



## **Methyl Isocyanate September 2003**

### **Introduction**

#### **Methyl Isocyanate – Overview**

Methyl isocyanate is a colorless liquid that has a distinctly sharp odor with an odor threshold of 2.1 parts per million. Its vapor pressure is 348 millimeters of mercury at 20° C and it is highly flammable with a low flash point. Methyl isocyanate is a chemical intermediate in the production of carbamate insecticides and herbicides, and is extremely toxic to humans in an acute exposure. In 1984, in Bhopal, India, an accidental acute inhalation exposure to the gas, estimated at 13 to 100 parts per million, resulted in the deaths of more than 3 to 5,000 people within 5 days and adverse health effects in greater than 170,000 survivors. However, the main source of potential exposure is an occupational one in those workers who use insecticides and herbicides produced from methyl isocyanate. It has also been found in cigarette smoke with about 4 µg per cigarette.

#### **Methyl Isocyanate -- Toxicity**

Methyl isocyanate is extremely toxic to people and most of our toxicity data comes from acute animal tests in rats. These studies have shown this agent to be extremely toxic in inhalation exposure with a LD<sub>50</sub> of less than 200 mg/m<sup>3</sup>, as well as being highly toxic from an oral exposure, with a LD<sub>50</sub> of 50-500 mg/kg. Acute exposure to concentrations of only 23 mg/m<sup>3</sup> is irritating to the eyes, nose, and throat; while levels of 68 mg/m<sup>3</sup> result in a risk of severe injuries; and 225 mg/m<sup>3</sup> may result in death. While the EPA has not established a Reference Concentration (RfC) or a Reference Dose (RfD) for methyl isocyanate, the California EPA has calculated a chronic inhalation reference exposure level of 0.001 mg/m<sup>3</sup> based on lung and body weight effects in rats. This reference exposure level is a concentration at or below which adverse health effects are not likely to occur. An experiment on human exposure revealed no irritation at levels of 0.4 parts per million, while exposure at 2 parts per million produced bronchial

irritation and lacrimation, and exposure at 21 parts per million was unbearable. Based on these and other data, an 8-hour threshold limit value of 0.02 parts per million, or  $46 \mu\text{g}/\text{m}^3$ , has been set by both OSHA and NIOSH.

### **Protective Equipment**

Methyl isocyanate diffuses through polyethylene and attacks most elastomers, although fluorocarbon resins are resistant. It is dangerous to use materials other than stainless steel, nickel, or glass/ceramic in contact with methyl isocyanate. In particular, the use of iron, steel, zinc, tin, copper, or their alloys can lead to dangerous reactions.

Because of this, special protective clothing must be worn by emergency personnel going into a contaminated area. In addition, a positive-pressure, self-contained breathing apparatus must be used to protect the lungs.

### **Detection**

A review of commercially available gas sensors and chemical monitoring equipment reveals no automated detection devices for methyl isocyanate.

### **Decontamination**

Remove the victim from the exposure area as quickly as possible and should receive 100% oxygen if an inhalation exposure occurred. All clothing and personal belongings must be removed and double bagged to prevent secondary exposures. For eye exposure, irrigate the exposed eyes with copious amounts of tepid water for at least 15 minutes. If the victim is wearing contact lenses, they should be removed, provided such removal does not cause further damage to the eyes. For dermal contact, remove contaminated clothing and flush the skin and hair with plain water for at least 5 minutes. Then wash all exposed areas thoroughly with soap and water for at least 15 minutes and rinse thoroughly.

### **Signs and Symptoms**

The early effects of acute gaseous exposure to methyl isocyanate are respiratory tract and mucous membrane irritation. Eye exposure, will cause intense burning of the eyes, photophobia, blepharospasm, profuse lacrimation, lid edema, and superficial corneal ulceration with a resulting reversible blindness. As the exposure continues, respiratory symptoms – difficulty breathing and cough – will develop and can progress to acute pulmonary edema and even acute respiratory distress syndrome, with damage noted to the alveolar septa.

### **Signs and Symptoms**

Methyl isocyanate is also a skin irritant that causes a burning sensation. It can be absorbed through the skin, although little is known about this route of exposure.

### **Signs and Symptoms**

The chemical is highly toxic with oral exposure, and once absorbed it reaches various organs in its active form. In animal studies, the systemic effects include a dose-dependent hypotension, hemoconcentration, hyperglycemia, clinical lactic acidosis and uremia. These will also be evident with inhalation.

Other systemic symptoms include nausea, gastritis, sweating, fever, and chills.

### **Signs and Symptoms**

In the Bhopal accident, the most frequently reported first symptom was burning eyes, followed by coughing, watering of the eyes, and vomiting in that order. Cough was significantly associated with a poor prognosis. Among less frequently mentioned symptoms, diarrhea was also strongly associated with mortality, while shortness of breath was strongly, inversely related to death. Many of the Bhopal deaths resulted from secondary respiratory infections such as bronchitis and bronchial pneumonia. Severe changes in lung function, renal tubular necrosis and reduced liver function have been reported as well.

### **Treatment**

Basic first aid is required at the scene. Following that, treatment is primarily supportive, with attention directed to treating pulmonary irritation and maintaining adequate ventilation and oxygenation.

### **Treatment**

For oral exposures, administer activated charcoal as a slurry of 240 milliliters water with 30 gm charcoal, at a dose of 25 to 100gm in adults and adolescents, 25 to 50gm in children ages 1 to 12 years, and 1 gm/kg in infants less than 1 year old. The use of a cathartic may be beneficial, but such benefits have not been proven.

### **Treatment**

Eye contact with liquid methyl isocyanate is extremely irritating and may cause permanent damage. Gaseous exposure, while irritating, does not tend to result in permanent injury. Mydriatics, systemic analgesics, and topical ophthalmic antibiotics may be used for corneal abrasions. Severe iritis may be treated with topical atropine or homatropine.

## **Treatment**

Dermal exposure is extremely irritating and should be treated topically as indicated. Patients who develop dermal hypersensitivity reactions may require treatment with systemic or topical corticosteroids or antihistamines.

## **Treatment**

Following inhalation, markedly symptomatic patients should receive oxygen, ventilatory support, and an intravenous line. If bronchospasm is evident, consider inhaled sympathomimetics, IV theophylline, parenteral sympathomimetics such as epinephrine or terbutaline, and steroids. All patients displaying pulmonary symptoms should be hospitalized and observed for at least 72 hours in order to detect a delayed onset of pulmonary edema. For pulmonary edema, maintain ventilation and oxygenation and evaluate with frequent arterial blood gas or pulse oximetry monitoring. Hypoxia may be controlled by O<sub>2</sub> supplementation; and the early use of positive airway pressure intermittent positive pressure breathing, a positive end-expiratory pressure mask or, if necessary, intubation may delay and/or minimize the pulmonary edema and reduce the degree of hypoxia.

## **Treatment**

Throughout a symptomatic victim's treatment course, monitor the ECG, chest x-ray, pulse oximetry, peak air flows, arterial blood gases, serum electrolytes, and renal and hepatic function.

## **Long-term Medical Sequelae**

The long term effects of acute methyl isocyanate exposure are being followed after the Bhopal accident. Survivors are showing chronic eye problems such as loss of vision, loss of visual acuity, and cataracts, and pulmonary damage as evidenced by bronchoalveolar lesions and decreased lung function. In addition, reproductive effects have been noted with an increased number of stillbirths, spontaneous abortions and low birth weight babies.

The EPA has placed methyl isocyanate in Group D, not classifiable as to human carcinogenicity. Its teratogenicity has not been defined.

## **Environmental Sequelae**

If methyl isocyanate is released to moist soil or to water, it will rapidly hydrolyze to N-carboxymethylamine, methylamine, carbon dioxide, and N,N'-dimethylurea. Based upon methyl isocyanate's measured vapor pressure, volatilization from dry near-surface soil or surfaces is likely. Since it rapidly hydrolyzes,

bioconcentration, volatilization, and adsorption to sediment and suspended solids are not expected to be significant processes.

## **Summary**

In summary, despite its toxicity, methyl isocyanate is difficult to make and safely store, making it less likely as a terrorist weapon. It is extremely poisonous, with exposures to only 3 parts per million posing an immediate danger to life and health, and it is equally dangerous by inhalation or oral exposure. The signs and symptoms of exposure range from eye irritation to full-blown ARDS, and it has numerous serious systemic effects. Treatment is primarily supportive, with attention directed to treating pulmonary irritation and maintaining adequate ventilation and oxygenation. Finally, its long-term medical consequences are being followed after a 1984 accidental release in Bhopal, India.