ENDRIN

CAS number: 72-20-8

Synonyms: 1,2,3,4,10,10-Hexachloro-6,7-epoxy-1,4,4a,5,6,7,8,8a-octahydro-endo, endo-1,4:5,8-dimethanonaphthalene

Chemical formula: $C_{12}H_8Cl_6O$

Structural formula: —

Workplace exposure standard (retained)

TWA: **0.1 mg/m^3**

STEL: **—**

Peak limitation: **—**

Notations: **Sk.**

IDLH: **2 mg/m^3**

Sampling and analysis: The recommended value is quantifiable through available sampling and analysis techniques.

Recommendation and basis for workplace exposure standard

A TWA of 0.1 mg/m^3 is recommended to protect for effects in the liver and central nervous system (CNS) in exposed workers including headache, dizziness, weakness, muscle tremors and convulsions.

Discussion and conclusions

Endrin was formerly used as an organochlorine insecticide and rodenticide. Its use was discontinued since the late 1980s (ACGIH, 2018) and it is prohibited for use in Australia.

Critical effects include liver toxicity and CNS effects including muscle tremors and convulsions. The ACGIH (2018) base its TLV-TWA recommendations by extrapolation of acute toxicity data from animal studies and note that this concentration does not appear to result in adverse effects in humans.

Given the limited human data available, the current TWA is retained, in line with the recommended TLV-TWA from ACGIH (2018). There are no available data to refute this position and the recommended TWA of 0.1 mg/m^3 is considered protective of liver and CNS effects in exposed workers.

Recommendation for notations

Not classified as a carcinogen according to the Globally Harmonized System of Classification and Labelling of Chemicals (GHS).

Not classified as a skin sensitiser or respiratory sensitiser according to the GHS.

A skin notation is recommended based on evidence suggesting potential dermal absorption and adverse systemic effects in animals.

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APPENDIX

Primary sources with reports

Source	Year set	Standard
SWA	***1991***	***TWA: 0.1 mg/m^3***
ACGIH	***2001***	***TLV-TWA: 0.1 mg/m^3***

TLV-TWA recommended to minimise CNS effects including headache, dizziness, weakness, muscle tremors, convulsion, as well as effects on the liver. TLV-TWA based on extrapolations (not clearly presented) from acute toxicity data and oral LD_{50} values obtained from experimental animal studies due to a lack of human data (including comparison to Aldrin and dieldrin).

Dermal exposure is also significant to the overall toxicity due to lethality observed in animals after dermal application.

Summary of data:

Human data:

- Oral dose between 0.2 and 0.25 mg/kg reported to induce convulsions
  - 1.0 mg/kg caused repeated seizures, which can manifest within 3 h of exposure
- Studies on carcinogenicity unable to identify association between exposure and increased incidence of cancer in a manufacturing setting
  - 1 case study involved 233 chemical workers in a Dutch manufacturing facility, and it was reported that after 15 yr of observation, there was no evidence of increased cancer incidence in the same group of workers following exposure durations 4-13 yr.

Animal data:

- Oral LD_{50}: 1.37 mg/kg (mice), 3.0 mg/kg (monkeys), 5.3 mg/kg (rats)
- LD_{50}: 15–18 mg/kg (female and male rats, dermal)
- Acute toxicity generally targets the CNS, manifesting in the form of twitching, convulsions and coma
- Rats and mice subjected through inhalation exposure to concentration of 0.36 ppm (15 mg/m^3) for 7 h/d, 5 d/wk for 26 wk, showed no signs of intoxication or retardation of growth. However, in an experiment involving 4 rabbits under identical conditions, 2 fatalities reported
- Carcinogenic studies on mice and rats concluded no effect on tumour growth
- Some studies suggest adverse reproductive/developmental effects, as a single dose of 2.5 mg/kg administered to pregnant hamsters resulted in higher incidence of foetal death, congenital anomalies and growth retardation.

A4 carcinogenicity classification assigned based on lack of evidence in animal or human case studies.

DFG	***2012***	***MAK: 0.05 mg/m^3***

Summary of additional data:

Human data:

- Some studies reported a dose of ~100 mg/kg considered lethal
- A plant worker suffered seizures following acute inhalation exposure (quantity unknown), whilst two workers following skin contact did not develop symptoms of intoxication

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Source	Year set	Standard
• Several studies examined workers exposed for 12–24 yr showed no signs of toxicity • No increase in chromosomal aberrations observed in a study involving the peripheral lymphocytes of 8 male workers. Animal data: • Study reported fatalities in groups of 10 rats following exposure to 2,000 mg/m^3 for 1 h • Chronic feeding studies identified NOAELs: mice 0.045 mg/kg/d, 0.05 mg/kg/d rats, dogs 0.025 mg/kg/d; toxicokinetic transfer of NOAEL to a concentration in air using the following: ○ daily exposure of animals compared to the 5-d work-week exposure (7/5) ○ species-specific toxicokinetic differences between animal and human: mouse (1:7), rat (1:4) and dog (1:1.4) ○ oral absorption 90% ○ human body weight 70 kg ○ the respiratory volume 10 m^3 ○ assumed 100% absorption in lungs humans ○ corresponding concentrations 0.06, 0.11 and 0.16 mg/m^3 • Based on the rat study derivation divided by 2 and rounded down: MAK value of 0.05 mg/m^3 is established.		
SCOEL	***NA***	***NA***
No report.		
OARS/AIHA	***NA***	***NA***
No report.		
HCOTN	***NA***	***NA***
No report.		

Secondary source reports relied upon

Source		Year	Additional information
US EPA	✓	2002	• Oral RfD of 0.0003 mg/kg-d based on NOEL of 0.025 mg/kg/d and LOAEL of 0.05 mg/kg/d for mild histological lesions in liver and occasional convulsions in dogs (chronic oral bioassay)
US NIOSH	✓	2018	• TWA: 0.1 mg/m^3 [skin]

Carcinogenicity — non-threshold based genotoxic carcinogens

Is the chemical mutagenic? No

The chemical is not a non-threshold based genotoxic carcinogen.

Notations

Source	Notations
SWA	Skin

Source	Notations
HCIS	—
NICNAS	NA
EU Annex	NA
ECHA	NA
ACGIH	Carcinogenicity – A4, Skin
DFG	H (skin)
SCOEL	NA
HCOTN	NA
IARC	Carcinogenicity – Group 3
US NIOSH	—

NA = not applicable (a recommendation has not been made by this Agency); — = the Agency has assessed available data for this chemical but has not recommended any notations

Skin notation assessment

Calculation	
Conclusion:	
Adverse effects in human case study:	no
Dermal LD_{50} ≤1000 mg/kg:	yes
Dermal repeat-dose NOAEL ≤200 mg/kg:	
Dermal LD_{50}/Inhalation LD_{50} <10:	
In vivo dermal absorption rate >10%:	
Estimated dermal exposure at WES >10%:	
	consider assigning a skin notation

IDLH

Is there a suitable IDLH value available? Yes

Additional information

Molecular weight:	380.93
Conversion factors at 25°C and 101.3 kPa:	1 ppm = 15.58 mg/m^3; 1 mg/m^3 = 0.064 ppm
This chemical is used as a pesticide:	✓
This chemical is a biological product:	☐

Molecular weight:	380.93
Conversion factors at 25°C and 101.3 kPa:	1 ppm = 15.58 mg/m^3; 1 mg/m^3 = 0.064 ppm
This chemical is used as a pesticide:	✓
This chemical is a by-product of a process:	☐
A biological exposure index has been recommended by these agencies:	☐ ACGIH ☐ DFG ☐ SCOEL

Workplace exposure standard history

Year	Standard
1991	TWA: 0.1 mg/m^3

References

American Conference of Industrial Hygienists (ACGIH®). (2018). TLVs® and BEIs® with 7th Edition Documentation, CD-ROM, Single User Version. Copyright 2018. Reprinted with permission. See the *TLVs® and BEIs® Guidelines section* on the ACGIH website.

Deutsche Forschungsgemeinschaft (DFG). (1998). Endrin – MAK value documentation.

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International Agency for Research on Cancer (IARC). (1987). Endrin. IARC Monographs on the evaluation of the carcinogenic risk to humans.

US Environmental Protection Authority (US EPA) (1998) Integrated Risk Information System (IRIS) Chemical Assessment Summary – Endrin.

US National Institute for Occupational Safety and Health (NIOSH). (1994). Immediately dangerous to life or health concentrations – Endrin.

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