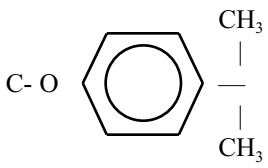
Cumene Hydroperoxide

Document History
Published: 1991
Revised: 2001
Rebranded: 2025

This OEL was originally established in 1991 and updated in 2001. A literature search to identify new toxicity information for Diallylamine was performed in August 2008. No new studies or data relevant to the OEL were identified.

I. IDENTIFICATION

Chemical Name: Cumene hydroperoxide
Synonyms: Isopropylbenzene hydroperoxide; CHP; alpha, alpha-dimethylbenzyl hydroperoxide; cumyl hydroperoxide
CAS Number: 80-15-9
Molecular Formula: $C_9H_{12}O_2$
Structural Formula:



II. CHEMICAL AND PHYSICAL PROPERTIES[1–4]

Physical State: Colorless to pale yellow liquid
Molecular Weight: 152.21
Conversion at 25°C (77°F) 760 mmHG: 1 ppm = 6.23 mg/rn^3 1 mg/rn^3 = 0.16 ppm (v/v)
Boiling Point: 153°C (307°F) at 760 mmHg (decomposed below the boiling point)
Melting Point: Below -40°C (-40°F)
Vapor Pressure: 2.0 mmHg at 20°C (68°F)
Saturated Vapor Concentration: 2632 ppm at 20°C 68°F)
Odor Description: Sharp, irritating odor
Flammability Limits: 0.9% Lower explosive limit; 6.5% Upper explosive limit
Flash Point: (Closed-cup) 56°C (132°F)
Specific Gravity (H2,O = 1): 1.03
Vapor Density (Air = 1): 4.1
Solubility (in water): 1.0% at 25°C (77°F)
Stability: Decomposes below boiling point
Reactivity and Incompatibility: Slight reaction with water, CHP undergoes vigorous and exothermic decomposition in contact with mineral acids, certain oxidizing agents (e.g., chlorine, ferric chloride, reducing agents, and other materials such as zinc.

III. USES[5]

CHP is used to produce phenol and acetone and as a polymerization catalyst. Technical grade CHP used by most industries is a mixture containing 80% to 85% CHP, 9.6% to 16.8% cumene, 2.9% to 4.6% phenyl carbinol, and 0.3% to 0.8% acetophenone.

IV. ANIMAL TOXICITY DATA

A. Acute Toxicity

1. *Oral Toxicity*

Rat: LD_{50} 382 mg/kg (73% active ingredient); kidney, ureter, and bladder effects noted.[6]

1000–2000 mg/kg administered as a 10% solution in corn oil[7]

800 mg/kg (effects included narcosis; methemoglobin induction; hematotropic effects)[8]

800–1600 mg/kg (83% active ingredient)[9]

Mouse: LD_{LO} 5000 mg/kg[10]

2. *Eye Toxicity*

Rabbit: Undiluted material (no volume given) produced severe irritation and corneal damage.[7]

An exposure to 80% CHP (no volume given) produced moderate irritation and corneal injury that had not healed 15 days after instillation.[11]

A drop of 10% CHP in propylene glycol caused a reaction (graded 46 and 79 on a scale of 100) that persisted at least a week. Washing with water within 4 sec prevented injury. A 1% concentration (no dose given) in

propylene glycol or dimethyl phthalate was not irritating.[6] An exposure to 1 mg of CHP (no concentration given) produced irritation of the palpebral conjunctiva and chemosis.[6]

3. Skin Toxicity

a. Irritation

Rabbit: Contact with 80% CHP (no dose given) for 10 mm, 1 hr. or 2 hr produced slight irritation. Edema developed after 2 hr of contact, and necrosis was apparent after 4.5 hr.[11]

One to two drops of 73% CHP applied to a circular area (2-cm diameter) produced erythema, edema, and vesiculation within 2 to 3 days.[6]

b. Absorption

Rat:

LD_{50} 500 mg/kg

(toxic effects were seen in the uro-genital area; convulsions were also noted)[12]

LD_{50} 515 to 1030 mg/kg[13] (occluded)

LD_{50} 1160 to 1475 mg/kg[13] (non-occluded)

Rabbit:

LD_{50} >500 mg/kg (80% solution) after 10 to 15 mm min exposure"[11]

Rabbits treated with 83% active ingredient CHP (no dose given) developed treatment-related changes necrotic-ulcerative dermatitis; degenerative lesions indicative of toxic nephrosis; degenerative hepatocellular cytoplasmic vacuolation; peiivascular and peiineuronal edema.[13]

4. Inhalation Toxicity

Rat: LC_{50} (4 hrs) 220 ppm, 73% solution).[6] Three rats exposed to nominal concentrations of CHP at 25°C for 7 hr showed signs of nasal irritation and weight loss. All rats survived.[7]

Mouse: LC_{50} (4 hrs) 200 ppm (73% solution)[6]

5. Other Toxicity

a. Intraperitoneal Toxicity

Rat: LD_{50} 95 mg/kg[6]

Mouse: LD_{LO} 90 mgfkg[14]

b. Subcutaneous Toxicity

Mouse: LD_{50} 400 mg/kg[15]

B. Genotoxicity

CHP was not mutagenic in the dominant lethal assay in mice at 90 mg/kg, single intraperitoneal dose.[14]

CHP was tested at doses of 0.03 to 167 micrograms per plate in five *Salmonella typhimurium* strains (TA1535, TA1537, TA97, TA98, and TA100) in the presence and absence of rat or hamster liver S-9. CHP was positive in these tests; the lowest positive dose tested in any strain was 33 micrograms per plate.[16]

CHP was mutagenic toward Neurospora Escherichia coli 15 and in a Drosophila melanogaster test.[17,19]

C. Metabolism and Pharmacokinetics

An *in vitro* study found that CHP penetrateshuman red blood cells and is reduced by glutathione in the reaction catalyzed by glutathione peroxidase to cumenol, water, and oxidized glutathione.[20] In another study, enzymatic-reduction of CHP led to the formation of cumenol *in vitro*.[2]

D. Developmental/Reproductive Toxicity

No studies were found.

E. Subacute/Subchronic Toxicity

Two female rats exposed to 50 ppm (41.5% in cumene) for three 4-hr periods exhibited in coordination, tremors, and narcosis. One rat died. Necropsy revealed lungand kidney congestion.[22]

Six female rats exposed to 31.5 ppm (CHP dissolved in ethanol) for seven 5-hr. periods exhibited salivation, respiratory difficulty, tremors, and hyperaemia of the ear and tail. Histologic evaluation revealed emphysema and thickening of the alveolar walls.[23]

Six female rats exposed to 16 ppm (CHP dissolved in ethanol) for twelve 4.5-hr periods experienced salivation and nasal irritation. Necropsy revealed all organs were normal.[22]

Groups of 10 male and 10 female rats were exposed to 1, 6, 31, or 124 mg/rn^3 (delivered as an aerosol) for 6 hr/day,5 days/week, for 3 months The 124 mg/rn^3 level was terminated after 5 days because of mortality, and the surviving animals were sacrificed on Day 12. Eye, respiratory tract, and stomach irritation were noted in this group. No effects were noted at 31 mg/rn^3 (5 ppm) or below.[23]

F. Chronic Toxicity and Carcinogenicity

Weekly subcutaneous injections of 3.3 mg CHP were administered to 30 mice. One fibrosarcoma

developed. Duration of test was 535 days.[24]

A 1% benzene solution of CHP was applied to the clipped skin of 30 mice three times per week, for their lifetime. Median survival time was 455 days. None of the mice developed papillomas or carcinomas.[25]

Female rats were administered 100 mg CHP subcutaneously once per week for 77 weeks. No tumors were produced.[26]

V. HUMAN USE AND EXPERIENCE

A manufacturer reported worker exposure levels to CHP of between <0.002 and 0.01 mg/rn^3 during the manufacturing of phenol. The manufacturer is not aware of any medical problems resulting from inhalation of CHP.[27]

VI. RATIONALE

CHP is severely irritating to the eyes and skin. CHP has moderate, acute toxicity by ingestion, inhalation, and dermal absorption. Even though there were conflicting data concerning acute inhalation toxicity, other CHP subacute and subchronic toxicity data support the Floyd study. A 3-month inhalation study established a no-effect level of 31 mg/rn^3 (5 ppm). Animals exposed to 16 ppm for 12 days experienced irritation; however, all organs were normal. Dermal carcinogenicity studies were negative. An occupational Exposure Level (OEL) guide of 1 ppm as an 8-hr time-weighted average (TWA) should prevent irritation and systemic effects in workers. A skin notation is recom-mended on the basis of dermal absorption data.

VII. RECOMMENDED OEL GUIDE

8-hr TWA: 1 ppm (6 mg/m^3), skin

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