environmental Health Criteria document, but on critical national reviews. The hazard evaluation in the Health and Safety Guide was made on the basis of carefully selected studies, after scrutiny of the original publications.

In order to assist the peer-review process of the present Health and Safety Guide, a background companion document was prepared by the IPCS and can be obtained from the Director on request; the IPCS does not intend that the background document should be published.

The first three sections of this Health and Safety Guide present essential technical information and the hazard evaluation. Section 4 includes advice on preventive and protective measures and emergency action; health workers should be thoroughly familiar with the medical information to ensure that they can act efficiently in an emergency. The section on regulatory information has been extracted from the legal file of the International Register of Potentially Toxic Chemicals (IRPTC) and from other United Nations sources.

The target readership includes occupational health services, those in ministries, governmental agencies, industry, and trade unions who are involved in the safe use of chemicals and the avoidance of environmental health hazards, and those wanting more information on this topic. An attempt has been made to use only terms that will be familiar to the intended user. However, sections 1 and 2 inevitably contain some technical terms.

Revision of the information in this Guide will take place in due course, and the eventual aim is to use standardized terminology. Comments on any difficulties encountered in using the Guide would be very helpful and should be addressed to:

The Director  
International Programme on Chemical Safety  
World Health Organization  
1211 Geneva 27  
Switzerland

THE INFORMATION IN THIS GUIDE  
SHOULD BE CONSIDERED AS A  
STARTING POINT TO A COMPREHENSIVE  
HEALTH AND SAFETY PROGRAMME



# 1. PRODUCT IDENTITY AND USES

## 1.1 Identity

The chemical names, synonyms, trade names, chemical formulae and CAS numbers of some inorganic arsenic compounds are given in Table 1.

Table 1. Chemical names, synonyms, trade names, and chemical formulae of some inorganic arsenic compounds

Chemical name	Formula	CAS-No.	Synonyms and trade names
Arsenic	As	7440-38-2	Arsen; arsenic black; grey arsenic; metallic arsenic
Arsenic pentoxide <sup>1</sup>	As <sub>2</sub> O <sub>5</sub>	1303-28-2	Arsenic acid; arsenic acid anhydride; arsenic [V] oxide; diarsenic pentoxide; arsenic oxide
Arsenic sulfide	As <sub>2</sub> S <sub>3</sub>	1303-33-9	Arsenic sesquisulfide; arsenic sulfide; arsenic tersulphide; arsenic trisulphide; arsenic yellow; arsenious sulphide; arsenous sulphide; auripigment; C.I. 77086; C.I. pigment yellow; diarsenic trisulphide; orpiment; King's Gold
Arsenic trichloride	AsCl <sub>3</sub>	7784-34-1	Arsenious chloride; arsenic butter; arsenous chloride; caustic arsenic chloride; caustic oil of arsenic; fuming liquid arsenic
Arsenic trioxide <sup>2</sup>	As <sub>2</sub> O <sub>3</sub>	1327-53-3	Arsenic[III]oxide; arsenic sesquioxide; arsenicum album; arsenious acid; arsenious oxide; arsenious trioxide; arsenite; arsenous acid; arsenous anhydride; arsenous oxide; arsenous oxide anhydride; crude arsenic; diarsenic trioxide; arsenic oxide; white arsenic; Arsenolite; Arsodent; Claudelite

## PRODUCT IDENTITY AND USES

Table 1 (continued)

Chemical name	Formula	CAS-No.	Synonyms and trade names
Calcium arsenate	$\text{Ca}_3(\text{AsO}_4)_2$	7778-44-1	Arsenic acid calcium salt; calcium orthoarsenate; tricalcium arsenate; Chipcal; Pencal; Spracal
Cupric acetoarsenite	$\text{C}_4\text{H}_6\text{As}_6\text{Cu}_4\text{O}_{16}$	12002-03-8	(Acetato) trimetaarsenitodicopper; bis(acetato)hexametaarsenitotetracopper; copper acetate arsenite; Paris green, emerald green, French green, mineral green, imperial green
Gallium arsenide	$\text{AsGa}$	1303-00-0	Gallium monoarsenide
Lead arsenate	$\text{PbHAsO}_4$	7784-40-9	Arsenic acid lead salt; acid lead arsenate; acid lead ortho-arsenate; arsenate of lead; arsinette; lead acid arsenate; plumbous arsenate; schultenite; standard lead arsenate; Gypsine; Soprabel; Talbot
Potassium arsenate	$\text{KH}_2\text{AsO}_4$	7784-41-0	Arsenic acid monopotassium salt; monopotassium arsenate; monopotassium dihydrogen arsenate; potassium acid arsenate; potassium arsenate, monobasic; potassium dihydrogen arsenate; potassium hydrogen arsenate; Macquer's salt
Potassium arsenite	$\text{KH}(\text{AsO}_2)_2$	10124-50-2	Arsenous acid, potassium salt; arsenious acid, potassium salt; arsonic acid, potassium salt; potassium metaarsenite; Fowler's solution
Sodium arsenate <sup>3</sup>	$\text{Na}_3\text{AsO}_4$	7631-89-2	Arsenic acid, sodium salt; arsenic acid, sodium ortho-arsenate; sodium metaarsenate

# PRODUCT IDENTITY AND USES

Table 1 (continued)

Chemical name	Formula	CAS-No.	Synonyms and trade names
Sodium arsenite	NaAsO <sub>2</sub>	7784-46-5	Arsenous acid, sodium salt; arsenious acid, sodium salt; sodium metaarsenite; sodanit; prodalumol

<sup>1</sup> The name "arsenic acid" is commonly used for the pentoxide as well as for the various hydrated products.

<sup>2</sup> Sometimes erroneously called "arsenic".

<sup>3</sup> The name "sodium arsenate" is applied both to the disodium and the trisodium salts.

## 1.2 Physical and chemical properties

Arsenic compounds are often unstable, and in many cases are not well-defined materials. For example, the arsenites of the alkali metals are slowly converted in solution to arsenates, by atmospheric oxygen. Arsenic trisulfide reacts vigorously with oxidizing agents, and hydrogen sulfide is generated on contact with strong acids. Arsenic trichloride is highly reactive with water, strong oxidants, ammonia, and some alkalis; the reaction results in the generation of hydrogen chloride and chlorine gas.

Inorganic arsenic compounds may generate highly toxic (and flammable) arsine gas when in contact with acids plus reducing metals (e.g., zinc or iron), or with sodium hydroxide plus aluminium. Some physical properties are summarized in Table 2.

## 1.3 Analysis

The techniques most commonly used for the determination of arsenic involve its transformation into arsine. Subsequent measurements of arsine are carried out using spectrophotometry, flame and electrothermal devices for atomic absorption spectroscopy (AAS), atomic fluorescence (AFS), or atomic emission spectroscopy (AES). The limit of detection for AAS is in the range of 2–20 ng/kg.

## 1.4 Composition

Arsenic is available as a technical grade product, usually with a typical purity of 99%, and as a high-purity grade for semiconductor use, with a purity of at least 99.999%. Arsenic pentoxide is usually available as

## PRODUCT IDENTITY AND USES

Table 2. Some physical properties of inorganic arsenic compounds <sup>a</sup>

Compound	Vapour pressure (mmHg)	Melting point (°C)	Boiling point (°C)	Description	Solubility (g/litre)
Arsenic	1 at 372 °C	817 (28 atm)	615 (sublimes)	grey, crystalline solid with metallic luster	insoluble in water; soluble in HNO <sub>3</sub>
Arsenic pentoxide	-	315 (decomp.)	-	white hygroscopic powder	soluble in cold water (1500); soluble in hot water (767)
Arsenic sulphide	-	300-325	707	yellow-red powder	insoluble in cold water (0.0005); slightly soluble in hot water; soluble in alkali, acids, ethanol
Arsenic trichloride	10 at 23.5 °C	16	130	oily, colourless liquid with acrid smell	decomposed by water; soluble in ethanol, ether, conc. mineral acids
Arsenic trioxide	66.1 at 312 °C	312	465	white, amorphous or crystalline powder	soluble in cold water, (12); hot water (115); alkali and HCl
Calcium arsenate	0	1455	decomp.	colourless, amorphous powder	soluble in water (0.13); soluble in dilute acids
Cupric acetoarsenite	-	n.a.	n.a.	emerald green, crystalline powder	insoluble in water, soluble in acids
Gallium arsenide	-	1238	n.a.	dark grey crystals	insoluble in water

## PRODUCT IDENTITY AND USES

Table 2 (continued)

Compound	Vapour pressure (mmHg)	Melting point (°C)	Boiling point (°C)	Description	Solubility (g/litre)
Lead arsenate	-	720 (decomp.)	decomp.	white, crystalline solid	slightly soluble in hot water; soluble in HNO <sub>3</sub> , caustic alkalis
Potassium arsenate	-	288	-	white, crystalline powder	soluble in cold water, (190); very soluble in hot water; soluble in acid, glycerol, ammonia
Potassium arsenite	-	300 (decomp.)	-	white powder	soluble in water; slightly soluble in ethanol
Sodium arsenate dodecahydrate	-	86	-	white powder	soluble in cold water, (389); ethanol, glycerol
Sodium arsenite	-	n.a.	n.a.	grey-whitish powder	very soluble in water; slightly soluble in ethanol

<sup>a</sup> n.a. = not available.  
decomp. = decomposes.

technical grade. Arsenic sulfide is available in some countries as optical grade (99.999%), as well as a powder (99% active). Arsenic trioxide is marketed as a 95%-pure, crude grade, and as a 99%-pure, refined grade, as well as a 1% solution in about 5% hydrochloric acid.

Commercial calcium arsenate usually contains about 60% calcium arsenate and 10% calcium arsenite. Lime and calcium carbonate are often also present. Lead arsenate is available as acid lead arsenate, which contains 33% arsenic pentoxide. It is sometimes available as a wettable powder (94-98%), as a dust or as a paste.

Potassium and sodium arsenates are generally available in purified as well as reagent grades. Potassium arsenite is marketed by chemical suppliers in a purified grade. It is also available, in some countries, in a 1% aqueous solution known as Fowler's solution.

## PRODUCT IDENTITY AND USES

Sodium arsenite is available commercially in some countries as a pure grade material of 95–98% purity, and in a technical grade of 90–95% purity. It was previously used as powders containing 90 or 94% of the chemical, and as solutions containing various concentrations (a 0.25% solution was available for use as a livestock dip, but most solutions contained 40–44% active ingredient).

### 1.5 Production and uses

World production of arsenic, as arsenic trioxide, has been estimated at around 60 000 tonnes annually; it has been estimated that about one-third is used for wood preservation. Metallic arsenic is currently used in alloys, in combination with lead and copper, in semiconductor devices, and in low-melting point glasses. The most important use of arsenic(III) oxide is in the manufacture of a variety of insecticides, herbicides, fungicides, algicides, sheep dips, and pharmaceutical products (Fowler's solution). Arsenic sulfide is used for dehairing skins in tanning, in the manufacture of pyrotechnics and semiconductors, and in the manufacture of special optical glass.

Calcium and lead arsenates have been used as insecticides, e.g., for the control of boll weevil and gypsy moth, but these arsenates have been largely replaced for this purpose by more effective organic chemicals. However, in many countries, lead arsenate is still used as an insecticide on fruit trees, vegetables, rubber, coffee, cacao, and grapefruit, and as a herbicide for the treatment of turf. Arsenic (as lead or calcium arsenate) is not a normal constituent of the fungicidal Bordeaux mixture (calcium hydroxide and copper sulfate), but it has occasionally been added to widen its action to control some insects. Sodium arsenite has been used in cattle and sheep dips, for debarking trees, and for non-selective weed control. Arsenic-containing wood preservatives are widely used and usually consist of a chromated copper arsenate, applied under pressure.

## 2. SUMMARY AND EVALUATION

### 2.1 Natural occurrence and biological transformations in the environment

As a result of its natural occurrence, humans are universally exposed to arsenic in various forms. The various naturally occurring inorganic and organic arsenic compounds are interlinked through complex biotic and abiotic transformations in the environment.

Inorganic arsenic is found chiefly in the form of its compounds with metals (arsenides), which usually occur in isomorphous mixture with sulfides. High levels of arsenic may also be present in some coals (up to 1500 mg/kg). As a result of the presence of arsenic in the parent rock, arsenic is present naturally in soils in various quantities. Soils overlying sulfide-ore deposits may contain several hundred mg/kg. Arsenic is more strongly bound to soils that have a high clay or high organic matter content and, in these circumstances, is less available to plants. Arsenic is phytotoxic. Plants take up arsenic in proportion to the soil concentration, except at very high soil concentrations. Plants growing on mine or smelter wastes have developed resistance to arsenic toxicity; such plants sometimes have concentrations of arsenic (6000 mg/kg has been found) that may be toxic to animals eating the plants. Arsenic taken up by plants is distributed to all tissues.

Inorganic arsenic can be converted to methylated species in soil by a number of microorganisms under aerobic, as well as anaerobic, conditions. In anoxic parts of the soil layer, arsenic can be immobilized as the sulfide. Arsenic is present in water at a concentration that varies greatly. Extremely high levels of inorganic arsenic have been found in some ground waters. Arsenic in aquatic systems partitions preferentially to the sediment.

A number of microorganisms (e.g., fungi and bacteria in soil, algae in water) have the capacity to methylate inorganic arsenic to the much less acutely toxic compounds methane-arsonic acid and dimethylarsinic acid (cacodylic acid); the latter is readily converted in soil to the volatile methylarsines. Algae (unicellular organisms and seaweeds) actively take up naturally occurring arsenate, and transform inorganic arsenic into a

## SUMMARY AND EVALUATION

variety of organic arsenic compounds. The bioconcentration of arsenic in unicellular algae has been reported to reach up to 3000 times the concentration in the surrounding water. This is a major source of arsenic for higher organisms. Fish and crustaceans accumulate arsenic compounds via the food-chain, in the form of arsenocholine and arsenobetaine. Arsenobetaine is metabolically very stable and is bioaccumulated in the higher trophic levels of the aquatic food-chains. Marine fish and crustaceans commonly contain 2–20 mg arsenic/kg—mainly as organic arsenic—on a wet weight basis, although higher values have been reported (up to 50–100 mg/kg).

### 2.2 Human exposure

Exposure of the general population occurs mainly through arsenic present in food and drinking-water. In some areas, the natural high arsenic content of the drinking-water has caused endemic, chronic arsenic poisoning. A significant portion of the population in other areas is exposed to arsenic levels in drinking-water that lie above the present WHO drinking-water guideline value for arsenic of 50  $\mu\text{g/litre}$ . In humans, the total daily intake of arsenic is greatly influenced by the amount of seafood in the diet, and consumers may reach several thousand  $\mu\text{g}$  of total arsenic per day. However, 85–95% of the arsenic present in marine products is present as the much less toxic, organic arsenic compounds.

In the working environment, if precautions are not taken, high inhalation exposures may be associated with the smelting of non-ferrous sulfide ores, glass manufacturing, wood preservation plants, and the agricultural application of arsenic-containing pesticides.

### 2.3 Effects on organisms in the environment

For most aquatic animal species, the acute toxicity of inorganic arsenic compounds is moderate to low (LC<sub>50</sub> 10–100 mg/litre). However, long-term exposure of immature fish populations to sublethal doses may result in toxic effects at about 4 mg/litre, and exposure of *Daphnia* may lead to slightly impaired reproduction at 0.5 mg/litre. In aquatic ecosystems, algal communities seem to suffer most from exposure to arsenic. The growth of some species of unicellular algae is inhibited at arsenate concentrations as low as 75  $\mu\text{g/litre}$ . Communities of some species of marine macro algae



## SUMMARY AND EVALUATION

(seaweed) may be eliminated at exposures of about 10  $\mu\text{g}/\text{litre}$ . Arsenic is also toxic to terrestrial plants.

### 2.4 Uptake, metabolism, and excretion

Studies on experimental animals, as well as on humans, have shown that over 90% of an ingested dose of dissolved inorganic trivalent or pentavalent arsenic is absorbed from the gastrointestinal tract. In the lungs, water-soluble compounds, such as oxides and arsenites, are rapidly absorbed, whereas there may be considerable retention of arsenic compounds of low solubility. Since inorganic arsenic compounds are considered to be poorly absorbed through the skin (except for corrosive compounds like arsenic trichloride), in the work environment, dermal exposure is usually of less significance than inhalation exposure.

Although high levels of arsenic are maintained for long periods of time in the bone, hair, and nails of exposed individuals, most inorganic arsenic is eliminated at a much higher rate with the urine, mainly as dimethylarsinic acid and methane-arsonic acid. Depending on the administered dose, the half-life in man, after short-term exposure, is in the range of 1-3 days. There is no long-term accumulation of arsenic in soft tissues. Placental transfer of inorganic arsenic has been demonstrated in both experimental animal and human studies.

With increasing arsenic intake, the proportion of arsenic detoxified (methylated) is reduced. Increases in the inorganic arsenic body burden may be expected at daily intakes exceeding about 200  $\mu\text{g}/\text{person}$ . The level at which overloading of the detoxification system occurs may be lowered by a protein-deficient diet. In persons with a low (stable) dietary arsenic intake, the urinary levels may be used to monitor exposure to inorganic arsenic. Since the elimination of arsenic takes place mainly via the kidneys, the concentration of arsenic in the urine is a good indication of exposure to inorganic arsenic.

### 2.5 Effects on experimental animals

In general, the toxic action of arsenic in experimental animals resembles that seen in man. The oral  $\text{LD}_{50}$  of arsenic ranges from 15 to 293  $\text{mg}/\text{kg}$  body weight in rats, and from 11 to 150  $\text{mg}/\text{kg}$  body weight in other experimental animals. Trivalent arsenic is, in general, more toxic than

## SUMMARY AND EVALUATION

pentavalent arsenic. With long-term oral administration, liver lesions, anaemia, and pathological skin changes have been produced in animal models. Studies on experimental animals have demonstrated the development of tolerance towards the acute effects of arsenic compounds.

There has been no consistent demonstration of carcinogenicity in tests with several species of animals, when various chemical forms of arsenic have been administered by the oral route, or to the skin. Teratogenic effects have been induced in pregnant golden hamsters given a high dose by either intravenous or intraperitoneal injection. Available mutagenicity data are equivocal; however, inorganic arsenic compounds have been shown to enhance the potency of other mutagenic agents.

### 2.6 Effects on humans

In man, the smallest recorded fatal dose is in the range of 70-180 mg, but recovery has been reported after much larger doses. Acute symptoms develop within 30 minutes to 2 hours, in the form of a sudden and explosive gastroenteritis. Common symptoms include: nausea, vomiting, abdominal pain, rice-water diarrhoea (which develops into bloody stools), progressive general weakness, and severe dehydration leading to collapse and heart failure. The patient complains of a metallic taste, salivation, hoarse voice, constriction of the throat, and difficulty in swallowing. The skin is pale and moist, and the stomach may be distended. Severely poisoned patients develop shock as a result of increased capillary permeability and loss of fluids and electrolytes. Death usually results from heart failure within 24 hours to 4 days. If the patient survives, hepatic and renal impairment and central nervous and peripheral nervous system damage may become evident. The sequelae of acute poisoning include loss of hair (which grows back with recovery) and brittle fingernails with white horizontal striae ("Mees" lines). Peripheral nervous disturbances, primarily of a sensory type, are frequently encountered in individuals surviving poisoning, and there may also be transient effects on the blood constituents. Irritant and vesicant arsenic compounds, such as arsenic trioxide and arsenic trichloride, have been known to cause severe damage to the respiratory system following inhalation.

Tolerance to arsenic can develop after repeated exposure. The chronic signs of toxicity are insidious and may be difficult to diagnose. They are chiefly related to the skin, gastrointestinal tract, and nervous system, but

## SUMMARY AND EVALUATION

also to the mucous membranes, lungs, and liver. Signs of poisoning are: progressive general weakness, anorexia, nausea, vomiting, stomatitis, colitis, salivation, nose bleed and bleeding gums, conjunctivitis, "Mees" lines, thirst, runny nose, hoarseness, dermatitis, severe skin exfoliation, low-grade fever, and weight loss. The following signs and symptoms might also be observed: garlic odour of breath, motor paralysis, tingling of the skin of extremities, foot and wrist drop, tremors, severe pain and ataxia, and loss of hair. Perforation of the nasal septum may be helpful in the diagnosis of chronic poisoning caused by inhalation of inorganic arsenic. A major symptom of chronic poisoning by arsenic is a symmetrical hyperkeratosis of the palms and soles, as well as melanosis. The skin changes may progress and cover the entire body in multiple forms, and eventually develop into skin cancer (mostly squamous cell epithelioma). In certain populations, a vascular disorder resulting in gangrene of the lower extremities ("Blackfoot disease") has also been observed. An allergic type of contact dermatitis is frequently seen among workers who are exposed to arsenic trioxide. A common finding among arsenic-exposed workers is conjunctivitis and perforation of the nasal septum as a result of irritation of the upper respiratory organs by arsenic dust.

In a number of studies of populations of smelter workers, as well as of pesticide applicators, a clear association between occupational arsenic exposure and an increased incidence of lung cancer has been established. The carcinogenic effect of arsenic taken up by inhalation is potentiated by smoking, and possibly also by other agents present in these occupational environments.

As to the chronic toxic effects caused by oral intake, it appears that the ingestion of 3 mg of inorganic arsenic per day, over a period of a few weeks, may give rise to severe poisoning in infants, and symptoms of toxicity in adults. Chronic arsenic poisoning, with skin lesions, is often accompanied by moderate anaemia and leukopenia. Chronic signs of intoxication may persist for several years after the cessation of exposure.

## 3. CONCLUSIONS AND RECOMMENDATIONS

### 3.1 Conclusions

Exposure of the general population to arsenic compounds occurs predominately via food and drinking-water. Over-exposure in the working environment and during agricultural application occurs mainly through inhalation.

The acute toxicity of inorganic arsenic compounds for man is very high. The smallest, fatal, single dose for a human is in the range of 70–180 mg. With long-term exposure, significant toxic effects can be expected to occur above a daily oral intake of 100–200  $\mu\text{g}$ .

The main chronic effects of inorganic arsenic compounds are damage to the nervous system and hyperkeratosis of the skin, leading to skin cancer.

Inorganic arsenic is a proven human carcinogen after long-term oral intake, as well as after inhalation.

Arsenic is moderately toxic for fish and aquatic invertebrates, but is highly toxic for some algal species. There is field evidence of arsenic affecting aquatic ecosystems.

### 3.2 Recommendations

To minimize the risk to humans, the use of inorganic arsenic compounds as pesticides should be stopped, wherever this is feasible.

Occupational exposure should be kept to a minimum.

Regularly exposed workers should be kept under strict medical surveillance.

## CONCLUSIONS AND RECOMMENDATIONS

A daily oral intake of 2  $\mu\text{g}$  of inorganic arsenic/kg body weight should not be exceeded.

The medicinal use of inorganic arsenic compounds, in particular potassium arsenite (Fowler's solution), is to be strongly discouraged.

## **4. HUMAN HEALTH HAZARDS, PREVENTION AND PROTECTION, EMERGENCY ACTION**

### **4.1 Human health hazards, prevention and protection, first aid**

#### *4.1.1 General population*

Where populations are exposed to naturally occurring arsenic in water, every effort should be made to provide drinking-water of better quality.

#### *4.1.2 Occupationally exposed population*

In order to interrupt the chain of generation/release/transmission of the hazardous agent, the main goal should be primary prevention through interventions in the work environment. These should include such measures as exhaust ventilation, closed systems, enclosure of sources, and good housekeeping practices. Local exhaust ventilation systems must include air cleaning devices, to prevent environmental pollution.

When these measures are not technically feasible, as is the case in the formulation and application of pesticides, or during temporary operations, the use of personal protective clothing and equipment (e.g., disposable dust masks) is recommended.

Respirators must be appropriately selected, used, and maintained. In the case of arsenic compounds in a particulate form, a respirator for particles should be used; however, when arsine is formed accidentally, this type of respirator is completely ineffective. Routine cleaning and maintenance of respirators is essential, including the renewal of filters or cartridges. This requires proper supervision and training of workers, and adequate facilities. The exposure limits adopted should be strictly observed.

Safe work practices are important preventive measures, particularly when the way a task is performed may influence the generation or release of the agent, or may influence exposure. In the case of arsenic compounds, conditions that can lead to the accidental generation of arsine must be spelled out in the work practices, as well as ways of preventing such generation.

## HUMAN HEALTH HAZARDS, PREVENTION AND PROTECTION, EMERGENCY ACTION

The following precautions should be observed during handling and use:

- Avoid contact with the skin and eyes, by using a face-mask and complete protective clothing.
- Do not smoke, drink, or eat in the workplace. Wash the hands and any exposed skin before eating, drinking, or smoking, and after work.

Regular medical supervision of workers occupationally exposed to arsenic is recommended. For employees exposed for 10 years or more, examinations should be repeated every 6 months. Owing to its corrosive properties, skin contact with arsenic trichloride is associated with a high risk of systemic intoxication.

Surveillance programmes should include:

- routine air monitoring, to ensure that air concentrations are below the acceptable standards;
- biological monitoring, by measuring arsenic concentrations in the urine.

Interpretation of results must take into consideration non-occupational values and, therefore, pre-exposure values.

### 4.1.3 *First aid*

Medical attention should be obtained as soon as possible. In the meantime, first aid should be commenced. If material has been spilled on the skin, immediately remove the patient from the source of contamination, remove all contaminated clothing, and wash affected areas with soap and water. If the material is in the eyes, flush with clean water for at least 15 minutes. In case of ingestion, immediate action is imperative: if the patient is conscious, give two glasses of milk (or water), or a beaten egg, induce vomiting and subsequently administer activated charcoal, if possible. Transport the patient to a hospital.

### 4.2 Advice to physicians

Diagnosis is based on history, symptoms, signs, and laboratory investigations, but treatment should start on suspicion of poisoning.

## HUMAN HEALTH HAZARDS, PREVENTION AND PROTECTION, EMERGENCY ACTION

### 4.2.1 *Treatment*

Prognosis is dependent on dose, as well as the time between ingestion of arsenic and first treatment. Gastric aspiration and lavage with warm water followed by sodium sulfate (30 g) is indicated. Keep patient warm and quiet; combat shock and dehydration. Apply artificial respiration, oxygen therapy, whole blood, or fluids as needed. Dimercaprol (BAL) by intramuscular injection has been found to be useful in cases of intoxication. A number of side-effects have been associated with BAL, and the use of this antidote for treatment of chronic intoxications is controversial. D-penicillamine has also been used, although its efficacy has been questioned. A water-soluble analogue of dimercaprol (meso-2,3-dimer-captosuccinic acid or DMSA) has proved to be more effective and less toxic; therefore, it is indicated as first choice chelator, if available. The sodium salt of 2,3-dimercaptopropanesulfonate (Unithiol, Dimaval, DMPS) has also been reported to be effective and to induce less severe side-effects, in comparison with dimercaprol.

### 4.3 Explosion and fire hazards

Finely divided arsenic metal may present an explosion risk. Most industrially important inorganic arsenic compounds are not combustible, but may evolve highly toxic and flammable arsine when heated, or in the presence of other agents (see section 1.2). Arsine may also be produced when arsenic is in contact with acids in the presence of some metals, e.g., zinc or iron, as a consequence of the liberation of hydrogen. Arsenic sulfides are combustible and yield toxic and flammable hydrogen sulfide gas on contact with strong acids.

Do not use water to extinguish fires involving arsenic trichloride; dry chemical or carbon dioxide extinguishers should be used.

Water sprays should only be used to cool undamaged stock; the use of large amounts of water should be avoided because of the possibility of highly toxic run-off from the site. Fire service personnel should be advised that self-contained breathing apparatus and totally encapsulated protective clothing are necessary.



## **HUMAN HEALTH HAZARDS, PREVENTION AND PROTECTION, EMERGENCY ACTION**

### **4.4 Storage and transport**

All products should be stored in secure buildings, kept dry and out of the reach of children and animals, and separated from food and animal feed. Containers should be sound and adequately labelled. Arsenic trichloride is highly corrosive and must not be stored in containers made from steel, galvanized steel, tin, or aluminium. Suitable containers are high density polyethylene bottles, resin-lined metal drums, and glass containers. Do not store near fertilizers, seeds, insecticides, or fungicides.

These products should be transported in a separate compartment to prevent contamination of food or feed.

### **4.5 Spillage**

Keep spectators away from any leakage. Prevent contamination of other goods or cargo, nearby vegetation, and surface waters. Absorb spillage of liquid products with sand or earth, sweep up and place in a separate container. Empty any product remaining in damaged or leaking containers into a clean empty container, which should be suitably labelled. Sweep up any spilt powder with damp sawdust, taking care not to raise a dust cloud. Place in a separate container for subsequent disposal. Contaminated absorbents, used containers, surplus product, etc., should not be incinerated.

### **4.6 Disposal**

Arsenic-containing wastes should not be buried in landfill sites, except in very small quantities interspersed with large volumes of non-hazardous wastes. Do not incinerate and do not discharge to sewers or water courses.

Precipitation and/or solidification are preferred methods but should be carried out by a specialist in toxic waste disposal, because of the persistence and toxicity of arsenic.

## **5. HAZARDS FOR THE ENVIRONMENT AND THEIR PREVENTION**

Inorganic arsenic compounds are moderately toxic for fish and aquatic invertebrates. They are highly toxic for some algae. Low concentrations have been shown to have serious effects on aquatic ecosystems. Biological transformation results in the production of less acutely toxic organic arsenic compounds. Inorganic arsenic in sediments may be released slowly over long periods. Groundwater contamination has proved to be a serious problem in some areas. Although persistent and taken up by plants and other organisms, inorganic arsenic as such is not subject to significant biological transfer through food-chains.

## 6. CURRENT REGULATIONS, GUIDELINES, AND STANDARDS

### 6.1 Previous evaluations by international bodies

The Joint FAO/WHO Expert Committee on Food Additives assigned a provisional tolerable weekly intake (PTWI) of 0.015 mg/kg body weight for inorganic arsenic, but stressed that there is a narrow margin between the PTWI and intakes reported in epidemiological studies to have toxic effects.

Arsenic trioxide has a minimum lethal dose for humans of 2 mg/kg body weight, and is classified in *The WHO recommended classification of pesticides by hazard and guidelines to classification* as an "extremely hazardous pesticide", the oral LD<sub>50</sub> for the rat being 180 mg/kg body weight.

The International Agency for Research on Cancer (IARC) evaluated arsenic and (inorganic) arsenic compounds and concluded that there is sufficient evidence of their carcinogenicity in humans, and limited evidence of their carcinogenicity in experimental animals (Group 1). Because of the inadequacy of the data, and the concern over the potential carcinogenicity of arsenic, no acceptable daily intakes (ADI) for calcium and lead arsenate pesticides have been established by the Joint FAO/WHO Meeting on Pesticide Residues.

A guideline value of 0.05 mg As(total)/litre has been recommended in the *WHO Guidelines for drinking-water quality*. In the *WHO Air quality guidelines for Europe* it was concluded that, because inorganic arsenic is carcinogenic and there is no known safe threshold, no safe level for arsenic can be recommended. At an arsenic air concentration of 1 µg/m<sup>3</sup>, a conservative estimate of lifetime risk is  $3 \times 10^{-3}$ .

### 6.2 Exposure limit values

The information given in this section has been extracted from the most recent International Register of Potentially Toxic Chemicals (IRPTC) legal file. Regulatory decisions about chemicals, taken in a certain country, can only be fully understood in the framework of the legislation of that country.

## CURRENT REGULATIONS, GUIDELINES, AND STANDARDS

The regulations and guidelines of all countries are subject to change and should always be verified with appropriate regulatory authorities before application. Some exposure limit values are given in Table 3.

### 6.3 Specific restrictions

No arsenic-containing pesticides (except for wood preservatives) or pharmaceutical products are permitted in Sweden. Lead arsenate has been prohibited from use as an insecticide in Japan since 1977.

In Germany, emissions of arsenic are controlled. The total concentration of dusts of arsenic, cobalt, nickel, selenium, and tellurium, including their inorganic compounds, may not exceed  $1 \text{ mg/m}^3$  at a mass flow of  $5 \text{ g/hour}$  or more.

In the United States of America, arsenic and compounds are classified as toxic pollutants, for which the US Environmental Protection Agency is required to set effluent limitations and pre-treatment standards for 21 major industries. Permits are required for the discharge of arsenic into USA national waters. Arsenic in outfalls must be reported. Inspection, monitoring, and reporting requirements after the issue of the permit are specified. Even if not required in the permit, discharge of arsenic must be reported if it exceeds the higher of the following levels: (a)  $100 \text{ } \mu\text{g/litre}$ ; (b) five times the maximum concentration reported in the application; (c) the level established by the US EPA.

### 6.4 Transport and labelling

The United Nations Committee of Experts on the Transport of Dangerous Goods has classified arsenic and most inorganic arsenic compounds as "Poisonous (toxic) substances". As such, strict regulations are applied to their transportation. The International Maritime Dangerous Goods code classifies such substances as marine pollutants, which require appropriate warning labels.

Within the European Economic Community, the mandatory labelling of arsenic, which is classified as "Toxic", includes the "skull and crossbones"

## CURRENT REGULATIONS, GUIDELINES, AND STANDARDS

Table 3. Exposure limit values

Medium	Specification	Country/ organization	Exposure limit description	Value (mg/m <sup>3</sup> )
Air	Occupational	Argentina	Maximum permissible limit (MPC) - Time-weighted average	0.5
		Australia	Threshold limit value (TLV) - Time-weighted average (TWA)	0.2
		Belgium	Threshold limit value (TLV) - Time-weighted average (TWA)	0.2
		Canada	Threshold limit value (TLV) - Time weighted average (TWA)	0.2
		Czechoslovakia	Maximum allowable concentration (MAC) - Time-weighted average (TWA)	0.2
		Finland	Maximum permissible limit (MPC) - Time-weighted average (TWA)	0.01
		Germany	Technical guiding concentration (TRK) - 8h - Time-weighted average (TWA)	0.1
		Hungary	Maximum allowable concentration (MAC) - Time-weighted average (TWA)	0.3

## CURRENT REGULATIONS, GUIDELINES, AND STANDARDS

Table 3. Exposure limit values (continued)

Medium	Specification	Country/ organization	Exposure limit description	Value (mg/m <sup>3</sup> )
Air	Occupational	Italy	Threshold limit value (TLV) (carcinogen)	0.25
		Netherlands	Maximum limit (MXL) - Time-weighted average (TWA)	0.5
	Poland	Maximum permissible limit (MPC) - Time-weighted average (TWA)	0.3	
	Romania	Maximum permissible limit (MPC) - Time-weighted average (TWA)	0.2	
	Sweden	Hygienic limit value (HLV) 1 day- Time-weighted average (TWA)	0.03	
	United Kingdom	Permissible exposure limit (PEL) 8h - Time-weighted average (TWA)	0.2	
	USA	Threshold limit value (TLV) - Time-weighted average (TWA)	0.2	
	USSR	Maximum allowable concentration (MAC) - Time-weighted average (TWA)	0.01	


Air	Ambient	Yugoslavia	Maximum allowable concentration (MAC) - Time-weighted average (TWA)	0.01
		Czechoslovakia	Maximum allowable concentration (MAC) - average/day	0.003
			- average/0.5h	0.01
Water	Drinking-	USSR	Maximum allowable concentration (MAC) - average/day	0.003
		Canada	Maximum allowable concentration (MAC)	0.05 mg/litre
		Czechoslovakia	Maximum allowable concentration (MAC)	0.05 mg/litre
		Germany	Maximum permissible limit (MPC)	0.04 mg/litre
		Japan	Maximum permissible limit (MPC)	0.05 mg/litre
		USA	Maximum permissible limit (MPC)	0.05 mg/litre
		USSR	Maximum allowable concentration (MAC)	0.05 mg/litre
		WHO	Guideline level (GL)	0.05 mg/litre
		EEC	Maximum allowable concentration (MAC)	0.05 mg/litre
		Water	Surface	Czechoslovakia
Japan	Maximum limit (MXL)			<0.05 mg/litre
Mexico	Maximum permissible limit (MPC) (depending on water use)			0.05-5.0 mg/litre
USSR	Maximum allowable concentration (MAC)			0.05 mg/litre

## CURRENT REGULATIONS, GUIDELINES, AND STANDARDS

design. The label should read "Toxic by inhalation and if swallowed", as well as:

*Keep locked up, keep out of reach of children. When using do not eat, drink, or smoke. After contact with skin, wash immediately with plenty of .... (to be specified by the manufacturer). If you feel unwell, seek medical advice (show the label where possible).*

Within the European Economic Community legislation, arsenic trioxide is classified as a carcinogen Class 1 (known human carcinogen) requiring the label:

T+	
	
	R: 45-28-34
	S: 53-45

*May cause cancer; very toxic if swallowed; causes burns; avoid exposure, obtain special instructions before use; in case of accident or if you feel unwell, seek medical advice immediately (show label where possible).*



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