ENFLURANE

CAS number: 13838-16-9

Synonyms: 2-Chloro-1,1,2-trifluoroethyl difluoromethyl ether, Ethrane

Chemical formula: $C_3H_2ClF_5O$

Workplace exposure standard (amended)

TWA: **20 ppm (150 mg/m^3)**

STEL: —

Peak limitation: —

Notations: —

IDLH: —

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

Recommendation and basis for workplace exposure standard

A TWA of 20 ppm (150 mg/m^3) is recommended to protect for liver, central nervous system (CNS) and cardiovascular system effects in exposed workers.

Discussion and conclusions

Enflurane is commonly used as an anaesthetic.

Data from humans and animal studies indicate that enflurane has low acute, chronic and inhalation toxicity (DFG, 1998). No hepatotoxic effects are reported in operating theatre personnel exposed at 20 ppm (DFG, 1998). An acute behavioural effect study reported a LOAEC for the sedation effect at 2,000 ppm (ACGIH, 2018). Multiple animal studies reported no adverse effects, including organ toxicity, with repeated exposure in the range 20 to 200 ppm (DFG, 1998).

Based on the weight of evidence presented in human and animal studies, a TWA of 20 ppm is recommended and is considered sufficiently low to minimise the potential for liver, CNS and cardiovascular system 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.

There are insufficient data to recommend a skin notation.

APPENDIX

Primary sources with reports

Source	Year set	Standard
SWA	***1991***	***TWA: 0.5 ppm (3.8 mg/m^3)***
ACGIH	***2001***	***TLV-TWA: 75 ppm (566 mg/m^3)***
TLV-TWA recommended to minimise the risk of CNS and cardiovascular system effects in exposed workers. Summary of data: Human data: • Exposure to 15,000–20,000 ppm causes anaesthesia • LOAEL: 2,000 ppm (inhalation) for behavioural effects. Animal data: • LD_{50}: 3,900 mg/kg (mice, intravenous) • Negative results in mutagenicity assays • TLV-TWA is recommended based on the assumption of lower toxicity than halothane or trichloroethylene. Assigned an A4, not classified as human carcinogen. Insufficient data to recommend a skin or sensitiser notation.		
DFG	***1994***	***MAK: 20 ppm (150 mg/m^3)***
Summary of additional data: Human data: • Anaesthesia at 12,000 ppm (8 h) produced mild reversible renal function impairment • Anaesthesia (unknown concentration for 30 min) resulted in a reduction of the plasma concentration of corpus luteum hormone to 75% • Anaesthetists exposed to 3.6–22 ppm did not show abnormal liver function and haematological parameters • No hepatotoxicity effects observed in occupationally exposed personnel at 20 ppm • Negative results in mutagenicity assays. Animal data: • LC_{50}: 14,000 and 8,100 ppm (rats and mice, 3 h) • LD_{50}: 5,450 and 5,000 mg/kg (rats and mice, oral) • Exposure at 20 ppm (rats, 8 h/d, 5 d/w, up to 99 wk) produced no symptoms, parameters included pathological changes in liver, kidney, lung, heart, spleen or testes • NOAEC: 5,000 ppm (mice, 4 hr/d, 5 d/w, 76 d) parameters included pathological changes in the liver, kidneys, testes • Exposure to 140–33,000 ppm (dogs and monkeys, 3 d/wk, 4 wk) produced no symptoms, parameters included bone marrow, urine values , liver enzymes, histopathological, haematological or ophthalmological effects • Exposure at 700 and 2,000 ppm (mice, rats and guinea pigs, 35 d): ○ all animals had a reduced weight gain at 2,000 ppm		

Source	Year set	Standard
○ in mice, weight loss and mortality were recorded in both dose groups after 5 d • Exposure at 3,000 ppm (mice, 4 hr/d, 52 wk) no effects on the haematopoietic system • Multiple reproductive toxicity studies produce no result with one exception, reproductive toxicity (slight fetotoxicity) occurred after inhalation exposure at 3,200 ppm in rats • An indication of a DNA-damaging effect *in vitro* is offset by several negative *in vitro* or *in vivo* findings on genotoxicity • In long-term carcinogenicity study, no statistically significant increase in tumours could be detected.		
SCOEL	***NA***	***NA***
No report.		
OARS/AIHA	***NA***	***NA***
No report.		
HCOTN	***NA***	***NA***
No report.		

Secondary source reports relied upon

NIL.

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	—
HCIS	NA
NICNAS	NA
EU Annex	NA
ECHA	NA
ACGIH	Carcinogenicity – A4
DFG	—
SCOEL	NA
HCOTN	NA
IARC	NA

Source	Notations
US NIOSH	NA

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

There are insufficient evidence to recommend a skin notation.

IDLH

Is there a suitable IDLH value available?	No

Additional information

Molecular weight:	184.49
Conversion factors at 25°C and 101.3 kPa:	1 ppm = 7.57 mg/m^3; 1 mg/m^3 = 0.132 ppm
This chemical is used as a pesticide:	☐
This chemical is a biological product:	☐
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
Click here to enter year	

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) Enflurane – MAK value documentation.