

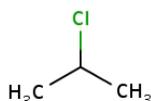
# WORKPLACE ENVIRONMENTAL EXPOSURE LEVEL<sup>®</sup>



## 2-Chloropropane (2016)

### I. IDENTIFICATION<sup>(1)</sup>

Chemical Name: 2-Chloropropane  
Synonyms: Isopropyl chloride; 2-propyl chloride, isoprid, 2-CP  
CAS Number: 75-29-6  
UN Number: 2653  
Molecular Formula: C<sub>3</sub>H<sub>7</sub>Cl  
Structural Formula:



### II. CHEMICAL AND PHYSICAL PROPERTIES<sup>(2-6)</sup>

Physical State: Colorless liquid  
Molecular Weight: 78.54  
Conversion Factors: 1 ppm = 3.21 mg/m<sup>3</sup>; 1 mg/m<sup>3</sup> = 0.31 ppm  
Melting Point: -117.2 °C (-179 °F) at 760 mm Hg  
Boiling Point: 35.7 °C (96.3 °F) at 760 mm Hg  
Vapor Pressure: 515.3 mm Hg at 25 °C (77 °F)  
Saturated Vapor Conc.: ~ 678,000 ppm at 25 °C (77 °F) (calculated)  
Odor Description: Chloroform-like, mildly sweet odor  
Threshold: Limited odor. Some subjects could not detect 500 ppm 2-CP vapor.  
Flammability Limits: 2.8-10.7% (in air at 25 °C)  
Flash Point: -32 °C (-26 °F) (closed cup)  
Autoignition Temp.: 593 °C (1100 °F)  
Specific Gravity: 0.8617 at 20 °C (68 °F)  
Vapor Density: 2.7 (air = 1)  
Solubility: In water = 3.05 g/L at 25 °C; soluble in benzene, acetone, and methanol; miscible with alcohol and ether  
Stability: Normally stable reactivity and incompatibilities: can react vigorously with oxidizing materials

### III. USES

Anesthetic properties of 2-chloropropane (2-CP) are described but significant use as an anesthetic is not reported. The primary uses of 2-CP are as a chemical intermediate, an industrial solvent or extractant.<sup>(3)</sup>

The use of 2-CP is anticipated to increase due to its acceptance by the EPA as an alternative foam-blowing agent. Many currently used foam-blowing agents are being phased out due to concern for atmospheric ozone depletion.<sup>(7)</sup>

### IV. ANIMAL TOXICITY DATA

#### A. Acute Toxicity

##### 1. Lethality Data

Species	Route	LD or LC(mg/kg)
Rat	Oral (LD <sub>50</sub> )	> 2,000 <sup>(8)</sup>
Guinea Pig	Oral (LD <sub>50</sub> )	> 3,000 <sup>(9)</sup>
Rat and Mouse	Oral (LD <sub>50</sub> )	> 3,200 <sup>(11)</sup>
Rat	Inhalation (LC <sub>100</sub> )	Saturated vapor exposure @ 23°C for 6 min <sup>(10)</sup>
Rat	Skin (LD <sub>50</sub> )	> 2,000 <sup>(11)</sup>

##### 2. Eye Irritation

A volume of 0.1 mL of 2-CP was instilled into the left conjunctival sac of six rabbits. 2-CP produced low-grade conjunctival effects (redness and swelling) at the 1- and 24-hour observation intervals. No findings on the cornea or iris were observed. All irritation resolved by 48 hours. 2-CP was classified as a non-irritant for the eye based on European Economic Commission (EEC) guidelines.<sup>(12)</sup>

##### 3. Skin Absorption

No data available other than lethality.

##### 4. Skin Irritation

A volume of 0.5 mL of 2-CP was applied on the intact and abraded dermal surface of the back of six rabbits. Test sites were wrapped for 4 hours and then unwrapped, gently cleaned (if necessary) and evaluated. No erythema or edema was observed. 2-CP was classified as non-irritating on skin based on EEC guidelines.<sup>(13)</sup>

##### 5. Skin Sensitization

2-CP was tested in guinea pigs for the potential to cause skin sensitization according to the experimental design of Magnusson and Kligman.<sup>(14)</sup> Twenty test and 20 control animals were studied. No irritation or sensitization was observed following challenge exposures.<sup>(15)</sup>

## 6. Acute Inhalation Toxicity

Rats exposed to a saturated atmosphere of 2-chloropropane were anaesthetized within 3 minutes and died within 6 minutes.<sup>(10)</sup> No lethality was seen in rats (5/sex) exposed by nose-only to 2030 ppm for 4-hrs.<sup>(16)</sup> Signs of central nervous system depression was seen in rats exposed to 8000 ppm for 4-hr.<sup>(10)</sup>

### B. Subacute Toxicity

Male and female Alderley Park SPF rats were exposed to 2-CP by inhalation at concentrations of 250 or 1000 ppm for 6 hours/day, five days/week for 4 weeks (20 exposures). Rats from both groups completed this exposure regimen without mortality or other clinical signs of toxicity. Rats exposed to 1000 ppm showed liver injury characterized by extensive vacuolation and necrosis. No adverse effects were seen in rodents exposed to 250 ppm.<sup>(17)</sup>

### C. Subchronic Toxicity

In the 1950s a series of investigations into the inhalation toxicity of 2-CP were conducted. Both acute (described in A3, above) and subchronic tests were run. Mice (10 females), rats (20 males and 20 females), guinea pigs (8 males and 8 females), rabbits (2 males and 2 females) and monkeys (2 females) were exposed by whole body inhalation to 1000 ppm 2-CP for approximately six months (7 hours/day, 5 days/week, 127 exposures). Air exposed controls and unexposed controls were run for valid comparison. No significant treatment-related changes were observed in mortality, appearance, growth, behavior, or final average body and organ weights. Microscopic examination of the tissues revealed adverse changes in the lungs of female rabbits and monkeys (edema or pneumonitis) and in the livers of all exposed species. In general the liver pathology was characterized by necrosis of the parenchymal cells of the portal region. Repeated exposure to 1000 ppm 2-CP also caused kidney injury in guinea pigs, rabbits and monkeys characterized by tubular degeneration of the epithelium with some necrosis.<sup>(18)</sup>

In a similar, but separate experiment, rats (24 males and 24 females), guinea pigs (12 males and 12 females), rabbits (2 males and 2 females) and dogs (2 females) were repeatedly exposed to 500 ppm of 2-CP vapor for six months. At 500 ppm no treatment-related adverse effects were observed in any of the exposed animals.

More recently, a 90-day inhalation toxicity study of 2-CP was completed according to OECD Guideline 413. Male and female Sprague Dawley rats (10 each per dose group) were exposed to 2-CP vapor at target concentrations of 0, 250, 500, or 1000 ppm for six hours per day, seven days per week for 90 days. A second high-concentration exposure group (satellite) was simultaneously exposed for 90 days and then held for an additional 30 days to determine the reversibility of any adverse findings identified in the main study groups. Histopathological evaluation included reproductive and endocrine organs,

neurological tissues and immune system tissues. No treatment-related mortality or changes in general appearance or behavior was observed in any treatment group. A slight decrease in food consumption and body weight was observed in male rats exposed to 1000 ppm. All other measured parameters including blood and clinical chemistry, organ weight determinations, histopathological evaluations (including liver and kidneys) and determination of laryngeal epithelial thickness showed no significant treatment-related adverse effects. Based on these results, 500 ppm was a clear NOEL.<sup>(19)</sup>

### D. Chronic Toxicity

No chronic toxicity studies have been conducted on this material.

### E. Reproductive/Developmental Toxicity

Pregnant Sprague–Dawley rats were exposed to 2-CP by inhalation at concentrations of 250, 500, 1000 or 2700 ppm from day 6 to 15 of gestation. No clinical signs of toxicity were observed in any of the treated dams. Dark red and beige foci were found in the lungs of treated dams at 2700 ppm (12/20) and to a lesser extent at 1000 ppm (2/20). No treatment-associated increase in fetal malformations was observed at any exposure level. At the highest concentration a slight increase in skeletal variations was found (86.3% compared to 72.0% in the controls). The results show that 1000 ppm was at or near the threshold for maternal toxicity (NOEL/LOEL). The NOEL for fetal effects was 1000 ppm.<sup>(20)</sup>

### F. Genotoxicity/Mutagenicity

#### 1. *In vitro*

2-CP was mutagenic to *S. typhimurium* after metabolic activation when tested in desiccators.<sup>(21)</sup> No mutagenic response was observed in a standard *S. typhimurium*/microsome test with 4 strains of bacteria and doses up to 10,000 µg/plate.<sup>(22)</sup> 2-CP failed to show any evidence of genotoxicity in a battery of short-term tests including HGPRT gene mutation in V79 cells, DNA single-strand breaks in V79 cells, unscheduled DNA synthesis in human fibroblasts and chromosomal aberrations in human blood lymphocytes.<sup>(23)</sup>

#### 2. *In vivo*

2-CP was not genotoxic in a mouse micronucleus test. Male and female mice were administered 2-CP at 2000 mg/kg by intraperitoneal injection and bone marrow was harvested for study at 24, 48 and 72 hours post-dosing. 2-CP exposure failed to produce an increase in the frequency of micronuclei in polychromatic erythrocyte stem cells.<sup>(19)</sup>

### G. Metabolism/Pharmacokinetics

It has been reported that 2-CP is enzymatically dechlorinated *in vitro* by rat liver microsomes.<sup>(24)</sup> Additional studies suggest that cytochrome P450 may catalyze this reaction.<sup>(25)</sup>

## V. HUMAN USE AND EXPERIENCE

Only a limited amount of industrial hygiene data is available for 2-CP. Individual worker TWA exposures were all below 0.11 ppm in a plant that used 2-CP as a chemical intermediate. The workers who were monitored in this study performed a variety of jobs at the plant including, process operators, pipe fitters, electricians, welders, machinists, and foremen. Exposures to 2-CP were slightly higher for maintenance personnel when cleaning lines and working on pumps (0.1–0.17 ppm).<sup>(26)</sup> Recent exposure studies of 2-CP in foam fabrication field trials indicate TWA workplace atmospheres of less than 6 ppm.<sup>(27)</sup>

## VI. RATIONALE

2-CP is a colorless liquid with a flash point of -26°F. This is coupled with a high odor threshold (500 ppm), therefore, it is a severe fire hazard with poor warning properties. Acute toxicity data indicates a low order of toxicity by oral, dermal and inhalation routes of exposure. Based on EEC guidelines, 2-CP was tested and found not to be an eye or skin irritant. 2-CP did not induce skin sensitization in guinea pigs. 2-CP is not genotoxic based on a robust battery of mammalian cell and whole animal genotoxicity tests. However, in one instance, when 2-CP was tested in a desiccator with *S. typhimurium*, 2-CP was mutagenic following metabolic activation.

A wide variety of animal species, mice, rats, guinea pigs, rabbits and monkeys, were exposed to 1000 ppm 2-CP vapor for six months in the 1950s. This exposure regimen revealed the critical effect to be adverse effects in the liver found in all species. A NOEL could not be established because 1000 ppm was the only exposure level used in the experiment. In follow up experiments using rats, guinea pigs, rabbits and dogs, a 500 ppm exposure regimen resulted in no treatment-related adverse effects. More recently (1993), a study using rats and a range of exposures (0, 250, 500, 1000 ppm) indicated minimal adverse effects [decreased body weight and food consumption; no liver or kidney pathological changes] in the 1000 ppm exposure group. This study included an extensive histopathological evaluation, clinical chemistry and a recovery group. Based on the results of these experiments, 500 ppm was a clear NOEL.

Developmental effects of 2-CP vapor have also been evaluated in rats. Pregnant rats showed limited evidence (color changes in the lung) of maternal toxicity at 1000 ppm (LOAEL). No fetal malformations were produced. An increase in skeletal variations in the exposed fetus was observed at 2700 ppm. The NOEL for fetal toxicity was 1000 ppm. The NOEL for maternal toxicity was 500 ppm.

The only studies of human exposure come from industrial hygiene monitoring in the workplace. Based on these monitoring reports, 2-CP TWA atmospheres averaged less than 6 ppm in foam fabrication field trials.

A WEEL guide of 50 ppm as an 8-hr TWA should allow an adequate margin of safety to protect against liver injury and potential adverse effects to the fetus.

## VII. RECOMMENDED WEEL

8-hr time-weighted average (TWA): 50 ppm (161 mg/m<sup>3</sup>)

This WEEL value was originally established in 2004. No significant new literature was identified since the WEEL was established (2004) that supports a change to the recommended WEEL value.

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