

**2-Ethyl-2-hexenal**  
**[645-62-5]**

**Review of Toxicological Literature**

*Prepared for*

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## EXECUTIVE SUMMARY

The nomination of 2-ethyl-2-hexenal (645-62-5) by the NIEHS to the ICCEC for testing is based on high production volumes and the potential for human exposure, and the lack of data on carcinogenicity.

In commercial production processes, 2-ethyl-2-hexenal is converted from n-butyraldehyde by an aldol condensation reaction. 2-Ethyl-2-hexenal is also an intermediate in the production of 2-ethylhexanol from n-butyraldehyde. Approximately 34 million pounds (15,419 metric tons [Mg]) of n-butyraldehyde was converted to 2-ethyl-2-hexenal in 1993, and the average annual growth rate for the U.S. consumption of 2-ethyl-2-hexenal is estimated to be 3.3% between 1993 and 1998.

2-Ethyl-2-hexenal is used in the manufacturing of insecticides, as an intermediate in organic synthesis, and in warning and leak detectors. 2-Ethyl-2-hexenal and its acid have a strong antifungal activity which makes them useful for the preservation of moist plant materials such as straw, grains, hay, and silage. In addition to its fungicidal activity, 2-ethyl-2-hexenal is also effective as an antimicrobial and acaricidal agent.

2-Ethyl-2-hexenal has been identified as a minor constituent found in both raw and cooked meat. Although no data on occupational exposure were found, there is the potential for exposure to 2-ethyl-2-hexenal during its production or during the production of 2-ethylhexanol from n-butyraldehyde.

In rats exposed to a concentrated vapor of 2-ethyl-2-hexenal (dose not provided) for 8 hours, no mortality was observed.

C3H-CUM mice exposed to undiluted 2-ethyl-2-hexenal (amount not provided) by skin-painting for up to 23 months did not exhibit observable tumors.

2-Ethyl-2-hexenal, in either the presence or absence of metabolic activation, did not induce *his* gene mutations in *Salmonella typhimurium*. Strains TA97, TA98, TA100, and TA1535 were exposed to doses of 3 to 666 µg/plate (0.02 to 5.28 µmol/plate) using the pre-incubation method. Metabolic activation consisted of 10% and 30% rat and hamster liver S9 mix. No other genetic toxicology data were found.

No data on chemical disposition, metabolism, toxicokinetics, teratogenicity and embryotoxicity, immunotoxicity, or structure-activity relationships were found.

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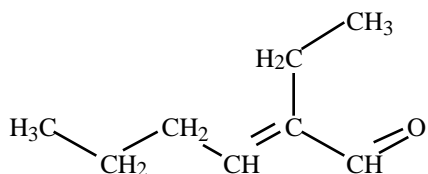
## 1.0 BASIS OF NOMINATION TO THE ICCEC

The nomination of 2-ethyl-2-hexenal [645-62-5] by the NIEHS to the ICCEC for testing is based on high production volumes and the potential for human exposure, and the lack of data on carcinogenicity.

## 2.0 CHEMICAL PROPERTIES

2-Ethyl-2-hexenal

[645-62-5]



### 2.1 Chemical Identification

2-Ethyl-2-hexenal (C<sub>8</sub>H<sub>14</sub>O, mol. wt. = 126.22) is also called:

Ethylpropylacrolein	2-Ethyl-3-propylacrolein
2-Ethyl-2-hexen-1-al	2-Ethyl-3-propylacrylaldehyde
2-Ethylhexenal	-Ethyl- -propylacrolein
2-Hexenal, 2-ethyl-	Acrolein, 2-ethyl-3-propyl-
-Ethyl- -N-propylacrolein	2-Ethylhex-2-enal

2-Ethyl-2-hexenal has the designation for shipping UN 1991.

## 2.2 Physical-Chemical Properties

Property	Information	Reference
Color	Yellow	HSDB (1996); Lewis (1993)
Physical State	Liquid	Lewis (1993)
Odor	Sharp, irritating	HSDB (1996)
Flash Point, °C	68.3	Lewis (1993)
Boiling Point, °C	175	HSDB (1996)
Specific Gravity (at 15 °C)	0.8518	HSDB (1996)
Vapor Pressure, mm Hg, at 20 °C	1	NTP Chem. Repository (1991)
Solubility at 21 °C:		
Water (g/100 mL)	0.07	HSDB (1996)
Organic Solvents (g/100 mL)	100	NTP Chem. Repository (1991)
Heat of Combustion (cal/g)	-8670	CHRIS (1991)

2-Ethyl-2-hexenal exhibits moderate flammability when exposed to heat or flame, and can react with oxidizing materials (OHM/TADS, 1985; HSDB, 1996). Fires caused by 2-ethyl-2-hexenal can be controlled using a dry chemical, carbon dioxide, or a halon extinguisher (NTP Chem. Repository, 1991). Technical grade 2-ethyl-2-hexenal can be stored at ambient conditions, and remains stable during transport (CHRIS, 1991; HSDB, 1996).

## 2.3 Purity and Commercial Availability

No data were found.

## 3.0 COMMERCIAL PRODUCTION PROCESSES

2-Ethyl-2-hexenal is converted from n-butyraldehyde by an aldol condensation reaction. 2-Ethyl-2-hexenal is also an intermediate in the production of 2-ethylhexanol from n-butyraldehyde (Anonymous, 1996; Kirshenbaum and Inchalik, 1985).

#### **4.0 PRODUCTION VOLUMES**

Approximately 34 million pounds (15,419 Mg) of n-butyraldehyde was converted to 2-ethyl-2-hexenal in 1993, and the average annual growth rate for the U.S. consumption of 2-ethyl-2-hexenal is estimated to be 3.3% between 1993 and 1998 (SRI International, 1997). Union Carbide is the only listed production site (OHM/TADS, 1985); however, in December, 1996, 5 domestic producers (Aristech, BASF, Eastman, Shell, and Union Carbide) of 2-ethylhexanol derived from n-butyraldehyde combined for a total domestic production of 865 million pounds (393,278 Mg) (Anonymous, 1996).

#### **5.0 USES**

2-Ethyl-2-hexenal is used in the manufacturing of insecticides, as an intermediate in organic synthesis, and in warning and leak detectors (Lewis, 1993; HSDB, 1996). 2-Ethyl-2-hexenal and its acid have a strong antifungal activity which makes them useful for the preservation of moist plant materials such as straw, grains, hay, and silage (Riedmann et al., 1981 abstr.; Lyr and Banasiak, 1983 abstr.; Banasiak et al., 1984 abstr.; Dunsing et al., 1987 abstr.). In addition to its fungicidal activity, 2-ethyl-2-hexenal is also effective as an antimicrobial and acaricidal agent (Beilfuss, 1976 abstr.; Lauche et al., 1989 abstr.).

#### **6.0 ENVIRONMENTAL OCCURRENCE**

##### **6.1 Occurrence**

No data were found on the environmental occurrence of 2-ethyl-2-hexenal; however, since this compound is produced in high volumes, the potential for environmental contamination exists.

##### **6.2 Persistence**

The biodegradation of 2-ethyl-2-hexenal was described as moderate (OHM/TADS,

1985).

The persistence of 2-ethyl-2-hexenal when used to inhibit fungi in moist grain storage was studied (Dunsing et al., 1987 abstr.). The oxidation of pure 2-ethyl-2-hexenal was found to be a first order reaction, and the main products were 2-ethyl-2-hexenoic acid, 3-heptanone, butyric acid, and an unidentified compound. The half life of 2-ethyl-2-hexenal on barley and wheat was 14 and 49 hours, respectively.

## 7.0 HUMAN EXPOSURE

2-Ethyl-2-hexenal has been identified as a minor constituent of both raw (King et al., 1993) and cooked beef (King et al., 1995). Although no data on occupational exposure were found, the potential for exposure to 2-ethyl-2-hexenal during its production or during the production of 2-ethylhexanol from n-butyraldehyde exists.

## 8.0 REGULATORY STATUS

No data were found.

## 9.0 TOXICOLOGICAL DATA

**Summary:** In rats exposed to a concentrated vapor of 2-ethyl-2-hexenal (dose not provided) for 8 hours, no mortality was observed.

C3H-CUM mice exposed to undiluted 2-ethyl-2-hexenal (amount not provided) via dermal application for up to 23 months did not exhibit observable tumors.

2-Ethyl-2-hexenal, with or without metabolic activation, did not induce *his* gene mutations in *Salmonella typhimurium*. Strains TA97, TA98, TA100, and TA1535 were exposed to doses of 3 to 666 µg/plate (0.02 to 5.28 µmol/plate) using the pre-incubation method in the presence and absence of 10% and 30% rat and hamster liver S9 mix. No other genetic toxicology data were found.

No data on chemical disposition, metabolism, toxicokinetics, teratogenicity and



embryotoxicity, immunotoxicity, or structure-activity relationships were found.

## 9.1 Human Data

The vapor of 2-ethyl-2-hexenal is a moderate skin and eye irritant (HSDB, 1996). Contact with the liquid form of 2-ethyl-2-hexenal may result in first-degree burns on short exposure, and second-degree burns on long exposure (CHRIS, 1991). 2-Ethyl-2-hexenal is an ingestive and inhalative toxin and may pose a biochemical oxygen demand problem in an acute exposure situation. The chronic hazard level for 2-ethyl-2-hexenal is unknown (OHM/TADS, 1985). 2-Ethyl-2-hexenal has been identified as an impurity in 2-ethylhexanol, which creates a potential risk for co- exposure of 2-ethyl-2-hexenal and 2-ethylhexanol (Novrocik et al., 1987 abstr.).

## 9.2 General Toxicology

### 9.2.1 Chemical Disposition, Metabolism, and Toxicokinetics

No data were found.

### 9.2.2 Acute Exposure

Acute toxicity values for 2-ethyl-2-hexenal are presented in **Table 1**; other acute exposure data are presented in **Table 2**.

No mortality was observed in 6 rats (age and strain not specified) exposed to concentrated 2-ethyl-2-hexenal vapor (dose not provided) for 8 hours (Gaunt et al. 1971; cited by Brabec, 1993).

**Table 1. Acute Toxicity Values for 2-Ethyl-2-hexenal**

Route	Species (strain)	LD <sub>50</sub>	Reference
dermal	guinea pig (strain n.p.)	> 17,036 mg/kg (> 135.0 mmol/kg)	Gaunt et al. 1971; cited by Brabec, 1993
oral	rat (strain n.p.)	3,000 mg/kg (23.8 mmol/kg)	Gaunt et al. 1971; cited by Brabec, 1993
	rat (strain n.p.)	500 to 5,000 mg/kg (4.0 to 39.6 mmol/kg)	CHRIS, 1991

Abbreviations: n.p. = not provided

### 9.2.3 Short-Term and Subchronic Exposure

No data were found.

### 9.2.4 Chronic Exposure

The only chronic exposure data found for 2-ethyl-2-hexenal is presented in **Section 9.4** and in **Table 3**.

### 9.3 Teratogenicity and Embryotoxicity

No data were found.

### 9.4 Carcinogenicity

The study described in this section is presented in **Table 3**.

Forty C3H-CUM mice were exposed to undiluted 2-ethyl-2-hexenal (dose not provided) by skin-painting (site not specified) for 23 months (dosing intervals not provided) (Union Carbide, 1962). Thirty-six mice survived the first 12 months of skin-painting, 20 were alive after 17 months, and the last mouse died during month 23. None of the mice developed observable

tumors.

**Table 2. Acute Toxicity of 2-Ethyl-2-hexenal**

Species Strain, Age	Number of Animals	Chemical Form, Purity	Dose	Exposure/ Observation Period	Results/Comments	Reference
rat (strain, age n.p.)	exposed: 6 controls: 0	2-ethyl-2-hexenal, purity n.p.	n.p.	8 hours	Exposed to a concentrated vapor; no mortality was observed.	Gaunt et al., 1971; cited by Brabec, 1993

Abbreviations: n.p. = not provided

**Table 3. Carcinogenicity of 2-Ethyl-2-hexenal**

Species Strain, Age	Number of Animals	Chemical Form, Purity	Dose	Exposure/ Observation Period	Results/Comments	Reference
mouse (C3H-CUM, age n.p.)	exposed: 40 controls: 0	2-ethyl-2-hexenal, purity n.p.	n.p.	23 months of exposure by skin-painting; no post-treatment observation period	36 mice survived at least one year, 20 mice survived at least 17 months, and the last mouse died in month 23. None of the mice developed observable tumors. No other data provided.	Union Carbide, 1962

Abbreviations: n.p. = not provided

## 9.5 Genotoxicity

The study described in this section is presented in **Table 4**.

As reported by Zeiger et al. (1988), 2-ethyl-2-hexenal in either the presence or absence of metabolic activation did not induce *his* gene mutations in *Salmonella typhimurium*. Strains TA97, TA98, TA100, and TA1535 were exposed to doses of 3, 10, 33, 100, 166, 333, and 666 µg/plate (0.02, 0.08, 0.26, 0.79, 1.32, 2.64, and 5.28 µmol/plate) using the pre-incubation method in the presence and absence of 10% and 30% rat and hamster liver S9 mix.

No other genetic toxicology data were found.

## 9.6 Immunotoxicity

No data were found.

## 10.0 STRUCTURE-ACTIVITY RELATIONSHIPS

No data were found.

## 11.0 ONLINE DATABASES AND SECONDARY REFERENCES

### 11.1 Online Databases

#### Chemical Information System Files

TSCATS (Toxic Substances Control Act Test Submissions)

CHRIS

SANSS

#### DIALOG Files

359 Chemical Economics Handbook

161 NIOSHTIC (Occupational Safety and Health)

302 Kirk-Othmer Encyclopedia of Chemical Technology

Internet Databases

NTP Chemical Repository. 1991. 2-Ethyl-2-hexenal. Radian Corporation. Last Updated: August 29, 1991. Internet URL: [http://ntpdb.niehs.nih.gov/NTP\\_Re...m\\_H&S/NTP\\_Chem6/Radian645-62-5.txt](http://ntpdb.niehs.nih.gov/NTP_Re...m_H&S/NTP_Chem6/Radian645-62-5.txt).

National Library of Medicine Databases

EMIC and EMICBACK (Environmental Mutagen Information Center)

**Table 4. Genotoxicity of 2-Ethyl-2-hexenal**

Test System	Biological Endpoint	S9 Metabolic Activation	Chemical Form, Purity	Dose	Endpoint Response	Comments	Reference
<i>S. typhimurium</i> strains TA97, TA98, TA100, and TA1535	<i>his</i> reverse gene mutations	-/+ 10% and 30% rat and hamster S9 mix	2-Ethyl-2-hexenal, purity n.p.	3, 10, 33, 100, 166, 333, and 666 µg/plate (0.02, 0.08, 0.26, 0.79, 1.32, 2.64, and 5.28 µmol/plate)	negative/negative	pre-incubation assay	Zeiger et al. (1988)

Abbreviations: n.p. = not provided

STN International Files

BIOSIS (Biological Abstracts)  
 CA File (Chemical Abstracts)  
 CANCERLIT  
 CEN (Chemical & Engineering News)  
 CHEMSAFE  
 CIN (Chemical Industry Notes)  
 CSNB (Chemical Safety News Base)  
 EMBASE (Excerpta Medica)  
 HODOC  
 HSDB (Hazardous Substances Data Bank)  
 MEDLINE (Index Medicus)  
 PROMT  
 RTECS (Registry of Toxic Effects of Chemical Substances)  
 TOXLINE  
 TOXLIT

TOXLINE includes the following subfiles:

Toxicity Bibliography	TOXBIB
International Labor Office	CIS
Hazardous Materials Technical Center	HMTC
Environmental Mutagen Information Center File	EMIC
Environmental Teratology Information Center File (continued after 1989 by DART)	ETIC
Toxicology Document and Data Depository	NTIS
Toxicology Research Projects	CRISP
NIOSHTIC7	NIOSH
Pesticides Abstracts	PESTAB
Poisonous Plants Bibliography	PPBIB
Aneuploidy	
Epidemiology Information System	EPIDEM
Toxic Substances Control Act Test Submissions	TSCATS
Toxicological Aspects of Environmental Health	BIOSIS
International Pharmaceutical Abstracts	IPA
Federal Research in Progress	FEDRIP



Developmental and Reproductive Toxicology

DART

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