

# Safety Data Sheet

# Methyl mercury

Division of Safety  
National Institutes  
of Health



## WARNING!

THIS COMPOUND IS ACUTELY TOXIC, TERATOGENIC, AND EMBRYOTOXIC IN THE FORM OF THE HYDROXIDE OR CHLORIDE. IT IS READILY ABSORBED BY VARIOUS BODY TISSUES THROUGH THE RESPIRATORY AND INTESTINAL TRACTS AND TRANSPLACENTALLY. IT MAY IRRITATE TISSUES (SKIN, EYES, MUCOUS MEMBRANES, AND LUNGS). AVOID FORMATION AND BREATHING OF AEROSOLS.

LABORATORY OPERATIONS SHOULD BE CONDUCTED IN A FUME HOOD, GLOVE BOX, OR VENTILATED CABINET.

AVOID SKIN CONTACT: IF EXPOSED, WASH WITH SOAP AND COLD WATER. AVOID WASHING WITH SOLVENTS. AVOID RUBBING OF SKIN OR INCREASING ITS TEMPERATURE.

FOR EYE EXPOSURE, IRRIGATE IMMEDIATELY WITH LARGE AMOUNTS OF WATER. FOR INGESTION, INDUCE VOMITING. DRINK MILK OR WATER. REFER FOR GASTRIC LAVAGE. FOR INHALATION, REMOVE VICTIM PROMPTLY TO CLEAN AIR. ADMINISTER RESCUE BREATHING IF NECESSARY. REFER TO PHYSICIAN.

IN CASE OF LABORATORY SPILL, WEAR PROTECTIVE CLOTHING DURING CLEANUP. AVOID SKIN CONTACT OR BREATHING OF AEROSOLS. USE WATER TO DISSOLVE THE HYDROXIDE AND ETHANOL TO DISSOLVE THE CHLORIDE. USE ABSORBENT PAPER TO MOP UP SPILL. WASH DOWN AREA WITH 1% SODIUM THIOSULFATE FOLLOWED BY SOAP AND WATER. DISPOSE OF WASTE SOLUTIONS AND MATERIALS APPROPRIATELY.

### Introductory Remarks

1. The chief interest in biomedical research laboratories is in the chemical, analytical, and biological properties of methylmercury hydroxide because of its use as a denaturing agent in nucleic acid electrophoresis, and this will be emphasized. Nevertheless, a good deal of the literature deals with methylmercury chloride, and physical and

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chemical data for this compound are also listed. In the animal body, because of the higher association constant of chloride than of hydroxide for methylmercury, administered hydroxide exists almost entirely in the chloride form, and therefore biological data for both compounds are cited.

2. The following abbreviations will be used: MM = methylmercury as a generic term;  $MM^+$  = methylmercury cation; MMOH = methylmercury hydroxide; MMCl = methylmercury chloride.

3. Useful conversion factors: 1 g MMOH contains 0.862 g Hg; 1 g MMCl contains 0.799 g Hg.

#### A. Background

MMOH is a crystalline, colorless, somewhat volatile solid with a faintly metallic odor. It is neurotoxic, embryotoxic, teratogenic, and a vesicant. It is readily absorbed from the respiratory and gastrointestinal tract, skin, and mucous membranes. Currently the most important use of MMOH is as a reversible denaturing agent for nucleic acids during electrophoresis on agarose and polyacrylamide gels (Bailey and Davidson, 1976; Maxwell et al., 1979; Chandler et al., 1979). In the past, other MM compounds have been used as antifungal seed dressing compounds but this application has been discontinued. MM discharged as an industrial waste has been taken up in fish and shellfish. These sources of human intoxication have led to epidemics of MM poisoning in Japan (Minamata, Niigata), Iraq, Sweden, and (on a smaller scale) in the U.S. Several comprehensive reviews of these outbreaks exist (see for instance Harada, 1978; Bakir et al., 1973; Friberg et al., 1971; WHO, 1976). A useful review of the toxic properties of MM, with special emphasis on hazards associated with laboratory use, has recently been published (Junghans, 1983).

The permissible exposure limit to MM is  $0.01 \text{ mg/m}^3$  as a time-weighted 8-hour average (ACGIH, 1987).

#### B. Chemical and Physical Data

1. Chemical Abstract Nos.: MMOH: 1184-57-2; MMCl: 115-09-3;  $MM^+$  22967-92-6.

2. Synonyms: MMOH: methylmercury hydroxide, methyl mercury hydroxide, hydroxymethyl mercury. MMCl: methylmercury chloride, methyl mercury chloride, chloromethyl mercury, methyl mercuric chloride, methyl meruic chloride.

3. Chemical structures and molecular weights: MMOH:  $\text{CH}_3\text{HgOH}$ , 232.6; MMCl:  $\text{CH}_3\text{HgCl}$ , 251.1.

4. Density: MMOH: no data; MMCl: 4.063.

Absorption spectroscopy: MMOH in solution shows end absorption in the short (<280 nm) wavelength UV, and a small absorbance peak at 300-310 nm. Beer's law is not followed in this range (for discussion including that of UV behavior in vapor form, see pp. 11 ff, Junghans (1983)). The Raman spectrum of MMOH, and Raman and infrared frequencies for MMCl, have been published (Goggin and Woodward, 1960, 1966).

Volatility: Vapor pressure at 20°C: MMOH, 3.6  $\mu\text{m Hg}$ ; MMCl: 8.5  $\mu\text{m Hg}$ .

Solubility: MMOH is highly soluble in water (about 0.58 g/ml) and very soluble in organic solvents (methanol, ethanol, benzene, carbon tetrachloride, petroleum ether, etc.). MMCl is far less soluble in water (about 5 mg/ml or 0.02 M) but is also soluble in organic solvents.

Description: MMOH and MMCl are colorless crystalline solids with a faintly metallic, disagreeable odor.

Boiling point: MMOH: no data; MMCl: volatilizes above 100°C.  
Melting point: MMOH: 95°C; MMCl: 170°-173°C.

Stability: Aqueous solutions of MMOH and MMCl are quite stable;  $10^{-4}$  M solutions show no degradation after 17.1 hr of mid-day sunlight (the bromide and iodide of MM are less stable) (Wolfe et al., 1973). High intensity UV irradiation of MMCl solution causes decomposition (Inoko, 1981). No specific literature data on heat stability are known, but it may be assumed that MMOH and MMCl are also fairly stable except for vaporization.

Chemical reactivity: MMOH is a weak base, reacting alkaline to litmus and acid to phenolphthalein (Sneed and Maynard, 1922); in other words, its pK is in the neighborhood of 8. The  $\text{CH}_3\text{-Hg}$  bond is chemically stable and is unaffected by weak acids or bases; this stability is due not to the strength of this bond but to the very low affinity of Hg for oxygen. MMOH (Goggin and Woodward, 1960) and MMCl are covalent, nonpolar compounds which accounts for their high solubility in organic solvents; other compounds, such as the sulfate or nitrate, are more salt-like in their properties (WHO, 1976). The actual ionic or nonionic species of MMOH in aqueous solution over the pH range 0.26 to 13.11 have been described (Erlenmeyer and Leo, 1932).  $\text{MM}^+$  behaves in many respects like the silver ion; for instance, MMCl is soluble in dilute ammonia, KCN, and  $\text{Na}_2\text{S}_2\text{O}_3$ . It has been calculated that, at pH 7, an aqueous solution of MMOH contains 500 times more MMOH than  $\text{MM}^+$ . If such a solution is made 0.1 M in NaCl (i.e., approximating physiological conditions), there is present 100 times more MMCl than MMOH (Hughes, 1957). The

association constants of MM for imino groups of nucleosides and for thiols (cysteine, glutathione, thiosulfate) are as high as, or higher than, that for OH (Simpson, 1961, 1964).

12. Flash point: No data.
13. Autoignition temperature: No data.
14. Explosive limits in air: No data.

#### Fire, Explosion, and Reactivity Hazard Data

1. Major hazards from MM compounds to fire-fighting personnel are due to their volatility (effects on nose and throat) and vesicancy (effects on skin). Therefore, complete protective clothing and air-supplied respirators with full face masks should be worn.
2. Flammability is likely to be low.
3. Conditions contributing to instability have not been identified but are likely to include high temperatures.
4. Hazardous decomposition products are mercury vapor and inorganic mercury salts.

#### Operational Procedures

The NIH Guidelines for the Laboratory Use of Chemical Carcinogens describe operational practices to be followed when potentially carcinogenic chemicals are used in NIH laboratories. The NIH Guidelines should be consulted to identify the proper use conditions required and specific controls to be implemented during normal and complex operations or manipulations involving MM.

It should be emphasized that this data sheet and the NIH Guidelines are intended as starting points for the implementation of good laboratory practices when using this compound. The practices and procedures described in the following sections pertain to the National Institutes of Health and may not be universally applicable to other institutions. Administrators and/or researchers at other institutions should modify the following items as needed to reflect their individual management system and current occupational and environmental regulations.

1. Chemical inactivation: Methods have been reported (Junghans, 1983).
2. Decontamination: Turn off equipment that could be affected by MM or the materials used for cleanup. If there is any uncertainty regarding the procedures to be followed for decontamination, call the NIH Fire Department (dial 116) for assistance. Use absorbent paper to mop up spill. Wipe off

surfaces with sodium thiosulfate solution, then wash with copious quantities of water. Glassware should be rinsed in a hood with sodium thiosulfate solution, followed by ammonia solution, deionized water, and ethanol (Westöö, 1967). Animal cages should be washed with water.

3. Disposal: No waste streams containing MM shall be disposed of in sinks or general refuse. Surplus MM or chemical waste streams contaminated with MM shall be handled as hazardous chemical waste and disposed of in accordance with the NIH chemical waste disposal system. Nonchemical waste (e.g., animal carcasses and bedding) containing MM shall be handled and packaged for incineration in accordance with the NIH medical-pathological waste disposal system. Potentially infectious waste (e.g., tissue cultures) containing MM shall be disinfected by heat using a standard autoclave treatment and packaged for incineration, as above. Burnable waste (e.g., absorbent bench top liners) minimally contaminated with MM shall be handled as potentially infectious waste and packaged for incineration, as above. Absorbent materials (e.g., associated with spill cleanup) grossly contaminated shall be handled in accordance with the chemical waste disposal system. Radioactive waste containing MM shall be handled in accordance with the NIH radioactive waste disposal system.
4. Storage: Store solid MM and its solutions in dark-colored, tightly closed containers under refrigeration. Avoid exposure to light. Store working quantities of MM and its solutions in an explosion-safe refrigerator in the work area.

#### Monitoring and Measurement Procedures Including Direct Field Measurements and Sampling for Subsequent Laboratory Analysis

Notes. a. Many procedures have been developed for the analysis of total mercury and for MM. Both are important because of the interconversion of MM and inorganic mercury in the environment and in animal metabolism, and therefore both types will be mentioned below.

b. Several methods for MM analysis of biological materials have been directed specifically to the analysis of fish (for ecological monitoring); there is no reason why some or all of these methods cannot be adapted to other biological materials as well.

1. Sampling: Officially proposed or approved methods have been published for the sampling of total mercury (NIOSH, 1979) or MM (NIOSH, 1980) in air by means of commercially available absorption tubes. These methods are adequate in the TWA and ceiling ranges. Other absorption tube fillings include MnO<sub>2</sub> for total mercury (Janssen et al., 1977), and segmented fillings for

differential (Hg, inorganic Hg<sup>++</sup>, MM, and (CH<sub>3</sub>)<sub>2</sub>Hg) analysis (Braman and Johnson, 1974; Takizawa et al., 1981). Tissue samples are usually wet digested (acid, or alkali + cysteine) and concentrated by multiple extractions (e.g., Westöö, 1966; Cappon and Smith, 1978; James, 1983). A differential method which does not require digestion has been described (Magos, 1971; Farrant et al., 1981). This is based on the principle that addition of SnCl<sub>2</sub> to biological samples releases Hg<sup>++</sup> while addition of SnCl<sub>2</sub> + CdCl<sub>2</sub> also releases MM.

2. Analysis: The state of analysis through 1970 has been reviewed (Friberg et al., 1971). The older colorimetric (dithizone) procedure has been largely superseded although an official (AOAC) procedure has recently been described (Horwitz, 1980a). The most commonly used method at present is atomic absorption spectroscopy which is the NIOSH recommended procedure for total mercury (NIOSH, 1979) and MM (NIOSH, 1980) in air and has also been described as an AOAC method (Horwitz, 1980b). It has been used in differential mercury analysis in air (with a detection limit of 0.2 ng Hg/m<sup>3</sup> (Takizawa et al., 1981), blood (Sharma and Davis, 1979), and in other biological samples with a limit of less than 0.5 ng Hg/200 µl of sample (Farant et al., 1981). Also widely used is gas chromatography, usually coupled with electron capture (Westöö 1966, 1967, 1968) or other detection systems which have higher selectivity and require less cleanup, such as microwave emission detection (Talmi, 1975) with a detection limit for MMCl of 0.5 pg. Gas chromatography has been applied to the analysis of MM in blood (Goolvard and Smith, 1980), urine (Ross and Gonzalez, 1973), and other biological material (James, 1983). Still other methods for MM analysis employ high performance liquid chromatography (Holak, 1982), neutron activation, and isotope dilution.

### Biological Effects (Animal and Human)

1. Absorption: MM is absorbed by ingestion, inhalation, through other mucous membranes, and by parenteral injection. Over 90% of orally administered MM is absorbed from the gastrointestinal tract. It is a skin vesicant but it is not known whether systemic toxic effects are produced via this route. MM is also absorbed transplacentally.
2. Distribution: Ingested or injected MM is initially distributed fairly uniformly to all tissues except that 80-90% of the activity of <sup>203</sup>Hg-labeled MM in blood is found in the red blood cells. There is a somewhat delayed uptake in central nervous tissue (cerebrum, cerebellum) and in muscle. After several days there is a redistribution within the CNS reflecting areas of highest toxicological involvement. Chronically the highest activity is found in the kidney (mostly in the form of inorganic Hg). In an experiment with three volunteers, oral administration of labeled MM nitrate followed by body scans revealed 50% of the radioactivity in the liver and 10% in the head (Aberg et al., 1969).

3. Metabolism and excretion: By far the largest amount of orally or parenterally administered MM binds quickly to SH groups of proteins (red blood cells, tissues) and lower molecular weight compounds; MM glutathione has been identified in the liver of subcutaneously injected rats (Omata et al., 1978). While the  $\text{CH}_3\text{-Hg}$  bond is chemically very stable, a fair amount of biotransformation of MM to inorganic mercury salts has been demonstrated in the guinea pig (Iverson et al., 1974; Iverson and Herlihy, 1974), rat (Norseth, 1972), and mouse (Mehra and Choi, 1981), with resulting high concentrations of inorganic mercury in the kidney and liver. Excretion of MM is mainly in the feces in the form of nonvolatile adducts (e.g., 42% in rats within 28 days of a single injection of  $\text{MMC1}$ ) as compared with 6-7% in the urine (Schäfer et al., 1982).
4. Toxic effects: The  $\text{LD}_{50}$ , in  $\text{mg Hg/kg}^{\text{A}}$  for  $\text{MMOH}$  is 10 (rabbit, iv) and 34 (rat, iv). Considerably more data exist for  $\text{MMC1}$ , and it appears that the  $\text{LD}_{50}$  varies with species and route of administration (mouse 27.4 ig, 10.4 ip, 24.8 iv, 38.2 sc; Lown et al., 1977; guinea pig 5.5 ip, 16.5 po; Iverson et al., 1973), and length of observation to death (24 hour vs. 10 day  $\text{LD}_{50}$ , ip: rat, 9.5 vs. 8; hamster, 18 vs. 12; squirrel monkey, >13.5 vs. 3.8-5.1; Hoskins and Hupp, 1978). These findings suggest a different mechanism of lethality for different species.

Toxic manifestations of intoxication with  $\text{MM}^{\text{B}}$  in animals vary somewhat between species, particularly in the subacute phase. In the rat the first changes are noted in the kidney (necrosis of tubular epithelium with no effect on renal function) followed by ataxic gait and a characteristic "crossing phenomenon" (crossing of hind legs when rat is held upside down) (Klein et al., 1972). In the cat there is anorexia, ataxia, proprioceptive impairment, blindness, vertical nystagmus, and convulsions with lesions in the cerebrum, cerebellum, and brain stem (Davies and Nielsen, 1977). The squirrel monkey shows, as the first neurological sign, increase in scotopic vision (Berlin et al., 1975) but this is not found in the macaque (Luschei et al., 1977). Because of the high affinity of MM not only for sulfhydryl but also for imino, carbonyl, and hydroxyl groups, no particular enzyme system can be pinpointed as the target of toxic action.

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<sup>A</sup>All literature values have been recalculated as  $\text{mg Hg/kg}$  for better intercomparison between  $\text{MMOH}$  and  $\text{MMC1}$ . See interconversion factors under Introductory Remarks, above.

<sup>B</sup>Effects are about the same whether  $\text{MMOH}$  or  $\text{MMC1}$  was administered, and no distinction is made between these two.

Effects in man have been amply described in connection with the outbreaks of MM poisoning in Japan, Iraq, and elsewhere (Harada, 1978; Bakir et al., 1973; Friberg et al., 1971; Hunter, 1978). Junghans (1983) has summarized them as follows: "The usual first manifestation...is paresthesia (abnormal sensation or numbness) in the skin of the hands and feet and around the mouth. At higher levels ataxia (effect on coordination in gait) and visual disorders (constriction of visual fields and blurring) are observed. Still higher levels of exposure can result in dysarthria (difficulty in speech), generalized impairment of motor functions, and some loss in muscle power. Severe cases of poisoning can result in deafness, blindness, myoclonic jerks (involuntary muscle spasms), general physical and mental debilitation, paralysis, and even death. Morphologically, damage from MM appears to be limited to the visual cortex, primary sensory, and motor areas of the brain. Even in cases of severe poisoning, higher functions of memory, intelligence, and motivation are unaffected. Less severely affected persons show some gradual improvement in muscle power, ataxia, and dysarthria after blood levels have fallen. Visual changes are the slowest to improve."

5. Carcinogenic effects: None have been reported.
6. Mutagenic and teratogenic effects: Mutagenicity of MM has not been reported. However, fetotoxic and teratogenic effects in a variety of animal species such as the cat (Khera, 1973), hamster (Harris et al., 1972), and mouse (Curle et al., 1983) have been observed. The usual results of maternal administration of MM are fetal resorption, clubfoot, cleft palate, hydrocephalus, and other fetal abnormalities.

### Emergency Treatment

1. Skin and eye exposure: For skin exposure, remove contaminated clothing and wash skin with soap and water. Skin should not be rinsed with organic solvents. Avoid rubbing of skin or increasing its temperature. For eye exposure, irrigate immediately with copious quantities of running water for at least 15 minutes. Obtain ophthalmological evaluation.
2. Ingestion: Drink plenty of water or milk. Induce vomiting. Refer for gastric lavage.
3. Inhalation: Remove victim promptly to clean air. Administer rescue breathing if necessary.
4. Refer to physician. Consider treatment for pulmonary irritation.

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