

made compulsory at the end of each shift prior to changing to street clothes.

#### BIBLIOGRAPHY

- Goodwin, J. W. 1972. Twenty years of handling TNT in a shell loading plant. *Am. Ind. Hyg. Assoc. J.* 33:41.
- McConnell, W. J., and R. H. Flinn. 1946. Summary of twenty-two trinitrotoluene fatalities in World War II. *J. Ind. Hyg. and Toxicol.* 20:76.
- Morton, A. R., M. V. Ranadive, and J. A. Hathaway. 1976. Biological effects of trinitrotoluene from exposure below the threshold limit value. *Am. Ind. Hyg. Assoc. J.* 37:56.
- Norwood, W. D. 1943. Trinitrotoluene (TNT), its effective removal from the skin by a special liquid soap. *Ind. Med.* 12:206.

## MISCELLANEOUS ORGANIC NITROGEN COMPOUNDS

This group of organic nitrogen compounds includes examples of heterocyclic compounds, hydrazines, substituted amides, an imine, and a nitrosoamine.

Heterocyclic nitrogen compounds contain one or more nitrogen atoms in the ring structure and are widely distributed in nature as well as in industrial use. The ring may be three, five, or six membered, and there may be other hetero atoms in addition to nitrogen.

The hydrazine compounds are characterized by their structure. Amides are derivatives of acids, and some have wide usage as solvents. Imines are highly reactive substances of the general structure, e.g.,  $R_2C=NH$ . Many of them appear to be biological alkylating agents and to have radiomimetic properties. They are somewhat similar in these respects to epoxy compounds, with the nitrogen group in place of an oxygen in a ring structure.

The nitroso group, e.g.,  $-N=O$ , forms another reactive class of nitrogen compounds widely used in synthetic chemical reactions. When combined with a carbon atom, e.g.,  $C-N=O$ , they often show skin irritant or sensitizing properties, and some are methemoglobin formers. When attached to the nitrogen of certain aliphatic amines, however, e.g.,  $(CH_3)_2-N-N=O$  (N-nitroso dimethyl amine), they sometimes become potent experimental animal carcinogens.

### ACRIDINE

#### DESCRIPTION

$C_{13}H_9N$ , acridine, is a colorless or light yellow crystal, very soluble in boiling water.

#### SYNONYMS

Dibenzopyridine, 10-azaanthracene.

## POTENTIAL OCCUPATIONAL EXPOSURES

Acridine and its derivatives are widely used in the production of dyestuffs such as acriflavine, benzoflavine, and chrysaniline, and in the synthesis of pharmaceuticals such as aurinacrine, proflavine, and rivanol.

A partial list of occupations in which exposure may occur includes:

Chemical laboratory workers	Drug makers
Coal tar workers	Dye makers
Disinfectant makers	Organic chemical synthesizers

## PERMISSIBLE EXPOSURE LIMITS

There is no Federal standard for acridine.

## ROUTE OF ENTRY

Inhalation of vapor.

## HARMFUL EFFECTS

*Local*—

Acridine is a severe irritant to the conjunctiva of the eyes, the mucous membranes of the respiratory tract, and the skin. It is a powerful photosensitizer of the skin. Acridine causes sneezing on inhalation.

*Systemic*—

Yellowish discoloration of sclera and conjunctiva may occur. Mutational properties have been ascribed to acridine, but its effect on humans is not known.

## MEDICAL SURVEILLANCE

Evaluate the skin, eyes, and respiratory tract in the course of any placement or periodic examinations.

## SPECIAL TESTS

None commonly used. Can be detected in blood or urine.

## PERSONAL PROTECTIVE METHODS

Prevent skin, eye, or respiratory contact with protective clothing, gloves, goggles, and appropriate dust respirators. In case of spills or splashes, the skin area should be thoroughly washed and the contaminated clothing changed. Clean work clothing should be supplied on a daily basis, and the worker should shower prior to changing to street clothes.

## BIBLIOGRAPHY

- Baldi G. 1953. Patologia professionale de acridina. *Med. Lav.* 44:240.  
Sawicki, E., and C. R. Engel. 1969. Fluorimetric estimation of acridine in air-borne and other particulates. *Mikrochim. Acta.* 1:91.

***N,N-DIMETHYLFORMAMIDE***

## DESCRIPTION

$\text{HCON}(\text{CH}_3)_2$ , dimethylformamide, is a colorless liquid which at

25 C is soluble in water and organic solvents. It has a fishy, unpleasant odor at relatively low concentrations, but the odor has no warning property.

#### SYNONYMS

DMF, the "universal organic solvent," DMFA.

#### POTENTIAL OCCUPATIONAL EXPOSURES

Dimethylformamide has powerful solvent properties for a wide range of organic compounds. Because of dimethyl formamide's physical properties, it has been used when solvents with a slow rate of evaporation are required.

It finds particular usage in the manufacture of polyacrylic fibers, butadiene, purified acetylene, pharmaceuticals, dyes, petroleum products, and other organic chemicals.

A partial list of occupations in which exposure may occur includes:

Acetylene purifiers	Organic chemical synthesizers
Butadiene makers	Petroleum refinery workers
Drug makers	Resin makers
Dye makers	Solvent workers
	Synthetic fiber makers

#### PERMISSIBLE EXPOSURE LIMITS

The Federal standard is 10 ppm (30 mg/m<sup>3</sup>).

#### ROUTES OF ENTRY

Inhalation of vapor, and it is readily absorbed through intact skin.

#### HARMFUL EFFECTS

##### *Local*—

Dimethylformamide exposure may cause dermatitis.

##### *Systemic*—

Inhalation of dimethylformamide or skin contact with this chemical may cause colicky abdominal pain, anorexia, nausea, vomiting, constipation, diarrhea, facial flushing (especially after drinking alcohol), elevated blood pressures, hepatomegaly, and other signs of liver damage. This chemical has produced kidney damage in animals.

#### MEDICAL SURVEILLANCE

Replacement and periodic examinations should be concerned particularly with liver and kidney function and with possible effects on the skin.

#### SPECIAL TESTS

None in common use.

#### PERSONAL PROTECTIVE METHODS

Organic vapor masks or air supplied respirators may be required in elevated vapor concentrations. Percutaneous absorption should be pre-

vented by gloves and other protective clothing. Goggles should be used to prevent eye splashes. In cases of spills or splashes, the wet clothing should be immediately removed and the skin area thoroughly cleaned. Clean clothing should be issued to workers on a daily basis and showers taken before changing to street clothes.

#### BIBLIOGRAPHY

- Clayton, J. W., Jr., J. R. Barnes, D. B. Hood, and G. W. H. Schepers. 1963. The inhalation toxicity of dimethylformamide (DMF). *Am. Ind. Hyg. Assoc. J.* 24:144.
- Martelli, D. 1960. Toxicology of dimethylformamide. *Med. Lav.* 51:123.
- Massmann, W. 1956. Toxicological investigations on dimethylformamide. *Br. J. Ind. Med.* 13:51.
- Potter, H. P. 1973. Dimethylformamide-induced abdominal pain and liver injury. *Arch. Environ. Health* 27:340.

## ETHYLENEIMINE

#### DESCRIPTION

$H_2CNHCH_2$ , ethyleneimine, is a colorless volatile liquid with an ammoniacal odor.

#### SYNONYMS

Azacyclopropane, aziridine, dimethyleneimine, ethyleneimine, vinylamine, azirane, dihydroazirine, EI.

#### POTENTIAL OCCUPATIONAL EXPOSURES

Ethyleneimine is a highly reactive compound and is used in many organic syntheses. The polymerization products, polyethyleneimines, are used as auxiliaries in the paper industry and as flocculation aids in the clarification of effluents. It is also used in the textile industry for increasing wet strength, flameproofing, shrinkproofing, stiffening, and waterproofing.

A partial list of occupations in which exposure may occur includes:

Effluent treaters	Organic chemical synthesizers
Paper makers	Textile makers
Polyethyleneimine makers	

#### PERMISSIBLE EXPOSURE LIMITS

Ethyleneimine was included in the Federal standard for carcinogens; all contact with it should be avoided.

#### ROUTES OF ENTRY

Inhalation and percutaneous absorption.

#### HARMFUL EFFECTS

##### *Local*—

The vapor is strongly irritating to the conjunctiva and cornea, the mucous membranes of the nose, throat, and upper respiratory tract, and the skin. The liquid is a severe irritant and vesicant in humans, and

severe eye burns have followed contact with the cornea. Skin sensitization has occurred.

#### *Systemic—*

Acute exposures in humans have caused nausea, vomiting, headaches, dizziness, and pulmonary edema. In mice acute lethal exposures to vapor produced pulmonary edema, renal damage, and hematuria. Compounds with the aziridine structure have some of the properties of alkylating agents. Ethyleneimine has been reported to induce mutagenic effects in *in vitro* cultures, microorganisms, plants, and animals.

In repeated exposures rodents have developed pancytopenia and gonadal effects. Rats given twice weekly subcutaneous injections of ethyleneimine in oil for about 33 weeks developed sarcoma at the injection site and one case of transitional cell carcinoma in the kidney was observed. Feeding experiments with mice at 13 ppm in the diet for 74 weeks produced hepatomas and pulmonary tumors. These effects have not been reported in humans.

#### MEDICAL SURVEILLANCE

Based partly on animal experimental data, examinations should include history of exposure to other carcinogens, smoking, alcohol, medications, and family history. The skin, eye, lung, liver, and kidney should be evaluated. Sputum or urine cytology may be helpful.

#### SPECIAL TESTS

None in common use. Chromosomal studies have been made, but are probably not useful for routine surveillance.

#### PERSONAL PROTECTIVE METHODS

These are designed to supplement engineering control and prevent all skin or respiratory exposure. Full body protective clothing and gloves should be used. Fullface supplied air respirators with continuous flow or pressure demand type should also be used. Eyes should be protected at all times. On exit from a regulated area employees should shower and change to street clothes, leaving their protective clothing and equipment at the point of exit, to be placed in impervious containers at the end of the work shift for decontamination or disposal.

#### BIBLIOGRAPHY

- Dermer, O. C., and G. E. Ham. 1969. Ethyleneimine and Other Aziridines. Academic Press, New York.
- Innes, J. R. M., B. M. Ulland, M. G. Valerio, L. Petrucelli, L. Fishbein, E. R. Hart, A. J. Pallota, R. R. Bates, H. L. Falk, J. J. Gart, M. Klein, I. Mitchell, and J. Peters. 1969. Bioassay of pesticides and industrial chemical for tumorigenicity in mice: a preliminary note. *J. Natl. Cancer Inst.* 41:1101.
- Walpole, A. L., D. C. Roberts, F. L. Rose, J. A. Hendry, and R. E. Homer. 1954. Cytotoxic agents: IV, the carcinogenic actions of some monofunctional ethyleneimine derivatives. *Br. J. Pharmacol. Chemother.* 9:306.

**HEXAMETHYLENETETRAMINE****DESCRIPTION**

$(\text{CH}_2)_6\text{N}_4$ , hexamethylenetetramine, is an odorless, crystalline solid.

**SYNONYMS**

Methenamine, hexamine, formamine, ammonioformaldehyde.

**POTENTIAL OCCUPATIONAL EXPOSURES**

Hexamethylenetetramine is used as an accelerator in the rubber industry, as a curing agent in thermosetting plastics, as a fuel pellet for camp stoves, and in the manufacture of resins, pharmaceuticals, and explosives.

A partial list of occupations in which exposure may occur includes:

Drug makers	Resin makers
Explosive makers	Rubber makers
Fuel tablet makers	Textile makers
Phenol-formaldehyde resin workers	Urea-formaldehyde resin workers

**PERMISSIBLE EXPOSURE LIMITS**

There is no Federal standard for hexamethylenetetramine.

**ROUTES OF ENTRY**

Ingestion and skin contact.

**HARMFUL EFFECTS***Local—*

Very mild skin irritant.

*Systemic—*

None. Side effects from ingestion are urinary tract irritation, skin rash, and digestive disturbances. Large oral doses can cause severe nephritis which may be fatal.

**MEDICAL SURVEILLANCE**

No specific considerations are necessary.

**SPECIAL TESTS**

None.

**PERSONAL PROTECTIVE METHODS**

If repeated or prolonged skin exposure is likely, gloves or protective clothing may be needed.

**HYDRAZINE and DERIVATIVES****DESCRIPTION**

Hydrazine ( $\text{H}_2\text{N}-\text{NH}_2$ ) is a colorless, oily liquid with an ammoniacal odor. Phenylhydrazine ( $\text{C}_6\text{H}_5\text{NHNH}_2$ ) is an oily, colorless liquid

or a crystalline solid. Dimethylhydrazine, UDMH,  $((\text{CH}_3)_2\text{N}-\text{NH}_2)$  is a hygroscopic mobile liquid. Hydrazine and UDMH are soluble in water and alcohol. Phenylhydrazine is slightly soluble in water.

#### SYNONYMS

Hydrazine: Hydrazine base, diamine.

Phenylhydrazine: Hydrazinobenzene.

Dimethylhydrazine: UDMH, 1,1-dimethylhydrazine, asymmetrical dimethylhydrazine.

#### POTENTIAL OCCUPATIONAL EXPOSURES

Both UDMH and hydrazine are used in liquid rocket fuels. Because of its strong reducing capabilities, hydrazine is used as an intermediate in chemical synthesis and in photography and metallurgy. It is also used in the preparation of anticorrosives, textile agents, and pesticides, and as a scavenging agent for oxygen in boiler water. Hydrazine salts find use as fluxes in soft soldering and aluminum soldering. Phenylhydrazine is very reactive with carbonyl compounds and is a widely used reagent in conjunction with sugars, aldehydes, and ketones, in addition to its use in the synthesis of dyes, pharmaceuticals such as antipyrin, cryogenin, and pyramidone, and other organic chemicals. The hydrochloride salt is used in the treatment of polycythemia vera.

A partial list of occupations in which exposure may occur includes:

Acrylic and vinyl textile dyers	Insecticide makers
Agricultural chemical makers	Jet fuel workers
Anticorrosion additive makers	Oxygen scavenger makers
Antioxidant workers	Photographic developer makers
Boiler operators	Rocket fuel workers
Chemists	Solder flux makers
Drug makers	Water treaters

#### PERMISSIBLE EXPOSURE LIMITS

The Federal standard compounds are:

Hydrazine 1 ppm (1.3 mg/m<sup>3</sup>)

Phenylhydrazine 5 ppm (22 mg/m<sup>3</sup>)

Dimethylhydrazine 0.5 ppm (1 mg/m<sup>3</sup>)

#### ROUTES OF ENTRY

Inhalation and percutaneous absorption.

#### HARMFUL EFFECTS

##### *Local—*

All three compounds have similar toxic local effects due to their irritant properties. The vapor is highly irritating to the eyes, upper respiratory tract, and skin, and causes delayed eye irritation. Severe exposure may produce temporary blindness. The liquid is corrosive, producing penetrating burns and severe dermatitis. Permanent corneal lesions may occur if the liquid is splashed in the eyes. A sensitization dermatitis may be produced.

*Systemic—*

Inhalation of hydrazine may cause dizziness and nausea. In animals hydrazine has caused liver and kidney damage and pulmonary edema. It has also been reported to cause adenocarcinoma of the lung and liver in animals.

**MEDICAL SURVEILLANCE**

Based partly on experimental animal data, placement should include a history of exposure to other carcinogens, smoking, alcohol, medications, and family history. The skin, eye, lungs, liver, kidney, blood, and central nervous system should be evaluated. Sputum or urine cytology may give useful information.

**SPECIAL TESTS**

Hydrazine may be detected in the blood; UDMH has been measured in blood and urine. Some phenylhydrazine metabolites are known. None of these are in common use, however.

**PERSONAL PROTECTIVE METHODS**

Protective clothing, gloves, and goggles should be worn to reduce any skin or eye contact. Fullface supplied air masks and full protective clothing may be required if vapor concentrations are significant. Clean work clothes should be supplied on a daily basis, and workers should shower prior to change to street clothes.

**BIBLIOGRAPHY**

- Jacobson, K. H., J. H. Clem, W. E. Rinehart, and N. Mayes. 1955. The acute toxicity of the vapors of some methylated hydrazine derivatives. *AMA Arch. Ind. Health.* 12:609.
- Krop, S. 1954. Toxicology of hydrazine. *AMA Arch. Ind. Hyg. Occup. Med.* 9:199.
- Shook, B. S., Sr., and O. H. Cowart. 1957. Health hazards associated with unsymmetrical dimethylhydrazine. *Ind. Med. Surg.* 26:333.
- Toth, B. 1973. 1,1-dimethylhydrazine (unsymmetrical) carcinogenesis in mice. Light microscopic and ultrastructural studies on neoplastic blood vessels. *J. Natl. Cancer Inst.* 50:181.
- Von Oettingen, W. F. 1941. The aromatic amino and nitro compounds, their toxicity and potential dangers. *Public Health Bulletin No. 271.* U.S. Public Health Service p. 158.

***N-NITROSODIMETHYLAMINE*****DESCRIPTION**

$(\text{CH}_3)_2\text{NN}=\text{O}$ , *n*-nitrosodimethylamine (DMN), is a yellow liquid of low viscosity, soluble in water, alcohol, and ether.

**SYNONYMS**

Dimethylnitrosamine, DMN.

**POTENTIAL OCCUPATIONAL EXPOSURES**

DMN is used in the manufacture of dimethylhydrazine. It has also been used as an industrial solvent and a nematocide. There are patents

for its use as a solvent in the fiber and plastics industry, as an antioxidant, as a softener for copolymers, as an additive for lubricants, and in condensers to increase the dielectric constant.

A partial list of occupations in which exposure may occur includes:

Dimethylhydrazine makers	Solvent workers
Nematocide makers	

#### PERMISSIBLE EXPOSURE LIMITS

DMN is included in the Federal standard for carcinogens; all contact with it should be avoided.

#### ROUTES OF ENTRY

Inhalation of vapor and possibly percutaneous absorption.

#### HARMFUL EFFECTS

##### *Local—*

The liquid and vapor are not especially irritating to the skin or eyes, and warning properties are poor.

##### *Systemic—*

DMN is a highly toxic substance in most species, including man. Systemic effects are characterized by onset in a few hours of nausea and vomiting, abdominal cramps, and diarrhea. Also headache, fever, weakness, enlargement of the liver, and jaundice may occur. Chronic exposures may lead to liver damage (central necrosis), with jaundice and ascites. There have been a number of reported cases, including severe liver injury in man and one death. Autopsy revealed an acute diffuse centrolobular necrosis. Recovery occurred in other cases.

In rats, guinea pigs, and other experimental animals, DMN is a highly potent carcinogen, producing malignant tumors, primarily of the liver and kidney, but also in the lung. Both ingestion and inhalation routes have produced tumors. These have not been reported in man, but in view of its potency in various other species, the material has been presumed to be carcinogenic in man also.

#### MEDICAL SURVEILLANCE

Based on human experience and on animal studies, preplacement and periodic examinations should include a history of exposure to other carcinogens, alcohol and smoking habits, medications, and family history. Special attention should be given to liver size and function, and to any changes in lung symptoms or X-rays. Renal function should be followed. Sputum and urine cytology may be useful.

#### SPECIAL TESTS

None commonly used.

#### PERSONAL PROTECTIVE METHODS

These are designed to supplement engineering controls and to prevent all contact with the skin, eyes, or respiratory tract. Full body pro-

tective clothing and gloves should be provided and also appropriate type fullface supplied air respirators of continuous flow or pressure demand type. On exit from a regulated area, employees should be required to shower before changing into street clothes, leaving their protective clothing and equipment at the point of exit, to be placed in impervious containers at the end of the work shift for decontamination or disposal.

#### BIBLIOGRAPHY

- Jacobson, K. H., H. G. Wheelwright, Jr., J. H. Clem, and R. N. Shannon. 1955. Studies on the toxicology of n-nitrosodimethylamine vapor. *AMA Arch. Ind. Health* 2:617.
- Le Page, R. N., and G. S. Christie. 1969. Induction of liver tumours in the rabbit by feeding dimethylnitrosoamine. *Br. J. Cancer* 23:125.
- World Health Organization, International Agency for Research on Cancer, 1972. IARC Monographs on the Evaluation of Carcinogenic Risk of Chemicals to Man, Vol. I. International Agency for Research on Cancer, Lyon.

## PYRIDINE

#### DESCRIPTION

$C_5H_5N$ , pyridine, is a colorless liquid with an unpleasant odor. It is both flammable and explosive when exposed to a flame and decomposes on heating to release cyanide fumes. Pyridine is soluble in water, alcohol, and ether. The odor can be detected well below 1 ppm.

#### SYNONYMS

Azine.

#### POTENTIAL OCCUPATIONAL EXPOSURES

Pyridine is used as a solvent in the chemical industry and as a denaturant for ethyl alcohol. It is used in the manufacture of paints, explosives, dyestuffs, rubber, vitamins, sulfa drugs, and disinfectants.

A partial list of occupations in which exposure may occur includes:

Alcohol denaturant makers	Paint makers
Alcohol denaturers	Rubber workers
Drug makers	Resin workers
Dye makers	Solvent workers
Explosive workers	Vitamin makers
Organic chemical synthesizers	

#### PERMISSIBLE EXPOSURE LIMITS

The Federal standard is 5 ppm ( $15 \text{ mg/m}^3$ ).

#### ROUTES OF ENTRY

Inhalation of vapor and percutaneous absorption of liquids.

#### HARMFUL EFFECTS

##### *Local—*

Irritation of the conjunctiva of the eye and cornea and mucous membranes of the upper respiratory tract and skin may occur. It oc-

asionally causes skin sensitization, and photosensitization has been reported.

*Systemic—*

Very high concentrations may cause narcosis. Repeated, intermittent, or continuous low level exposure may lead to transient effects on the central nervous system and gastrointestinal tract. The symptoms include headache, dizziness, insomnia, nervousness, anorexia, nausea, vomiting, and diarrhea. Low back pain and urinary frequency with no changes in urine sediment or liver or renal function and complete recovery have been reported to follow exposures to about 100 ppm. Liver and kidney injury have been reported from its use as an oral medication.

**MEDICAL SURVEILLANCE**

Placement and periodic examinations should consider possible effects on skin, central nervous system, and liver and kidney function.

**SPECIAL TESTS**

None in common use. Metabolites are known and can be determined in blood and urine.

**PERSONAL PROTECTIVE METHODS**

Rubber and plastic gloves should not be relied upon to prevent contact with pyridine as its salts penetrate the material. The odor is detectable at less than 1 ppm but cannot be relied upon as a preventive. In areas of elevated vapor concentration, workers should be supplied with fullface supplied air masks and protective clothing. Clothing that is contaminated by spills or splashes should be immediately changed and discarded and the area of involved skin thoroughly washed. Clean work clothes should be supplied daily with the worker showering after his shift before changing to street clothes.

**BIBLIOGRAPHY**

Baldi, D. 1953. Patologia professional da piridina. Med. Lav. 44:244.

***N,N-DIMETHYLACETAMIDE***

**DESCRIPTION**

$\text{CH}_3\text{CON}(\text{CH}_3)_2$ , dimethylacetamide, is a colorless, nonvolatile liquid.

**SYNONYMS**

Acetic acid dimethylamide, DMA, DMAC, acetyl dimethylamide.

**POTENTIAL OCCUPATIONAL EXPOSURES**

Dimethylacetamide is used commercially as a solvent in various industries.

A partial list of occupations in which exposure may occur includes:  
Solvent workers

PERMISSIBLE EXPOSURE LIMITS

The Federal standard is 10 ppm (35 mg/m<sup>3</sup>), skin.

ROUTES OF ENTRY

Inhalation of vapor and absorption through intact skin.

HARMFUL EFFECTS

*Local*—

None known.

*Systemic*—

Jaundice has been noted in workers exposed chronically to dimethylacetamide vapor although skin absorption may also have occurred. Liver injury consists of cord-cell degeneration, but recovery is usually rapid. Other symptoms from large oral doses as an anticancer drug include depression, lethargy, and visual and auditory hallucinations.

MEDICAL SURVEILLANCE

Preplacement and periodic medical examinations should give special attention to skin, central nervous system, and liver function or disease.

SPECIAL TESTS

None commonly used.

PERSONAL PROTECTIVE METHODS

Organic vapor masks or air supplied respirators may be required in elevated vapor concentrations. Percutaneous absorption should be prevented by gloves and other protective clothing. Goggles should be used to prevent eye splashes. In cases of spills or splashes, the wet clothing should be immediately removed and the involved skin area thoroughly cleaned. Clean clothing should be issued to workers on a daily basis and showers taken before changing to street clothes.

BIBLIOGRAPHY

Horn, H. J. 1961. Toxicology of dimethylacetamide. *Toxicol. Appl. Pharmacol.* 3:12.

## MISCELLANEOUS ORGANIC CHEMICALS

### *BETA-PROPIOLACTONE*

DESCRIPTION

OCH<sub>2</sub>CH<sub>2</sub>CO, beta-propiolactone, is a colorless liquid which slowly hydrolyzes to hydracrylic acid and must be cooled to remain stable.

SYNONYMS

2-Oxetanone, propiolactone, BPL, 3-hydroxy-beta-lactone-propanoic acid.

**POTENTIAL OCCUPATIONAL EXPOSURES**

beta-Propiolactone is used as a chemical intermediate in synthesis of acrylate plastics and as a vapor sterilizing agent, disinfectant, and a viricidal agent.

A partial list of occupations in which exposure may occur includes:

Acrylate plastic makers	Plastic makers
Chemists	Resin makers
Disinfectant workers	Viricidal agent makers

**PERMISSIBLE EXPOSURE LIMITS**

beta-Propiolactone is included in the Federal standards for carcinogens; all contact with it should be avoided.

**ROUTES OF ENTRY**

Inhalation of vapor and percutaneous absorption.

**HARMFUL EFFECTS***Local—*

Repeated or prolonged contact with liquid may cause erythema, vesication of the skin, and, as reported in animals, hair loss and scarring. In rodents, beta-propiolactone has also produced skin papilloma and sarcoma by skin painting, subcutaneous injection, and oral administration. Tumors of the connective tissue are also suspected. Direct eye contact with concentrated liquid may result in permanent corneal opacification. Skin cancer has not been reported in man.

*Systemic—*

The systemic effect of beta-propiolactone in humans is unknown due to lack of reported cases. Acute exposure in animals has caused liver necrosis and renal tubular damage. Death has occurred following rapid development of spasms, dyspnea, convulsions, and collapse at relatively low levels (less than 5 ml/kg.) Beta propiolactone has been implicated as a carcinogen by a number of animal studies which produced a variety of skin tumors, stomach tumors, and hepatoma depending on the route of administration.

**MEDICAL SURVEILLANCE**

Based on its high toxicity and carcinogenic effects in animals, pre-placement and periodic examinations should include a history of exposure to other carcinogens, alcohol and smoking habits, medication and family history. The skin, eye, lung, liver, and kidney should be evaluated. Sputum cytology, may be helpful in evaluating the presence or absence of carcinogenic effects.

**SPECIAL TESTS**

None in common use.

**PERSONAL PROTECTIVE METHODS**

These are designed to supplement engineering controls and to pre-

vent all contact with skin or respiratory tract. Full body protective clothing and gloves should be provided as well as fullface supplied air respirators of continuous flow or pressure demand type. Employees should remove and leave protective clothing and equipment at the point of exit, to be placed in impervious containers at the end of work shift for decontamination or disposal. Showers should be taken before dressing in street clothes.

#### BIBLIOGRAPHY

- Palmes, E. O., L. Orris, and N. Nelson. 1962. Skin irritation and skin tumor production by beta-propiolactone (BPL). *Am. Ind. Hyg. Assoc. J.* 23:257.
- Van Duuren, B. L., L. Langseth, B. M. Goldschmidt, and L. Orris. 1967. Carcinogenicity of epoxides, lactones, and peroxy compounds. VI. Structure and carcinogenic activity. *J. Natl. Cancer Inst.* 39:1217.

### TRICRESYL PHOSPHATES

#### DESCRIPTION

Tricresyl phosphates are available as the ortho-isomer (TOCP), the meta-isomer (TMCP), and the para-isomer (TCP). The ortho-isomer is the most toxic of the three; the meta- and para-isomers are relatively inactive. The commercial product may contain the ortho-isomer as a contaminant unless special precautions are taken during manufacture. Pure tri-para-cresylphosphate is a solid, and ortho- and meta- are colorless, oily, odorless liquids.

#### SYNONYMS

Tritolyl phosphate, TCP.

#### POTENTIAL OCCUPATIONAL EXPOSURES

Tricresyl phosphate is used as a plasticizer for chlorinated rubber, vinyl plastics, polystyrene, polyacrylic, and polymethacrylic esters, as an adjuvant in milling of pigment pastes, as a solvent and as a binder in nitrocellulose and various natural resins, and as an additive to synthetic lubricants and gasoline. It is also used as hydraulic fluid, fire retardant and in the recovery of phenol in coke-oven waste waters.

A partial list of occupations in which exposure may occur includes:

Gasoline additive makers	Polystyrene makers
Gasoline blenders	Polyvinyl chloride makers
Hydraulic fluid workers	Solvent workers
Lead scavenger makers	Surgical instrument sterilizers
Nitrocellulose workers	Waterproofing makers
Plasticizer workers	

#### PERMISSIBLE EXPOSURE LIMITS

The Federal standard for tri-ortho-cresyl phosphate is 0.1 mg/m<sup>3</sup>; there is no standard for the meta- and para-isomers.

#### ROUTES OF ENTRY

Inhalation of ortho-isomer vapor or mist, especially when heated;

ingestion and percutaneous absorption of liquids. The widespread epidemics of poisoning that have occurred have been due to ingested ortho-isomer as a contaminant of foodstuff. There have been relatively few reports of neurological symptoms in workers handling these substances. Experimental human studies with labeled phosphorus derivatives show only 0.4% of the applied dose was absorbed.

#### HARMFUL EFFECTS

##### *Local—*

None reported.

##### *Systemic—*

The major effects from inhaling, swallowing, or absorbing tricresyl phosphate through the skin are on the spinal cord and peripheral nervous system; the poison attacking the anterior horn cells and pyramidal tract as well as the peripheral nerves. Gastrointestinal symptoms on acute exposure (nausea, vomiting, diarrhea, and abdominal pain) are followed by a latent period of 3 to 30 days with the progressive development of muscle soreness and numbness of fingers, calf muscles, and toes, with foot and wrist drop. In chronic intoxication, the g.i. symptoms pass unnoticed, and after a long latent period, flaccid paralysis of limb and leg muscles appear. There are minor sensory changes and no loss of sphincter control.

#### MEDICAL SURVEILLANCE

Preplacement and periodic examinations should include evaluation of spinal cord and neuromuscular function, especially in the extremities, and a history of exposure to other organo-phosphate esters, pesticides, or neurotoxic agents. Periodic cholinesterase determination may relate to exposure, but not necessarily to neuromuscular effect.

#### SPECIAL TESTS

None used except for determination of serum or red cell choline or acetylcholine esterases.

#### PERSONAL PROTECTIVE METHODS

Protective clothing should be worn to prevent skin absorption and, where dust or vapor concentrates, masks should be supplied to employees.

#### BIBLIOGRAPHY

- Hodge, H. C., and J. H. Sterner. 1943. Skin absorption of triorthocresyl phosphate as shown by radioactive phosphorus. *J. Pharmacol. Exp. Ther.* 79:225.
- Hunter, D., K. M. A. Perry, and R. B. Evans. 1944. Toxic polyneuritis arising during the manufacture of tricresyl phosphate. *Br. J. Ind. Med.* 1:227.
- Prineas, J. 1969. Triorthocresyl phosphate myopathy. *Arch. Neurol.* 21:150.
- Tabershaw, I. R., and M. Kleinfeld. 1957. Manufacture of tricresyl phosphate and other alkyl phenyl phosphates: an industrial hygiene study. II. Clinical effects of tricresyl phosphate. *AMA Arch. Ind. Health* 15:541.

**CARBON DISULFIDE****DESCRIPTION**

$CS_2$ , carbon disulfide, is a highly refractive, flammable liquid which in pure form has a sweet odor and in commercial and reagent grades has a foul smell. It can be detected by odor at about 1 ppm but the sense of smell fatigues rapidly and, therefore, odor does not serve as a good warning property. It is slightly soluble in water, but more soluble in organic solvents.

**SYNONYMS**

Carbon bisulfide, dithiocarbonic anhydride.

**POTENTIAL OCCUPATIONAL EXPOSURES**

Carbon disulfide is used in the manufacture of viscose rayon, ammonium salt, carbon tetrachloride, carbanilide, xanthogenates, flotation agents, soil disinfectants, dyes, electronic vacuum tubes, optical glass, paints, enamels, paint removers, varnishes, varnish removers, tallow, textiles, explosives, rocket fuel, putty, preservatives, and rubber cement; as a solvent for phosphorus, sulfur, selenium, bromine, iodine, alkali cellulose, fats, waxes, lacquers, camphor, resins, and cold vulcanized rubber. It is also used in degreasing, chemical analysis, electroplating, grain fumigation, oil extraction, and drycleaning.

A partial list of occupations in which exposure may occur includes:

Ammonium salt makers	Putty makers
Bromine processors	Rayon makers
Carbon tetrachloride makers	Resin makers
Degreasers	Rocket fuel makers
Drycleaners	Rubber cement makers
Electroplaters	Rubber workers
Fat processors	Sulfur processors
Flotation agent makers	Tallow makers
Iodine processors	Textile makers
Oil processors	Vacuum tube makers
Paint workers	Varnish makers
Preservative makers	Wax processors

**PERMISSIBLE EXPOSURE LIMITS**

The Federal standard is 20 ppm (60 mg/m<sup>3</sup>) determined as an 8-hour TWA. The acceptable ceiling concentration is 30 ppm (90 mg/m<sup>3</sup>) with a maximum peak above this for an 8-hour workshift of 100 ppm (300 mg/m<sup>3</sup>) for a maximum duration of 30 minutes.

**ROUTES OF ENTRY**

Inhalation of vapor which may be compounded by percutaneous absorption of liquid or vapor.

**HARMFUL EFFECTS****Local—**

Carbon disulfide vapor in sufficient quantities is severely irritating to

eyes, skin, and mucous membranes. Contact with liquid may cause blistering with second and third degree burns. Skin sensitization may occur. Skin absorption may result in localized degeneration of peripheral nerves which is most often noted in the hands. Respiratory irritation may result in bronchitis and emphysema, though these effects may be overshadowed by systemic effects.

#### *Systemic—*

Intoxication from carbon disulfide is primarily manifested by psychological, neurological, and cardiovascular disorders. Recent evidence indicates that once biochemical alterations are initiated they may remain latent; clinical signs and symptoms then occur following subsequent exposure.

Following repeated carbon disulfide exposure, subjective psychological as well as behavioral disorders have been observed. Acute exposures may result in extreme irritability, uncontrollable anger, suicidal tendencies, and a toxic manic depressive psychosis. Chronic exposures have resulted in insomnia, nightmares, defective memory, and impotency. Less dramatic changes include headache, dizziness, and diminished mental and motor ability, with staggering gait and loss of coordination.

Neurological changes result in polyneuritis. Animal experimentation has revealed pyramidal and extrapyramidal tract lesions and generalized degeneration of the myelin sheaths of peripheral nerves. Chronic exposure signs and symptoms include retrobulbar and optic neuritis, loss of sense of smell, tremors, paresthesias, weakness, and, most typically, loss of lower extremity reflexes.

Atherosclerosis and coronary heart disease have been significantly linked to exposure to carbon disulfide. Atherosclerosis develops most notably in the blood vessels of the brain, glomeruli, and myocardium. Abnormal electroencephalograms and retinal hypertension typically occur before renal involvement is noted. Any of the above three areas may be affected by chronic exposure, but most often only one aspect can be observed. A significant increase in coronary heart disease mortality has been observed in carbon disulfide workers. Studies also reveal higher frequency of angina pectoris and hypertension. Abnormal electrocardiograms may also occur and are also suggestive of carbon disulfide's role in the etiology of coronary disease.

Other specific effects include chronic gastritis with the possible development of gastric and duodenal ulcers; impairment of endocrine activity, specifically adrenal and testicular; abnormal erythrocytic development with hypochromic anemia; and possible liver dysfunction with abnormal serum cholesterol. Also in women, chronic menstrual disorders may occur. These effects usually occur following chronic exposure and are subordinate to the other symptoms.

Recently human experience and animal experimentation have indicated several possible biochemical changes. Carbon disulfide and its metabolites (i.e., dithiocarbamic acids and isothiocyanates) show amino acid interference, cerebral monoamine oxidase inhibition, endocrine dis-

orders, lipoprotein metabolism interference, blood protein, and zinc level abnormalities, and inorganic metabolism interference due to chelating of polyvalent ions. The direct relationship between these biochemical changes and clinical manifestations is only suggestive.

#### MEDICAL SURVEILLANCE

Replacement and periodic medical examinations should be concerned especially with skin, eyes, central and peripheral nervous system, cardiovascular disease, as well as liver and kidney function. Electrocardiograms should be taken.

#### SPECIAL TESTS

CS<sub>2</sub> can be determined in expired air, blood, and urine. The iodine-azide test is most useful although non-specific, and it may indicate other sulfur compounds.

#### PERSONAL PROTECTIVE METHODS

Local exhaust, general ventilation, and personal protective equipment should be utilized. In modern manufacture, CS<sub>2</sub> fumes are generally controlled by closed operations. Where fumes are present in unacceptable concentrations, vapor gas mask with fullface or used air respirators should be used. In all areas where there is likelihood of spill or splash on any skin area, protection should be afforded by protective clothing, goggles, face shields, aprons, and coats.

#### BIBLIOGRAPHY

- Brieger, H. H., and J. J. Teisinger, eds. 1967. International Symposium on Toxicology of Carbon Disulfide, organized by the Sub-Committee for Occupational Health in the Production of Artificial Fibers of the Permanent Commission and International Association of Occupational Health. Prague, September 15th-17th, 1966. Excerpta Medica Foundation, Amsterdam.
- Davidson, M., and M. Feinleib. 1972. Disulfide poisoning: a review. *Am. Heart J.* 83:100.
- Hanninen, H. 1971. Psychological picture of manifest and latent carbon disulfide poisoning. *Br. J. Ind. Med.* 28:374.
- Hernberg, S., T. Partanen, C. H. Nordman, and P. Sumari. 1970. Coronary heart disease among workers exposed to carbon disulfide. *Br. J. Ind. Med.* 27:313.
- Kleinfeld, M., and I. R. Tabershaw. 1955. Carbon disulfide poisoning. Report of two cases. *J. Am. Med. Assoc.* 159:677.
- U.S. Department of Health, Education, and Welfare, Public Health Service, Center for Disease Control, National Institute for Occupational Safety and Health, 1974. Case Report, Occupational Health Case Report - No. 1. *J. Occup. Med.* 16:22.

## DIMETHYL SULFATE

#### DESCRIPTION

(CH<sub>3</sub>)<sub>2</sub>SO<sub>4</sub>, dimethyl sulfate, is an oily, colorless liquid slightly soluble in water, but more soluble in organic solvents.

#### SYNONYMS

Sulfuric acid dimethyl ester.

## POTENTIAL OCCUPATIONAL EXPOSURES

Industrial use of dimethyl sulfate is based upon its methylating properties. It is used in the manufacture of methyl esters, ethers and amines, in dyes, drugs, perfume, phenol derivatives, and other organic chemicals. It is also used as a solvent in the separation of mineral oils.

A partial list of occupations in which exposure may occur includes:

Amine makers	Organic chemical synthesizers
Drug makers	Perfume makers
Dye makers	Phenol derivative makers
Methylation workers	

## PERMISSIBLE EXPOSURE LIMITS

The Federal standard is 1 ppm (5 mg/m<sup>3</sup>).

## ROUTES OF ENTRY

Inhalation of vapor; percutaneous absorption of liquid.

## HARMFUL EFFECTS

*Local—*

Liquid is highly irritating and causes skin vesiculation and analgesia. Lesions are typically slow-healing and may result in scar tissue while analgesia may last several months. Liquid and vapor are irritating to the mucous membranes, and exposure produces lacrimation, rhinitis, edema of the mucosa of the mouth and throat, dysphagia, sore throat, and hoarseness. Irritation of the skin and mucous membranes may be delayed in appearance. Eye irritation may result in conjunctivitis, keratitis, and photophobia. In severe cases corneal opacities, perforation of the nasal septum and permanent or persistent visual disorders have been reported.

*Systemic—*

The toxicity of dimethyl sulfate is based upon its alkylating properties and its hydrolysis to sulfuric acid and methyl alcohol. Acute exposure may cause respiratory dysfunctions such as pulmonary edema, bronchitis, and pneumonitis following a latent period of 6 to 24 hours. Cerebral edema and other central nervous system effects such as drowsiness, temporary blindness, tachycardia or bradycardia may be linked to dimethyl sulfate's effect on nerve endings. Secondary pulmonary effects such as susceptibility to infection, as well as, more pronounced effects in those persons with preexisting respiratory disorders, are also noteworthy. Chronic poisoning occurs only rarely and is usually limited to ocular and respiratory disabilities. It has been reported to be carcinogenic in rats, but this has not been verified in man.

## MEDICAL SURVEILLANCE

Preplacement and periodic medical examinations should give special consideration to the skin, eyes, central nervous system, lung. Chest X-rays should be taken and lung, liver, and kidney functions evaluated.

Sputum and urinary cytology may be useful in detecting the presence or absence of carcinogenic effects.

#### SPECIAL TESTS

None in common use.

#### PERSONAL PROTECTIVE METHODS

These are designed to supplement engineering controls and to reduce skin, eye, or respiratory contact to a negligible level. The liquid and the vapor of dimethyl sulfate are extremely irritating so that the skin, eyes, as well as the respiratory tract should be protected at all times. Protective clothing, gloves, goggles, face shields, aprons, and boots should be used in areas where there is danger of splash or spill. Fullface vapor masks or supplied air respirators may be necessary in areas of vapor build up or leaks. Attention should be given to personal hygiene with a change of work clothes daily and shower before change to street clothes.

#### BIBLIOGRAPHY

- Haswell, R. W. 1960. Dimethyl sulphate poisoning by inhalation. *J. Occup. Med.* 2:454.
- Littler, T. R., and R. B. McConnell. 1955. Dimethyl sulphate poisoning. *Br. J. Ind. Med.* 12:54.
- Thiess, A. M., and P. J. Goldman. 1968. Arbeitsmedizinische fragen im Zusammenhang mit der dimethylsulfat-intoxikation. Beobachtungen aus 30 Jahren in der BASF. *Zentralbl. Arbeitsmed.* 18:195.

## MERCAPTANS

#### DESCRIPTION

Methyl mercaptan:  $\text{CH}_3\text{SH}$ ; ethyl mercaptan:  $\text{CH}_3\text{CH}_2\text{SH}$ ; n-butyl mercaptan:  $\text{CH}_3(\text{CH}_2)_2\text{CH}_2\text{SH}$ ; and perchloromethyl mercaptan:  $\text{CCl}_3\text{-SH}$ .

These compounds are typically flammable liquids except methyl mercaptan which is a gas. Perchloromethyl mercaptan is yellow; the rest are colorless. A strong unpleasant odor is the most characteristic property of mercaptans and may be detected at very low levels, i.e. less than 0.5 ppm. Perchloromethyl mercaptan is insoluble in water, but others are slightly soluble.

#### SYNONYMS

Methyl mercaptans: Methanethiol, mercaptomethane, thiomethyl alcohol, methyl sulfhydrate.

Ethyl mercaptan: Ethanethiol, mercaptoethane, ethyl sulfhydrate, thioethyl alcohol.

n-Butyl mercaptan: 1-Butanethiol, n-butyl thioalcohol, thiobutyl alcohol.

#### POTENTIAL OCCUPATIONAL EXPOSURES

In general, mercaptans find use as intermediates in the manufacture of pesticides, fumigants, dyes, pharmaceuticals, and other chemicals, and as gas odorants, i.e., to serve as a warning property for hazardous odor-

less gases. Particular usages for methyl mercaptan include the synthesis of methionine and the manufacture of fungicides and jet fuels. Ethyl mercaptan is used as an adhesive stabilizer and butyl mercaptan may be used as a solvent.

A partial list of occupations in which exposure may occur includes:

Drug makers	Methionine makers
Dye makers	Organic chemical synthesizers
Fumigant makers	Pesticide makers
Fumigators	Warning agent workers
Jet fuel blenders	

#### PERMISSIBLE EXPOSURE LIMITS

The Federal standard for each mercaptan is:

Methyl mercaptan	10 ppm	20 mg/m <sup>3</sup>
Ethyl mercaptan	10 ppm	25 mg/m <sup>3</sup>
Butyl mercaptan	10 ppm	35 mg/m <sup>3</sup>
Perchloromethyl mercaptan	0.1 ppm	0.8 mg/m <sup>3</sup>

The above standards are determined as TWAs except ethyl and methyl mercaptan which are ceiling values. ACGIH has lowered the TLVs of all but perchloromethyl mercaptan: Methyl mercaptan, 0.5 ppm (1 mg/m<sup>3</sup>); ethyl mercaptan, 0.5 ppm (1.0 mg/m<sup>3</sup>); butyl mercaptan, 0.5 ppm (1.5 mg/m<sup>3</sup>); all TWAs.

#### ROUTE OF ENTRY

Inhalation of gas or vapor.

#### HARMFUL EFFECTS

##### *Local—*

Mercaptans have an intensely disagreeable odor and are irritating to skin, eyes, and mucous membranes of the upper respiratory tract. Liquid may cause contact dermatitis and vapor may cause irritation to nose and throat. Perchloromethyl mercaptan is stronger in its irritant ability than the other mercaptans which cause only slight to moderate irritation.

##### *Systemic—*

Methyl mercaptan acts toxicologically like hydrogen sulfide and may depress the central nervous system resulting in respiratory paralysis and death. Victims who survive severe exposures may suffer from headache, dizziness, staggering gait, nausea, and vomiting. Respiratory tract irritation may lead to pulmonary edema and possibly renal and hepatic damage. The above effects are based primarily on animal experimentation. In a recent case of acute methyl mercaptan exposure, a worker developed acute anemia and methemoglobinemia 24 hours following coma.

## MEDICAL SURVEILLANCE

Preplacement and periodic medical examinations should consider skin, eyes, lung and central nervous system as well as liver and kidney functions. Blood studies may be helpful in following acute intoxication from methyl mercaptan.

## SPECIAL TESTS

None commonly used.

## PERSONAL PROTECTIVE METHODS

In areas where liquid mercaptan is likely to be spilled or splashed on the skin, impervious clothing, gloves, gauntlets, aprons, and boots should be supplied. Otherwise protective methods are as for sulfur dioxide. (See Sulfur Dioxide.)

## BIBLIOGRAPHY

- Blinova, E. A. 1965. O normirovanii konstantratsii veshchestv s sil'nym zapakhom v vozdukhie proizvodstvennykh pom eshchenit. Gig. Sanit. 30:18.
- Fairchild, E. J., H. E. Stokinger. 1958. Toxicologic studies on organic sulfur compounds. 1. Acute toxicity of some aliphatic and aromatic thiols (mercaptans). Am. Ind. Hyg. Assoc. J. 19:171.
- Gobbato, F., and P. M. Terribile. 1968. Toxicologic properties of mercaptans. Folia Medica (Napoli) 51:329.
- Schults, W. T., E. N. Fountain, and E. C. Lynch. 1970. Methanethiol poisoning. J. Am. Med. Assoc. 211:2153.

*TETRAMETHYLTHIURAM DISULFIDE*

## DESCRIPTION

$C_6H_{12}N_2S_4$ , tetramethylthiuram disulfide, is a white or yellow crystal insoluble in water, but soluble in organic solvents.

## SYNONYMS

Thiram, bis-(dimethylthiocarbamyl) disulfide, TMTD, thirad, thiuram.

## POTENTIAL OCCUPATIONAL EXPOSURES

Tetramethylthiuram disulfide is used as a rubber accelerator and vulcanizer; a seed, nut, fruit, and mushroom disinfectant; a bacteriostat for edible oils and fats; and as an ingredient in sun-tan and antiseptic sprays and soaps. It is also used as a fungicide, rodent repellent, wood preservative, and may be used in the blending of lubricant oils.

A partial list of occupations in which exposure may occur includes:

Food disinfectant makers	Rubber makers
Fungicide workers	Soap makers
Lubricating oil blenders	Wood preservative makers
Rat repellent makers	

## PERMISSIBLE EXPOSURE LIMITS

The Federal standard for thiram (tetramethylthiuram disulfide) is 5 mg/m<sup>3</sup>.

## ROUTE OF ENTRY

Inhalation of dust, spray, or mist.

## HARMFUL EFFECTS

### *Local—*

Irritation of mucous membranes conjunctivitis, rhinitis, sneezing, and cough may result from excessive exposures. Skin irritation with erythema and urticaria may also occur. Allergic contact dermatitis has been reported in workers who wore rubber gloves containing tetramethylthiuram disulfide.

### *Systemic—*

Systemic effects have not been reported in the U.S. literature. Bronchitis was mentioned in one European report in workers exposed to thiram or other products during synthesis. Intolerance to alcohol has been observed in workers exposed to thiram, manifested by flushing of face, palpitation, rapid pulse, dizziness, and hypotension. These effects are thought to be due to the blocking of the oxidation of acetaldehyde. It should be noted in this connection that the diethyl homologue of this compound, tetraethylthiuram disulfide, is marketed as the drug "Antabuse" and that severe and disagreeable symptoms ensue immediately in subjects who ingest the smallest amount of ethyl alcohol after they have been "premedicated" with the drug.

## MEDICAL SURVEILLANCE

Replacement and periodic medical examinations should give special attention to history of skin allergy, eye irritation, and significant respiratory, liver, or kidney disease. Workers should be aware of the potentiating action of alcoholic beverages when working with tetramethylthiuram disulfide.

## SPECIAL TESTS

None in common use.

## PERSONAL PROTECTIVE METHODS

Skin and eye protection should be provided by protective clothing, gloves, and goggles. Employees should be encouraged to shower following each shift and to change to clean work clothes at the start of each shift. In areas where dust, spray, or mist are excessive, respiratory protection by dust masks or gas mask respirators with proper canister or supplied air respirators should be provided.

## BIBLIOGRAPHY

- Finulli, M., and M. Magistretti. 1961. Antabuse-like toxic manifestations in workmen employed in the manufacture of a synthetic anticyptogamic: TMTD (tetramethylthiuram disulfide). *Med. Lav.* 52:132.
- Gleason, M. N., R. E. Gosselin, and H. C. Hodge. 1963. *Clinical Toxicology of Commercial Products*, William and Wilkins, Baltimore.

**HALOGENS*****BROMINE/HYDROGEN BROMIDE*****DESCRIPTION**

Br, bromine, is a dark reddish-brown, fuming, volatile liquid with a suffocating odor. Bromine is soluble in water and alcohol. HBr, hydrogen bromide, is a corrosive colorless gas.

**SYNONYMS**

Bromine: none.

Hydrogen bromide: anhydrous hydrobromic acid.

**POTENTIAL OCCUPATIONAL EXPOSURES**

Bromine is primarily used in the manufacture of gasoline antiknock compounds (1,2-dibromoethane). Other uses are for gold extraction, in brominating hydrocarbons, in bleaching fibers and silk, in the manufacture of pharmaceuticals, military gas, dyestuffs, and as an oxidizing agent.

Hydrogen bromide and its aqueous solutions are used in the manufacture of organic and inorganic bromides, as a reducing agent and catalyst in controlled oxidations, in the alkylation of aromatic compounds, and in the isomerization of conjugated diolefins.

A partial list of occupations in which exposure may occur includes:

Drug makers	Organic chemical synthesizers
Dye makers	Petroleum refinery workers
Gasoline additive makers	Photographic chemical makers
Gold extractors	Silk and fiber bleachers

**PERMISSIBLE EXPOSURE LIMITS**

The Federal standards are: bromine 0.1 ppm (0.7 mg/m<sup>3</sup>); and hydrogen bromide 3 ppm (10 mg/m<sup>3</sup>).

**ROUTES OF ENTRY**

Inhalation of vapor or gas. Bromine may be absorbed through the skin.

**HARMFUL EFFECTS*****Local—***

Bromine and hydrogen bromide and its aqueous solutions are extremely irritating to eyes, skin, and mucous membranes of the upper respiratory tract. Severe burns of the eye may result from liquid or concentrated vapor exposure. Liquid bromine splashed on skin may cause vesicles, blisters, and slow healing ulcers. Continued exposure to low concentrations may result in acne-like skin lesions. These are more common in the oral use of sodium bromide as a sedation.

***Systemic—***

Inhalation of bromine is corrosive to the mucous membranes of

the nasopharynx and upper respiratory tract, producing brownish discoloration of tongue and buccal mucosa, a characteristic odor of the breath, edema and spasm of the glottis, asthmatic bronchitis, and possibly pulmonary edema which may be delayed until several hours following exposure. A measles-like skin rash may occur. Exposure to high concentrations of bromine can lead to rapid death due to choking caused by edema of the glottis and pulmonary edema.

Bromine has cumulative properties and is deposited in tissues as bromides, displacing other halogens. Exposures to low concentrations result in cough, copious mucous secretions, nose bleeds, respiratory difficulty, vertigo, and headache. Usually these symptoms are followed by nausea, diarrhea, abdominal distress, hoarseness, and asthmatic type respiratory difficulty.

Other effects from chronic exposure have been reported in Soviet literature, e.g., loss of corneal reflexes, joint pains, vegetative disorders, thyroid dysfunction, and depression of the bone marrow. These have not been noted in the U.S. literature.

Hydrogen bromide (hydrobromic acid) is less toxic than bromine, but is an irritant to the mucous membranes of the upper respiratory tract. Long term exposures can cause chronic nasal and bronchial discharge and dyspepsia. Skin contact may cause burns.

#### MEDICAL SURVEILLANCE

The skin, eyes, and respiratory tract should be given special emphasis during preplacement and periodic examinations. Chest X-rays as well as general health, blood, liver, and kidney function should be considered. Exposure to other irritants or bromine compounds in medications may be important.

#### SPECIAL TESTS

None commonly used. Blood bromides can be determined but are probably not helpful in following exposures.

#### PERSONAL PROTECTIVE METHODS

Respiratory protection with gas masks with acceptable canister or supplied air respirators is essential in areas of excessive vapor concentration. Where aqueous solutions or liquids are used, or high vapor concentrations are present, skin and eyes should be protected against spills or splashes by impervious clothing, gloves, aprons, and face shields or goggles.

#### BIBLIOGRAPHY

- Degenhart, J. J. 1972. Estimation of Br in plasma with a Br selective electrode. *Clin. Chim. Acta.* 38:217.
- Dunlop, M. 1967. Simple colorimetric method for the determination of bromide in urine. *J. Clin. Pathol.* 20:300.
- Edmonds, A. 1966. Toxicity of vaporizing liquids. *Ann. Occup. Hyg.* 9:235.
- Goodwin, J. F. 1971. Colorimetric measurement of serum bromide with a bromate-rosaniline method. *Clin. Chem.* 17:544.
- Gutsche, B., and R. Herrmann. 1970. Flame-photometric determination of bromine in urine. *Analyst.* 95:805.
- Leong, B. K. J., and T. R. Torkelson. 1970. Effects of repeated inhalation of

vinyl bromide in laboratory animals with recommendations for industrial handling. *Am. Ind. Hyg. Assoc. J.* 31:1.

Ohno, S. 1971. Determination of iodine and bromine in biological materials by neutron-activation analysis. *Analyst.* 96:423.

## CHLORINATED LIME

### DESCRIPTION

Chlorinated lime is a white or grayish-white hygroscopic powder with a chlorine odor. It is a relatively unstable chlorine carrier in solid form and is a complex compound of indefinite composition. Chemically, it consists of varying proportions of calcium hypochlorite, calcium chlorite, calcium oxychloride, calcium chloride, free calcium hydroxides, and water. The commercial product generally contains 24-37% available chlorine. On exposure to moisture, chlorine is released.

### SYNONYMS

Chloride of lime, bleaching powder.

### POTENTIAL OCCUPATIONAL EXPOSURES

Chlorinated lime is a bleaching agent, i.e., it has the ability to chemically remove dyes or pigments from materials. It is used in the bleaching of wood pulp, linen, cotton, straw, oils, and soaps, and in laundering, as an oxidizer in calico printing, a chlorinating agent, a disinfectant, particularly for drinking water and sewage, a decontaminant for mustard gas, and as a pesticide for caterpillars.

A partial list of occupations in which exposure may occur includes:

Disinfectant makers	Straw bleachers
Dyers	Textile bleachers
Laundry workers	Textile printers
Oil bleachers	Water treaters
Sewage treaters	Wood pulp bleachers
Soap bleachers	

### PERMISSIBLE EXPOSURE LIMITS

There is no Federal standard for chlorinated lime. (See Chlorine.)

### ROUTES OF ENTRY

Inhalation of dust. Inhalation of vapor and ingestion.

### HARMFUL EFFECTS

#### *Local—*

The toxic effects of chlorinated lime are due to its chlorine content. The powder and its solutions have corrosive action on skin, eyes, and mucous membranes, can produce conjunctivitis, blepharitis, corneal ulceration, gingivitis, contact dermatitis, and may damage the teeth.

#### *Systemic—*

The dust is irritating to the respiratory tract and can produce laryn-

gitis and pulmonary edema. Chlorinated lime is extremely hygroscopic and with the addition of water evolves free chlorine. Inhalation of the vapor is extremely irritating and toxic. (See Chlorine.) Ingestion of chlorinated lime causes severe oral, esophageal, and gastric irritation.

#### MEDICAL SURVEILLANCE

Consider possible effects on skin, teeth, eyes, or respiratory tract. There are no specific diagnostic tests.

#### SPECIAL TESTS

None commonly used.

#### PERSONAL PROTECTIVE METHODS

In dusty areas, the worker should be protected by appropriate respirators. Simple dust masks should not be used since the moisture present in expired air will release the chlorine. Skin effects can be minimized with protective clothing. Most important is the fact that free chlorine is liberated when chlorinated lime comes in contact with water. All precautions should be followed to protect the worker under these circumstances. (See Chlorine.)

## CHLORINE

#### DESCRIPTION

Cl, chlorine, is a greenish-yellow gas with a pungent odor. It is slightly soluble in water and is soluble in alkalis. It is the commonest of the four halogens which are among the most chemically reactive of all the elements.

#### SYNONYMS

None.

#### POTENTIAL OCCUPATIONAL EXPOSURES

Gaseous chlorine is a bleaching agent in the paper and pulp and textile industries for bleaching cellulose for artificial fibers. It is used in the manufacture of chlorinated lime, inorganic and organic compounds such as metallic chlorides, chlorinated solvents, refrigerants, pesticides, and polymers, e.g. synthetic rubber and plastics; it is used as a disinfectant, particularly for water and refuse, and in detinning and dezincing iron.

A partial list of occupations in which exposure may occur includes:

Aerosol propellant makers	Paper bleachers
Bleachers	Pesticide makers
Chlorinated solvent makers	Plastic makers
Disinfectant makers	Rayon makers
Dye makers	Refrigerant makers
Flour bleachers	Silver extractors
Iron workers	Swimming pool maintenance workers
Laundry workers	Tin recovery workers

PERMISSIBLE EXPOSURE LIMITS

The Federal standard is 1 ppm (3 mg/m<sup>3</sup>). NIOSH has recommended a ceiling limit of 0.5 ppm for a 15-minute sampling period.

ROUTE OF ENTRY

Inhalation of gas.

HARMFUL EFFECTS

*Local*—

Chlorine reacts with body moisture to form acids. It is itself extremely irritating to skin, eyes, and mucous membranes, and it may cause corrosion of teeth. Prolonged exposure to low concentrations may produce chloracne.

*Systemic*—

Chlorine in high concentrations acts as an asphyxiant by causing cramps in the muscles of the larynx (choking), swelling of the mucous membranes, nausea, vomiting, anxiety, and syncope. Acute respiratory distress including cough, hemoptysis, chest pain, dyspnea, and cyanosis develop, and later tracheobronchitis, pulmonary edema, and pneumonia may supervene.

MEDICAL SURVEILLANCE

Special emphasis should be given to the skin, eye, teeth, cardiovascular status in placement and periodic examinations. Chest X-rays should be taken and pulmonary function followed.

SPECIAL TESTS

None in common use.

PERSONAL PROTECTIVE METHODS

Whenever there is likelihood of excessive gas levels, workers should use respiratory protection in the form of fullface gas mask with proper canister or supplied air respirator. The skin effects of chlorine can generally be controlled by good personal hygiene practices. Where very high gas concentrations or liquid chlorine may be present, full protective clothing, gloves, and eye protection should be used. Changing work clothes daily and showering following each shift where exposures exist are recommended.

BIBLIOGRAPHY

- Chasis, H., J. A. Zapp, J. H. Bannon, J. L. Whittenburger, J. Helm, J. J. Doheny, and C. M. MacLeod. 1947. Chlorine accident in Brooklyn. *Occup. Med.* 4:152.
- Dixon, W. M., and D. Drew. 1968. Fatal chlorine poisoning. *J. Occup. Med.* 10:249.
- Henefer, D. 1969. *Disease of the Occupations*, 4th Ed. Little, Brown and Co., Boston.
- Joyner, R. E., and E. G. Durel. 1947. Accidental liquid chlorine spill in a rural community. *J. Occup. Med.* 4:152.
- Kaufman, J., and D. Burkons. 1971. Clinical, roentgenologic, and physiologic effects of acute chlorine exposure. *Arch. Environ. Health* 23:29.
- Kramer, C. G. 1967. Chlorine. *J. Occup. Med.* 9:193.

## FLUORINE and COMPOUNDS

### DESCRIPTION

F, elemental fluorine, is a yellow gas. Sulfuric acid reacts with fluorspar producing hydrofluoric acid (HF) which is starting material for synthesis of most fluorine compounds. Fluorine forms fluorides but not fluorates or perfluorates.

### SYNONYMS

Fluorine: none.

Hydrogen fluoride: hydrofluoric acid gas, fluohydric acid gas, anhydrous hydrofluoric acid.

Fluorides: none.

### POTENTIAL OCCUPATIONAL EXPOSURES

Elemental fluorine is used in the conversion of uranium tetrafluoride to uranium hexafluoride, in the synthesis of organic and inorganic fluorine compounds, and as an oxidizer in rocket fuel.

Hydrogen fluoride, its aqueous solution hydrofluoric acid, and its salts are used in production of organic and inorganic fluorine compounds such as fluorides and plastics; as a catalyst, particularly in paraffin alkylation in the petroleum industry; as an insecticide; and to arrest the fermentation in brewing. It is utilized in the fluorination processes, especially in the aluminum industry, in separating uranium isotopes, in cleaning cast iron, copper, and brass, in removing efflorescence from brick and stone, in removing sand from metallic castings, in frosting and etching glass and enamel, in polishing crystal, in decomposing cellulose, in enameling and galvanizing iron, in working silk, in dye and analytical chemistry, and to increase the porosity of ceramics.

Fluorides are used as an electrolyte in aluminum manufacture, a flux in smelting nickel, copper, gold, and silver, as a catalyst for organic reactions, a wood preservative, a fluoridation agent for drinking water, a bleaching agent for cane seats, in pesticides, rodenticides, and as a fermentation inhibitor. They are utilized in the manufacture of steel, iron, glass, ceramics, pottery, enamels, in the coagulation of latex, in coatings for welding rods, and in cleaning graphite, metals, windows, and glassware. Exposure to fluorides may also occur during preparation of fertilizer from phosphate rock by addition of sulfuric acid.

A partial list of occupations in which exposure may occur includes:

Aluminum fluoride makers	Fluorochemical workers
Aluminum makers	Glass etchers
Bleachers	Incandescent lamp frosters
Brass cleaners	Insecticide makers
Casting cleaners	Ore dissolvers
Ceramic workers	Stone cleaners
Copper cleaners	Uranium refiners
Crystal glass polishers	Yeast makers
Fermentation workers	

## PERMISSIBLE EXPOSURE LIMITS

The applicable Federal standards are: fluorine 0.1 ppm (0.2 mg/m<sup>3</sup>), fluoride as dust (2.5 mg/m<sup>3</sup>), hydrogen fluoride 3 ppm, ceiling 5 ppm, and peak 10 ppm for 30 minutes. For hydrogen fluoride NIOSH has recommended 2.5 mg/m<sup>3</sup> (fluoride ion) TWA with a ceiling of 5 mg/m<sup>3</sup> (fluoride ion) for a 15-minute sampling period.

## ROUTES OF ENTRY

Inhalation of gas, mist, dust, or fume; ingestion of dust.

## HARMFUL EFFECTS

*Local—*

Fluorine and some of its compounds are primary irritants of skin, eyes, mucous membranes, and lungs. Thermal or chemical burns may result from contact; the chemical burns cause deep tissue destruction and may not become symptomatic until several hours after contact, depending on dilution. Nosebleeds and sinus trouble may develop on chronic exposure to low concentration of fluoride or fluorine in air. Accidental fluoride burns, even when they involve small body areas (less than 3%), can cause systemic effects of fluoride poisoning by absorption of the fluoride through the skin.

*Systemic—*

Inhalation of excessive concentration of elemental fluorine or of hydrogen fluoride can produce bronchospasm, laryngospasm, and pulmonary edema. Gastrointestinal symptoms may be present. A brief exposure to 25 ppm has caused sore throat and chest pain, irreparable damage to the lungs, and death.

Most cases of acute fluoride intoxication result from ingestion of fluoride compounds. The severity of systemic effects is directly proportional to the irritating properties and the amount of the compound that has been ingested. Gastrointestinal symptoms of nausea, vomiting, diffuse abdominal cramps, and diarrhea can be expected. Large doses produce central nervous system involvement with twitching of muscle groups, tonic and clonic convulsions, and coma.

The systemic effects of prolonged absorption of fluorides from either dusts or vapors have long been a source of some uncertainty. Fluorides are retained preferentially in bone, and excessive intake may result in an osteosclerosis that is recognizable by X-ray. The first signs of changes in density appear in the lumbar spine and pelvis. Usually some ossification of ligaments occurs. Recent investigations suggest that rather severe skeletal fluorosis can exist in workers without any untoward physiological effects, detrimental effects on their general health, or physical impairment.

Fluorides occur in nature and enter the human body through inhalation or ingestion (natural dusts and water). In children, mottling of the dental enamel may occur from increased water concentrations. These exposures are usually minimal and occur over extended periods.

Residential districts which adjoin manufacturing areas can be subjected to continual exposures at minimal levels, or to heavy exposure in the event of accident or plant failure, as in the case of the Meuse Valley disaster.

#### MEDICAL SURVEILLANCE

Preemployment and periodic examinations should consider possible effects on the skin, eyes, teeth, respiratory tract, and kidneys. Chest X-rays and pulmonary function should be followed. Kidney function should be evaluated. If exposures have been heavy and skeletal fluorosis is suspected, pelvic X-rays may be helpful. Intake of fluoride from natural sources in food or water should be known.

#### SPECIAL TESTS

In the case of exposure to fluoride dusts, periodic urinary fluoride excretion levels have been very useful in evaluating industrial exposures and environmental dietary sources.

#### PERSONAL PROTECTIVE METHODS

In areas with excessive gas or dust levels for any type of fluorine, worker protection should be provided. Respiratory protection by dust masks or gas masks with an appropriate canister or supplied air respirator should be provided. Goggles or fullface masks should be used. In areas where there is likelihood of splash or spill, acid resistant clothing including gloves, gauntlets, aprons, boots, and goggles or face shield should be provided to the worker. Personal hygiene should be encouraged, with showering following each shift and before change to street clothes. Work clothes should be changed following each shift, especially in dusty areas. Attention should be given promptly to any burns from fluorine compounds due to absorption of the fluorine at the burn site and the possibility of developing systemic symptoms from absorption from burn sites.

#### BIBLIOGRAPHY

- Biologic Assay Committee, American Industrial Hygiene Association. 1971. Biologic monitoring guides: fluorides. *Am. Ind. Hyg. Assoc. J.* 32:274.
- Burke, W. J., U. R. Hoegg, and R. E. Phillips. 1973. Systemic fluoride poisoning resulting from a fluoride skin burn. *J. Occup. Med.* 15:39.
- Dinman, B. D., W. J. Bovard, T. B. Bonney, J. M. Cohen, and M. O. Colwell. 1976. Absorption and excretion of fluoride immediately after exposure — Pt. I. *J. Occup. Med.* 18:7.
- Hodge, H. C., and F. A. Smith. 1970. Air quality criteria for the effects of fluorides on man. *J. Air. Pollut. Control Assoc.* 20:232.
- Kaltreider, N. L., M. J. Elder, L. V. Cralley, and M. O. Colwell. 1972. Health survey of aluminum workers with special reference to fluoride exposure. *J. Occup. Med.* 17:531.
- Neefus, J. D., J. Cholak, and B. E. Saltzman. 1970. The determination of fluoride in urine using a fluoride-specific ion electrode. *Am. Ind. Hyg. Assoc. J.* 31:96.
- Princi, F. 1960. Fluorides: a critical review. III. The effects on man of the absorption of fluoride. *J. Occup. Med.* 2:92.

**HYDROGEN CHLORIDE****DESCRIPTION**

HCl, hydrogen chloride, is a colorless, nonflammable gas, soluble in water. The aqueous solution is known as hydrochloric acid or muriatic acid and may contain as much as 38% HCl.

**SYNONYMS**

Anhydrous hydrochloric acid, chlorohydric acid.

**POTENTIAL OCCUPATIONAL EXPOSURES**

Hydrogen chloride itself is used in the manufacture of pharmaceutical hydrochlorides, chlorine, vinyl chloride from acetylene, alkyl chlorides from olefins, arsenic trichloride from arsenic trioxide; in the chlorination of rubber; as a gaseous flux for babbiting operations; and in organic synthesis involving isomerization, polymerization, alkylation, and nitration reactions.

The acid is used in the production of fertilizers, dyes, dyestuffs, artificial silk, and paint pigments; in refining edible oils and fats; in electroplating, leather tanning, ore refining, soap refining, petroleum extraction, pickling of metals, and in the photographic, textile, and rubber industries.

A partial list of occupations in which exposure may occur includes:

Battery makers	Organic chemical synthesizers
Bleachers	Photoengravers
Chemical synthesizers	Plastic workers
Dye makers	Rubber makers
Electroplaters	Soap makers
Fertilizer makers	Tannery workers
Food processors	Textile workers
Galvanizers	Tantalum ore refiners
Glue makers	Tin ore refiners
Metal cleaners	Wire annealers
Oil well workers	

**PERMISSIBLE EXPOSURE LIMITS**

The Federal standard for hydrogen chloride is 5 ppm (7mg/m<sup>3</sup>) as a ceiling value.

**ROUTE OF ENTRY**

Inhalation of gas or mist.

**HARMFUL EFFECTS***Local—*

Hydrochloric acid and high concentrations of hydrogen chloride gas are highly corrosive to eyes, skin, and mucous membranes. The acid may produce burns, ulceration, and scarring on skin and mucous membranes, and it may produce dermatitis on repeated exposure. Eye con-

tact may result in reduced vision or blindness. Dental discoloration and erosion of exposed incisors occur on prolonged exposure to low concentrations. Ingestion may produce fatal effects from esophageal or gastric necrosis.

#### *Systemic—*

The irritant effect of vapors on the respiratory tract may produce laryngitis, glottal edema, bronchitis, pulmonary edema, and death.

#### MEDICAL SURVEILLANCE

Special consideration should be given to the skin, eyes, teeth, and respiratory system. Pulmonary function studies and chest X-rays may be helpful in following recovery from acute overexposure.

#### SPECIAL TESTS

None in common use.

#### PERSONAL PROTECTIVE METHODS

Appropriate gas masks with canister or supplied air respirators should be provided when vapor concentrations are excessive. Acid resistant clothing including gloves, gauntlets, aprons, boots, and goggles or face shield should be provided in all areas where there is likelihood of splash or spill of liquid. Personal hygiene and showering after each shift should be encouraged.

#### BIBLIOGRAPHY

- American Medical Association. 1946. Effects of hydrochloric acid fumes. *J. Amer. Med. Assoc.* 131:1182.
- Thiele, E. 1953. Fatal poisoning from use of hydrochloric acid in a confined space. *Zentralbl. Arbeitsmed. Arbeitsschutz.* 3:146. (*Indust. Hyg. Digest Abst.* No. 387, 1954.)

## METALLIC COMPOUNDS

### *ALUMINUM AND COMPOUNDS*

#### DESCRIPTION

Al, aluminum, is a light, silvery-white, soft, ductile, malleable amphoteric metal, soluble in acids or alkali, insoluble in water. The primary sources are the ores cryolite and bauxite; aluminum is never found in the elemental state.

#### SYNONYMS

None.

#### POTENTIAL OCCUPATIONAL EXPOSURES

Most hazardous exposures to aluminum occur in smelting and refining processes. Aluminum is mostly produced by electrolysis of  $Al_2O_3$  dissolved in molten cryolite ( $Na_3AlF_6$ ). Aluminum is alloyed with