

CHLOROPICRIN (CCI₃NO₂)

Attachment E.1. Introduction

This Attachment contains general information on chloropicrin which is used as a warning agent in some of the methyl bromide products. More extensive review will be presented in the risk characterization document for chloropicrin as an active ingredient. References cited in this Attachment are included in **VII. REFERENCES**.

Chloropicrin (trichloronitromethane, nitrochloroform, nitrotrichloromethane) is a colorless, slightly oily, heavy liquid with an intense irritating tear gas odor (The Merck Index, 1989; Farm Chemicals Handbook, 1998). In a mixture with methyl bromide, it volatilizes readily when released from the tanks (Extoxnet, 1999). Chloropicrin has been used as an insecticide since 1917 and as a soil fumigant since 1920 (Extonet, 1999). As a pesticide for space and soil fumigation, it controls nematodes, bacteria, fungi, insects, and weeds. In 1999, there are 44 active registered products with chloropicrin in California. The registrants for these products are: Ameribrom, Inc.; Great Lakes Chemical Corp.; Soil Chemicals Corp.; Niklor Chemical Co.; Holtrachem Manufacturing Co.; Trical, Trinity Manufacturing, Inc.; Osmose Wood Preserving, Inc.; and Shadow Mountain Products Corp. Twenty-six of the products are in combination with methyl bromide, while 8 of the products are in combination with 1,3-dichloropropene (Telone^R).

From 1993 to 1998, the use of chloropicrin increased from 2.1 million pounds in 1993 to 3.0 million pounds in 1998. The majority of the total use (>67%) was for strawberry fields in efforts to decrease the amount of methyl bromide applied. The use of methyl bromide for all uses are under strict use permit conditions requiring a minimum buffer zone of 100 feet for residents and 30 feet for workers.

From 1982 to 1996, there were a total of 363 cases with health effects “definitely”, “probably”, or “possibly” related to chloropicrin exposure reported in the California Pesticide Illness Surveillance Program (Mehler, 1999). Systemic effects (such as headache, nausea) as well as local effects to the eye and skin were reported. Some of the reported cases were due to drift from application sites. The highest number of cases was reported in 1987 where 71 residents in a nearby labor camp were exposed to chloropicrin being applied to a 9 acre field. Fumes were detected and the residents exhibited symptoms of exposure.

As a warning agent, the odor threshold is 1.1 ppm while 0.3 to 0.37 ppm resulted in painful irritation to the eyes in 3-30 seconds (ACGIH, 1997). For occupational exposure, the American Conference of Governmental Industrial Hygienists (ACGIH) has recommended a Threshold Limit Value (TLV^R) of below 0.1 ppm for occupational exposure and measured as an 8-hour time-weighted average air concentration. This level would protect for eye irritation. This level has been adopted as the Permissible Exposure Limit (PEL) by the Occupational Safety and Health Administration and the California Occupational Safety and Health Administration. Respiratory protection for workers is required if the air level exceed 0.1 ppm. National Institute of Occupational Safety and Health has established 2 ppm as the Immediately Dangerous to Life and Health (IDLH) level (NIOSH, 1999). In California, the Reference Exposure Levels are 4.4 ppb and 13 ppb for mild and severe effects, respectively (OEHHA, 1999).

Attachment E.2. Toxicology

2.a. Acute Toxicity

Because of its acute toxicity, chloropicrin is in toxicity category I, under FIFRA toxicity classification, and is a restricted use pesticide. Undiluted liquid or concentrated chloropicrin is a severe irritant to the eye, skin, and upper respiratory tract. The dose response for chloropicrin is considered steep. In humans, the no observable effect is 100 ppb (ACGIH, 1997). At 300 ppb, cough, nausea, and vomiting occur, and severe skin irritation from direct skin contact. A summary list of the air concentrations for lethality and acute effect is presented in Table E1.

2.b. Other Toxicity Studies

Toxicity studies submitted for the fulfillment of SB 950 data requirement and reviewed under FIFRA guidelines are summarized in Table E2. The review of all submitted studies in the Summary of Toxicology Data is available upon request to the Registration Branch of DPR.

Table E1. Acute toxicity of chloropicrin in experimental animals and human.

Species	Inhalation LC 50	Inhalation (non-lethal)	Oral LD50	Dermal LD50	Ref ^a
Human	2000 ppm (10 min), lethal		5 to 50 mg/kg as lethal dose		1
Human	200 ppm (10 min), lethal				2
Rat	25.5 ppm (1 hr) ^b		37.5 mg/kg ^b	100 mg/kg ^b	3
Rat	11.9 ppm (4 hr) ^c				4
Rat	16.7-20.1 ppm (4 hr)				5
Rat	(4 hr) whole body 14.4 ppm nose only 6.6 ppm				6
Mouse		7.98 ppm (10 min) ^d			7
Mouse	9.9 ppm (4 hr)				1
Mouse		2.34 ppm(30 min)			8
Dog	111-131ppm (30 min) 53% dead				9, 10
Cat	120 ppm (20 min)				1
G. Pigs	120 ppm (20 min)				1

^{a/} References: 1. HSDB, 1994; 2. Prentiss, 1937; 3. Harton and Rawl, 1976; 4. Yoshida et al., 1987a; 5. Hoffman, 1999a; 6. Yoshida et al., 1991; 7. Kane et al., 1979; 8. Hoffman, 1999b; 9. Lambert and Jackson, 1920; 10. Underhill, 1920.

^{b/} Lethal doses were based on deaths within 14 days.

^{c/} Rats were exposed to chloropicrin (0, 8.8 to 16 ppm) for 4 hours. Necropsy showed lung lesions (edema, emphysema) and gastric distension. All animals showed reduced body weights.

^{d/} RD50= dose which caused 50% decrease in the respiration rate.

Table E2. Summary of findings from toxicity studies in the SB 950 database.

Species /Route (Dose)	NOEL	Effects	Ref
Subchronic Toxicity			
Rat / inhalation (0.37-2.93 ppm)	0.67 ppm	↓ Body weights, food consumption; ↑ lung weights; lung epithelial hypertrophy	1
Rat/ oral gavage (10-80 mg/kg/day for 10 days)	<10 mg/kg/day	Forestomach lesions	2
Rat/ oral gavage (2-32 mg/kg/day for 90 days)	8 mg/kg/day	↓ Body weight, hematological changes and forestomach histological changes	2
Chronic Toxicity/Oncogenicity			
Rat / oral gavage (0.1- 10 mg/kg/day for 2 years)	0.1mg/kg/day	↓ Body weight, periportal vacuolization of hepatocytes Stomach papilloma (1 male), ↑ mammary fibroadenomas in 10 mg/kg females	3*
Dog / oral capsule (0.1- 5.0 mg/kg/day for 1 year)	1.0 mg/kg/day	↓ Body weight (male), clinical signs and clinical pathology	4*
Rat / inhalation (0.1-1.0 ppm for 107 weeks)	0.1 ppm (0.12 mg/kg/day)	↓ Survival	5
Mouse/ inhalation (0.1-1.0 ppm for at least 78 weeks)	0.1 ppm (0.22 mg/kg/day)	↓ Body weight/ gain, food consumption; ↑ lung weights; and lung lesions. No oncogenic effects	6*
Reproductive Toxicity			
Rat / inhalation (0.5-1.5 ppm for 2 generations)	Maternal 0.5 ppm Repro. ≥ 1.5 ppm	↓ Body weight, and lung lesions No pup or reproductive effects	7*
Developmental Toxicity			
Rat / inhalation (0.4-3.5 ppm, gd 6 to 15)	Maternal 1.2ppm Fetal 0.4 ppm	↓ Body weight, body weight gain, and food consumption; ↑ clinical sign ↑ Skeletal variations	8*
Rabbit / inhalation (0.4-2.0 ppm, gd 7 to 20)	Maternal 0.4 ppm Fetal 0.4 ppm	↑ Clinical signs, abortions, and mortality ↑ Skeletal variations	9*
Genotoxicity			
Mouse lymphoma cells	NA	No increase in forward mutation frequency	10*
<i>S. typhimurium</i> 5 strains	NA	↑ revertant colonies ± rat liver S9	11*
Chinese hamster ovary cells	NA	↑ chromosomal aberrations	12*
Rat primary hepatocytes	NA	No effect on unscheduled DNA synthesis	13*

a/ * Studies were considered acceptable under FIFRA guidelines. Reference: 1. Yoshida *et al.*, 1987b; 2. Condie *et al.*, 1994; 3. Slauter, 1995; 4. Wisler, 1994; 5. Burleigh-Flayer and Benson, 1995; 6. Burleigh-Flayer *et al.*, 1995; 7. Schardein, 1994; 8. Schardein, 1993; 9. York, 1993; 10. San and Sigler, 1990a; 11. San and Sigler, 1990b; 12. Putman and Morris, 1990; and 13. Curren, 1990. NA= not applicable.