

## EMERGENCY MEDICAL TREATMENT GUIDE

# CHLOROPICRIN VAPOR EXPOSURE RESULTING FROM TREATED FIELD VAPOR

---

**SYNONYMS:** Chloropicrin, Trichloronitromethane, Nitrochloroform (label names such as Tri-Clor and Tri-Pic).

**USE:** Agricultural pesticide applied for soil treatment

**APPEARANCE and PHYSICAL FORM:** Not visible as airborne vapor. Chloropicrin vapor is heavier than air and can concentrate in low areas during calm or no wind conditions.

**ADVERSE EFFECTS:** Chloropicrin behaves as a mild sensory irritant at concentrations between 75 ppb and 150 ppb and is usually detected through odor and eye sensation within 5 minutes of exposure. Lacrimation may occur. At concentrations of about 75 ppb, eye sensation (prickliness or pinching) can be felt in about 20 minutes. At levels above 150 ppb headache, nausea and vomiting may occur. These symptoms are temporary and reversible following termination of exposure. At levels above 580 ppb for 8 hours or 2000 ppb for 10 minutes, life-threatening effects including pulmonary edema can occur. Severe pulmonary responses can be delayed following onset of exposure. Symptoms of exposure are concentration dependent. Systemic effects including reproductive or developmental effects are unlikely at exposure levels of 150 ppb or lower.

### CLINICAL EFFECTS:

#### MILD EXPOSURE - (up to 150 ppb)

Mild exposure such as that likely to result from inhalation and eye contact with low vapor concentrations, which may move off of a treated field (up to approximately 150 ppb)

- ◆ Irritation of eyes, mucous membrane and upper respiratory tract
- ◆ Eye irritation may include lacrimation.
- ◆ Cough
- ◆ Nausea and headache may develop
- ◆ Possible skin irritation

These signs and symptoms will reverse with termination of exposure but have been reported to persist for up to two days post exposure.

CLINICAL EFFECTS:

MODERATE EXPOSURE (150ppb to 300 ppb)

- ◆ Exposure to airborne concentrations in the range of 150 ppb to 300 ppb or lower but for extended periods can produce the same symptoms as above but with increased severity and may include cough, bronchospasm and other respiratory symptoms.

These signs and symptoms can appear more quickly following elevated exposures and will reverse with termination of exposure. Symptoms have been reported to persist for up to two days post exposure.

CLINICAL EFFECTS:

SEVERE EXPOSURE (>300 ppb)

- ◆ In addition to eye and mucous membrane irritation, systemic symptoms (nausea, vomiting, headache) can occur
- ◆ Dyspnea and respiratory symptoms are likely with increasing exposure concentrations or duration
- ◆ Orthostatic hypotension has been reported
- ◆ Chest wall pain and rhabdomyolysis have occasionally been reported following industrial inhalation exposures but are unlikely to result from nonoccupational exposure as a result of chloropicrin vapor offgassing from a treated field
- ◆ Delayed pulmonary effects are possible
- ◆ Exposures to air concentrations above 500 ppb for 8 hours or 2000 ppb for 10 minutes can cause life-threatening pulmonary effects including immediate or delayed edema.

DIFFERENTIAL  
DIAGNOSIS

In mild exposure symptoms and signs may resemble seasonal or other allergy or viral upper respiratory tract infection. If breathing difficulties occur or if tracheobronchial tree or pulmonary parenchyma become involved, signs and symptoms must be differentiated from cardiogenic pulmonary edema, severe viral or bacterial pneumonia, and adult respiratory distress syndrome.

SPECIAL TESTS

Monitoring of patient: Monitor vital signs, CBC and electrolytes after significant ingestion. Monitor for occult GI hemorrhage (ingestion), respiratory distress and increasing pain. Chest radiograph and pulse oximetry in any patient with respiratory signs or symptoms.

**TREATMENT** Treatment is symptomatic and supportive. There is no specific antidote for overexposure to chloropicrin vapor. If eyes are irritated, flush with water. Where instances of direct contact with liquid or undiluted chloropicrin can be ruled out, skin surface decontamination is usually unnecessary. If necessary, remove person to fresh air and provide ventilator support.

Bronchospasm: Treat with oxygen, inhaled beta agonists and consider systemic corticosteroids.

Injury of globe of eye: Copious irrigation until pH neutral; perform slit lamp exam. Ophthalmology consult. Antibiotics and mydriatics may be indicated.

Contact a Regional Poison Control Center at 1-800-222-1222 for clinical assistance.

#### REFERENCES

Barry, T., et al. (2010). Community Exposure Following a Drip-Application of Chloropicrin. *J of Agromedicine*, 15: 24-37.

Goldman, L.R., et al., (1987). Acute Symptoms in Persons Residing Near a Field treated With the Soil Fumigants Methyl Bromide and Chloropicrin. *West J Med*, July 147: 95-98.

Chloropicrin: Hazardous Substances Data Bank (2011). National Library of Medicine, National Institutes of Health and Human Services, Bethesda.  
<http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?HSDB>

#### TOXICOLOGY BACKGROUND

##### Undiluted chloropicrin:

Undiluted or concentrated liquid chloropicrin is highly toxic following ingestion or direct contact with the skin or eyes

Inhalation exposure to 4000 ppb for a few seconds may cause some degree of incapacitation and very brief exposure (a few seconds) to 15,000 ppb can cause respiratory tract injury. Exposure to concentrations above 15,000 ppb if allowed to continue for a minute or longer, can cause pulmonary edema and possibly death.

##### Airborne chloropicrin vapor:

Exposure to airborne concentrations of chloropicrin vapor that may be present near a field during or immediately after treatment with chloropicrin or a chloropicrin-containing pesticide is unlikely to produce more than local, transient sensory irritation effects such as eye and upper respiratory irritation.

Human Subject Testing Controlled human subject testing with a study population consisting of young adults, a population more sensitive to sensory irritant effects than the general population including asthmatics and children, showed that sensory irritation as manifest primarily by eye irritation was the most sensitive indication of chloropicrin exposure. The threshold for ocular irritation in humans was 73 ppb calculated as a BMCL10. The BMCL10 was derived for a sensitive endpoint and represented the lower bound on the response of a small percentage (10%) of the test population selected to represent the sensitive end of the general population.

Laboratory Animal Inhalation Studies. Animal studies using inhalation exposure have been conducted with male and female CD rats and CD-1 mice. The animals were exposed in whole body inhalation chambers to chloropicrin vapor at concentrations of 0, 300, 1000 or 3000 ppb for 6 hours per day 5 days per week for 13 weeks. The animals were observed for standard toxicological parameters during the in-life phase of the investigation and were subjected to necropsy and extensive histopathological examination following termination. Ocular examination, organ-body weight ratios were performed and special attention was given to respiratory tissues and all lesions. Mortality occurred in 3 of 10 male rats in the high-dose group during the exposures. Clinical signs of exposure in this group included discoloration in rats and dehydration in mice. Increases in hemoglobin concentration, hematocrit and total erythrocyte count were observed for male mice in all exposure groups. Female mice showed a dose-related decrease in monocyte count. Increased relative and absolute lung weight was seen in rats and mice in the mid- and high-dose groups. Accompanying these increased weights were microscopic lesions in the lungs and airways consistent with acute and chronic inflammation and nonspecific irritation. These changes included hyperplasia of the respiratory epithelium of the nasal cavities, goblet cell hyperplasia, bronchial/bronchiolar epithelial hyperplasia and peribronchial fibrosis. The respiratory tissue changes were confined almost entirely to animals in the mid- and high-exposure groups; however, two female mice from the low exposure group (300 ppb) had evidence of hyalin inclusion in the respiratory tissue. Treatment related changes were not seen in organs or tissue other than the respiratory tract or in the eyes or in hematological, biochemical or urine parameters other than those specified above. Subchronic and chronic toxicity studies in three species receiving chloropicrin orally or by inhalation did not produce clinical or histological signs of cardiac effects. Direct cardiac toxicity was not demonstrated in any investigation of chloropicrin toxicity.

Reproductive Function Studies. Chloropicrin vapor was administered by whole body inhalation for six hours per day, seven days per week to male and female CD rats at concentrations of 0, 500, 1000 or 1500 ppb through two generations. The No Observable Adverse Effect (NOAEL) level established for this study was 100 ppb for systemic toxicity and greater than 1500 ppb for developmental toxicity and reproductive parameters. These data indicate that reproduction fitness is not adversely affected by chloropicrin inhalation even at systemically toxic levels.

Developmental Toxicity Studies. Sexually mature virgin female Sprague-Dawley rats were impregnated and exposed by whole body inhalation to chloropicrin vapor for 6 hours per day in 16 m<sup>3</sup> stainless steel and glass chamber for days 6-15 of gestation. Exposure levels were 400, 1200 and 3500 ppb. The animals were observed for survival, appearance, behavior, body weight. The No Observable Adverse Effect Level (NOAEL) for maternal toxicity in this study

was 400 ppb and 1200ppb for fetal toxicity indicating that the developing fetus is not target tissue for chloropicrin.

The developmental toxicity of chloropicrin has also been evaluated in a non-rodent species. Sexually mature virgin female New Zealand White SPF rabbits were impregnated and exposed by whole body inhalation to chloropicrin vapor for 6 hours per day in 16 m<sup>3</sup> stainless steel and glass chamber for days 7-20 of gestation. Exposure levels were 400, 1200 and 2000 ppb. The No Observable Adverse Effect Level (NOAEL) for maternal toxicity in this study was 400ppb and 1200ppb for fetal toxicity indicating that the developing fetus is not a target tissue for chloropicrin toxicity.

Carcinogenicity Testing. At least six long-term bioassays have been completed with chloropicrin to evaluate the potential of this compound to cause chronic and/or carcinogenic effects. The bioassays have employed two strains of rats, two strains of mice and Beagle dogs. Lifetime exposures via whole body inhalation to CD-1 mice and CD rats have been reported for chloropicrin, Chloropicrin has been shown to not cause cancer in animal studies following long-term inhalation.