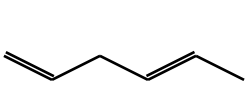
1,4-Hexadiene

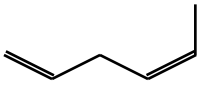
Document History
Published: 2029
Rebranded: 2025

I. IDENTIFICATION

Chemical Name: 1,4-Hexadiene
Synonyms: 1-Allylpropene (exists as cis- and trans-stereoisomers)
CAS Number: 592-45-0 (mixture of cis- and trans-isomers); 7319-00-8 (trans-isomer); 7318-67-4 (cis-isomer)
Molecular Formula: C_6H_{10}
Structural Formula:



trans-1,4-hexadiene



cis-1,4-hexadiene

II. CHEMICAL AND PHYSICAL PROPERTIES[1–5]

Physical State: clear, colorless liquid.
Molecular Weight: 82.15
Conversion Factors: 1 ppm = 3.36 mg/m^3; 1 mg/m^3 = 0.298 ppm (v/v) at 25°C
Boiling Point: 64-66°C (147–151°F) at 760 mm Hg
Melting Point: -170°C (-274°F)
Vapor pressure: 170 mm Hg at 25°C (77°F)
Saturated Vapor Concentration: 224,000 ppm at 25°C (77°F)
Odor Description and Threshold: no information found
Vapor Density: 2.83
Flammability Limits:
Lower explosive limit: 2% in air
Upper explosive limit: 6% in air
Flash Point (closed cup): -25°C (-13°F)
Specific Gravity: 0.71 @ 20°C (68°F)
Solubility: insoluble in water; soluble in ethanol
Log P_{ow}: 2.94
Stability: Stable
Reactivity and Incompatibilities: Avoid strong oxidizers.

III. USES

1,4-hexadiene is used in the production of synthetic elastomers.

IV. ANIMAL TOXICITY DATA

A. Acute Toxicity and Irritancy

1. Oral Toxicity

No deaths were observed in rats administered 20,000 mg/kg.[2]

Doses of 1,4-hexadiene (99% cis-isomer) made up to 2 ml with ethanol were administered by oral gavage to B6C3F1 male mice with the following results[3]:

1,4-hexadiene	Ethanol	Mortality
1.5 mL/kg (1050 mg/kg)	0.5 mL/kg	4/4
0.75 mL/kg (525 mg/kg)	1.25 mL/kg	1/4
0.15 mL/kg (105 mg/kg)	1.85 mL/kg	2/4
0 mL/kg (0 mg/kg)	2.0 mL/kg	0/4

2. Eye Irritation

1,4-hexadiene caused slight to mild transient conjuctival irritation with no injury to the cornea or iris in a rabbit.[2]

3. Skin Absorption

No information found.

4. Skin Irritation

No information found.

5. Skin Sensitization

No information found.

6. Inhalation Toxicity

Single exposure of groups of four albino ChR-CD male rats to 1,4-hexadiene vapors in a bell jar resulted in the following:

Concentration	Duration	Mortality
60,000 ppm	44 min	4/4
30,000 ppm	4 hr	1/4
15,000 ppm	4 hr	0/4

Signs of toxicity included rapid and forced respiration at 60,000 ppm and rapid and shallow respiration at 15,000 and 30,000 ppm. Tremors and unconsciousness were observed at 30,000 and 60,000 ppm. Recovery was rapid in animals that survived exposure. Necropsy findings in animals that died during exposure showed pulmonary congestion, edema of the brain, and distension of the urinary bladder.[2]

A 2-day 6-hr/day inhalation study was conducted with 1,4-hexadiene (99% cis-isomer inhibited with approximately 100 ppm tert-butyl catechol by weight) using B6C3F1 male mice and Crl CDBR male rats with the following results[3]:

Concentration (v/v in air)	Mortality	
	Rats	***Mice***
10,000 ppm	0/4	4/4
3260 ppm	0/4	4/4
1000 ppm	0/4	0/4

B. Subacute

In a 2-week inhalation study, groups of rats were exposed 6/hr/day 5 days/week to 500; 2500; or 10,000 ppm of 1,4-hexadiene. No clinical signs of toxicity were observed in the exposed rats. During the exposure portion of the study at 10,000 ppm, body weights and body weight gain were decreased; relative liver weights were increased and clinical pathology revealed leukopenia, lymphopenia, eosinopenia and hypercholesterolemia. Urine was increased in volume and pH and decreased in osmolality of. None of these differences from controls was found in rats allowed a 14-day recovery period after exposure. No histopathological change was found in any of the exposed rats. The no observed effect adverse level (NOAEL) was 2500 ppm.[2]

C. Subchronic Toxicity

No information found.

D. Chronic Toxicity and Carcinogenicity

No information found.

E. Developmental and Reproductive Toxicity

No information found.

F. Genotoxicity and Mutagenicity

1,4-hexadiene was tested for mutagenic activity in *Salmonella typhimurium* strains TA1535, TA97, TA98 and TA100 in the presence and absence of activation. Under the conditions of this assay 1,4-hexadiene is negative.[2]

Three trials were conducted in an *in vitro* mouse lymphoma assay. The test material was weakly mutagenic in two out of three trials in the presence of microsomes at the top dose of 200 µg/mL. A linear trend was obtained in those trials where weak mutagenicity was noted. Significant cytotoxicity was also observed.[6]

A mouse bone marrow micronucleus study was conducted on 1,4-hexadiene (99% cis-isomer) with groups of ten 8 to 9 week old B6C3F1 male mice with 1,3-butadiene used as a positive control. The mice were exposed by inhalation 6 hr/day for 2 days as shown below[7]:

Group	Description	Test Material	Concentration (ppm)
I	Control	Air	0
II	Low	1,4-hexadiene	492
III	High	1,4-hexadiene	1010
IV	Positive Control	1,3-butadiene	1081

Bone marrow samples were collected for evaluation 24 hr after exposure.

Based on overall information obtained from the two statistical analyses 1,4-hexadiene seems to induce a statistical increase ($p = 0.05$) in micronucleus formation in the bone marrow at 492 ppm and 1010 ppm when compared to air controls. Also, a dose-response ($p < 0.05$) was observed for the mean micronucleated polychromatic erythrocytes. A dose-related statistically significant decrease ($p < 0.01$) in the mean percent of polychromatic erythrocytes at 1010 ppm when compared with air control was also observed. This decrease is considered to be an indication of bone marrow cytotoxicity. Under the conditions of the test 1,4-hexadiene is considered to be weakly clastogenic in bone marrow.[4]

1,4-hexadiene was tested in an *in vitro* cytogenics assay using duplicate human lymphocyte cultures from male and female donors in two independent experiments with and without microsomes. The highest concentration level of 821.5 µg/mL was cytotoxic. 1,4-hexadiene induced a significantly higher frequency in chromosome aberrations at concentrations of 281.8 and 402.5 µg/mL in Trial 1 and 436.6 and 485.1 µg/mL in Trial 2 than those in the concurrent negative control cultures. 1,4-Hexadiene was weakly clastogenic without activation only.[6]

G. Metabolism and Pharmacokinetics

1. Metabolism

No information found.

2. Pharmacokinetics

No information found.

V. HUMAN USE AND EXPERIENCE

No information found.

VI. RATIONALE

In a 2-day inhalation study no deaths were observed in mice at 1000 ppm 1,4-hexadiene and in rats up to 30,000 ppm 1,4-hexadiene. The no observed adverse effect level (NOAEL) was 2500 ppm in a 2-week 6/hr/day 5 days/week study in mice and 15,000 ppm in rats.

1,4-hexadiene was found to be weakly mutagenic in the mouse lymphoma assay and negative in the Ames. 1,4-Hexadiene was also weakly clastogenic in the mouse micronucleus assay and in human lymphocytes.

Based on the ten-fold interspecies difference in toxicity between rats and mice and weak mutagenic and clastogenic effects, an OEL of 10 ppm is recommended.

VII. RECOMMENDED OEL

10 ppm (34 mg/m^3) as an 8-hour time weighted average.

VIII. REFERENCES

1. **Sax, N.I. and R.J. Lewis, Sr.:** *Hawley's Condensed Chemical Dictionary*, 11th edition. New York: Van Nostrand Reinhold Co., 1987. p. 598.
2. **E.I. DuPont de Nemours Company:** 1,4-Hexadiene Studies (Report No. 42-62), Haskell Laboratory. Newark, DE: E.I. du Pont de Nemours Co., 1993.
3. **Exxon Chemical Company:** Notification of Substantial Risk Under TSCA Section 8(e). [Letter to U.S. Environmental Protection Agency Containing Report on 1,4-Hexadiene, with Attachment (EPA/OTS Doc. #88-900000231)]. Houston, TX: Exxon Chemical Co., August 15, 1990.
4. **Acros Organics:** Material Safety Data Sheet for 1,4-hexadiene (Mixture of Cis and Trans), 99%. Fairlawn, NJ: Acros Organics, 1996.
5. **Weast, R.C., Ph.D. (ed.):** *CRC Handbook of Chemistry and Physics*, 69th edition. Boca Raton, Florida: CRC Press Inc., 1989. p C-302.
6. **E.I. DuPont de Nemours Company:** Support Letter from DuPont Haskell Laboratory to U.S. EPA Re Results of 2 Genetic Toxicity Studies (Mutagenicity and Chromosomal Aberration Assay) of 1,4-Hexadiene. Microfiche No. OTS 0527776-2. Newark, DE: E.I. DuPont de Nemours Company, June 24, 1998.
7. **Exxon Chemical Company:** *In Vivo* Mammalian Bone Marrow Micronucleus Assay — Inhalation Dosing Method, Project No. 181430. [Follow-up Information to U.S. EPA on 8E HQ-0990-1061] Exxon Biomedical Sciences, Inc. East Millstone, NJ: Exxon Chemical Co., February 28, 1991.