

DISULFIRAM

CAS number: 97-77-8

Synonyms: Tetraethyl thiuram disulphide, Antabuse, bis(Diethylthiocarbamoyl) disulphide, TETD, tetraethylthiuram

Chemical formula: $C_{10}H_{20}N_2S_4$

Structural formula: —

Workplace exposure standard (retained)

TWA: 2 mg/m³

STEL: —

Peak limitation: —

Notations: DSEN

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 2 mg/m³ is recommended to minimise potential for “Antabuse-like” effects, including increased heart rate, shortness of breath, nausea and vomiting in exposed workers.

Given the limited data available from the primary sources, it is recommended that a review of additional sources be conducted at the next scheduled review.

Discussion and conclusions

Disulfiram is a drug (Antabuse™) used in the treatment of chronic alcoholism by producing an acute sensitivity to ethanol.

Critical effects include vasodilation, tachycardia and nausea. There are a lack of data for inhalation and dermal exposures in animals and humans; studies largely focus on oral exposure of the pharmaceutical grade chemical. Studies report that some workers involved in the manufacture and handling of disulfiram developed Antabuse-like effects. Experimental animal studies demonstrate the hepatotoxic effects of disulfiram following oral exposure and evidence of carcinogenicity, genotoxicity and reproductive and developmental effects remain inconclusive (ACGIH, 2018).

The recommended TWA of 2 mg/m³ is adopted from ACGIH (2001) and DFG (2007). ACGIH does not present the derivation of the TWA. DFG report that the MAK is based on observations in adults exposed at 125 mg/day which may be the therapeutic oral dose recommended for treatment of alcoholism (not qualified by DFG the daily dose nor describe how TWA was derived). This TWA is considered to be protective of the critical effects. However, an investigation of additional sources is recommended at the next scheduled review.



Recommendation for notations

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

Classified as a dermal sensitiser and not a respiratory sensitiser according to the GHS.

There are insufficient data to recommend a skin notation.

DRAFT

APPENDIX

Primary sources with reports

Source	Year set	Standard
SWA	1991	TWA: 2 mg/m³
ACGIH	2001	TLV-TWA: 2 mg/m³
<p>TLV-TWA recommended to minimise possible Antabuse-like effects in exposed workers.</p> <p>Summary of data:</p> <p>Human data:</p> <ul style="list-style-type: none"> Many studies examine disulfiram used as medication to treat chronic alcoholism report Antabuse-like symptoms including vasodilation of face and neck, tachycardia, tachypnoea followed by nausea, vomiting pallor and hypotension; occasionally, convulsion, cardiac arrhythmias and myocardial infarction may occur, amongst other complications Workers who manufacture and handle the chemical may experience these symptoms, and one investigation indicated 9% of workers developed skin irritation <ul style="list-style-type: none"> there is insufficient evidence to directly link exposure to skin irritation Consumption has been shown to have a possible therapeutic effect in severe trichloroethylene poisoning. <p>Animal data:</p> <ul style="list-style-type: none"> Oral LD₅₀: 8.6 g/kg (rats), 2.05 g/kg (rabbits) Animal studies reported that oral exposure results in increased incidence of liver cell tumours in rats and mice, and an increase in lung tumours for select mice strains Negative evidence of carcinogenic effects on male and female rats <ul style="list-style-type: none"> limited data exists for carcinogenic effects Genotoxicity studies report mixed results; positive for the induction of SCE and negative for the induction of chromosomal aberrations. <p>A4 carcinogenicity category assigned due to limited data available to allow classification. Limited animal and human studies exist regarding inhalation exposure.</p> <p>No TLV-STEL is available, and no skin or SEN notations are assigned.</p>		
DFG	2007	MAK: 2 mg/m³
<p>Summary of additional data:</p> <p>Human data:</p> <ul style="list-style-type: none"> MAK based on observations in adults exposed to 125 mg/d, symptoms included fatigue, muscle weakness and shortness of breath Sensitiser, causing allergic response upon dermal contact, reported in several human case studies Incidence cases of exposure to high concentrations lead to peripheral neuropathy Human cases reported repeated chronic exposure (>250 mg/d) can potentially cause hepatotoxicity, encephalopathy and adverse effects on the endocrine system (impotence), among other complications. 		



Source	Year set	Standard
Animal data:		
<ul style="list-style-type: none"> Repeated exposure at 12 mg/kg/d in rats reduced glutathione levels in the liver and brain, with increased concentrations resulting in thyroid hyperplasia Results on carcinogenicity data are equivocal, with some studies reporting an increased incidence of subcutaneous fibrosarcomas and hepatomas in certain mouse strains, and other studies concluding that exposure had no effect on tumour growth Animal studies report developmental/teratogenic effects are inconclusive Experimental animal studies for inhalation and dermal exposure are not available. 		
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
NICNAS	✓ 2016	<ul style="list-style-type: none"> LD₅₀: >2,000 mg/kg (rats, dermal) Dermal application on rabbits (2,000 mg/kg) resulted in hepatotoxicity Several <i>in vitro</i> and <i>in vivo</i> studies reported positive genotoxicity results, indicating that disulfiram has a genotoxic response Animal studies did not show evidence of carcinogenicity, or reproductive/developmental toxicity.

Carcinogenicity — non-threshold based genotoxic carcinogens

Is the chemical mutagenic? Insufficient data

Is the chemical carcinogenic with a mutagenic mechanism of action? No

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

Notations

Source	Notations
SWA	Sen
HCIS	Skin sensitisation – category 1
NICNAS	Skin sensitisation
EU Annex	NA



Source	Notations
ECHA	Skin Sens. 1
ACGIH	Carcinogenicity – A4
DFG	Sh (dermal sensitiser)
SCOEL	NA
HCOTN	NA
IARC	Carcinogenicity – Group 3
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

Calculation	
Adverse effects in human case study:	No
Dermal LD ₅₀ ≤ 1000 mg/kg:	No
Dermal repeat-dose NOAEL ≤ 200 mg/kg:	No data
Dermal LD ₅₀ /Inhalation LD ₅₀ < 10:	No data
In vivo dermal absorption rate > 10%:	No data
Estimated dermal exposure at WES > 10%:	No data
A skin notation is not warranted	

IDLH

Is there a suitable IDLH value available? No

Additional information

Molecular weight:	296.54
Conversion factors at 25°C and 101.3 kPa:	1 ppm = 12.13 mg/m ³ ; 1 mg/m ³ = 0.08 ppm
This chemical is used as a pesticide:	<input type="checkbox"/>
This chemical is a biological product:	<input type="checkbox"/>
This chemical is a by-product of a process:	<input type="checkbox"/>
A biological exposure index has been recommended by these agencies:	<input type="checkbox"/> ACGIH <input type="checkbox"/> DFG <input type="checkbox"/> SCOEL

Workplace exposure standard history

Year	Standard
1991	TWA: 2 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). (2007). Disulfiram – MAK value documentation.

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European Chemicals Agency (ECHA). (2019). Disulfiram – REACH assessment.

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

National Industrial Chemicals Notification and Assessment Scheme (NICNAS). (2016).

Thioperoxydicarbonic diamide ([H₂N)C(S)]₂S₂, tetraethyl-: Human health tier II assessment – IMAP report.