DIISOPROPYLAMINE

CAS number: 108-18-9

Synonyms: N-(1-Methylethyl)-2-propanamine

Chemical formula: $C_6H_{15}N$

Workplace exposure standard (interim)

TWA: **5 ppm (21 mg/m^3)**

STEL: **—**

Peak limitation: **—**

Notations: **Sk.**

IDLH: **200 ppm**

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

Recommendation and basis for workplace exposure standard

A TWA of 5 ppm (21 mg/m^3) is recommended to protect for irritation to the eyes, skin, and respiratory tract, nausea, headache and disturbances to vision 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

Diisopropylamine is used in the production of paint pigments, pharmaceuticals, cosmetics and pesticides.

Critical effects are irritation to eyes, skin, and respiratory tract, and at higher concentrations, nausea, headache and disturbances to vision.

No primary sources (ACGIH, 2018; HCOTN, 2013) report a derivation of the currently adopted exposure standard (5 ppm), which appears to be recommended by analogy to other alkyl amines (ACGIH, 2018). Limited human data suggests that exposure at 50 ppm (100 mg/m^3) causes visual disturbances, nausea and headache. HCOTN (2013) has proposed an amended exposure limit of 1.2 ppm (5 mg/m^3) based on a sub-chronic repeat inhalation study in rats that identified a LOAEC of 100 mg/m^3 for nasal and corneal lesions and inflammation. An overall uncertainty factor of 27 is applied by HCOTN (2013) to the LOAEC of 100 mg/m^3 and the value is rounded to 5 mg/m^3.

There is no evidence for carcinogenicity in the sources, with data suggesting analogies to other structurally related alkyl amines in the absence of substance-specific information (HCOTN, 2013; OECD, 2013). There is some evidence for increased severity of the critical effects within an order of magnitude of the current TWA and this should be considered during subsequent reviews (ACGIH, 2018).

Given the inconsistencies in the primary sources, it is recommended that the TWA of 5 ppm be retained in the interim with a recommendation that a broader evaluation be conducted 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).

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

A skin notation may not be warranted based on the available evidence. However, there were inconsistencies in the data from primary sources, including dermatitis. Therefore, the skin notation is retained and an evaluation of additional sources, including dermal studies, are recommended at the next scheduled review.

APPENDIX

Primary sources with reports

Source	Year set	Standard
SWA	***1991***	***TWA: 5 ppm (21 mg/m^3)***
ACGIH	***2001***	***TLV-TWA: 5 ppm (21 mg/m^3)***
TLV-TWA intended to minimise potential for irritation to the eyes, skin, and respiratory tract, as well as nausea, headache, and disturbances to vision. A skin notation is assigned by analogy to several structurally related alkyl amines. Insufficient data available to recommend a TLV-STEL or notations for carcinogenicity or sensitisation. Summary of data: Derivation of the TLV-TWA is not discussed in the assessment. The value is based on experiences in industrial practice, which are not thoroughly documented, but informed by assessments of isopropyl amine and other structurally related alkyl amines. Human data: • Disturbance in vision, nausea, and headache reported for workers exposed to an average 25–50 ppm (no further information provided) • Prolonged skin contact likely to cause dermatitis, but no evidence supporting the assertion Animal data: • Oral LD_{50}: 770 mg/kg (rats) • Severe pulmonary irritant in both acute and chronic exposures with several animal models (no further information provided) • Corneal clouding at >600 ppm in several animal models (no further information provided) • Exposure to 2,200 ppm was lethal (guinea pigs, rabbits, cats, rats, <3 h); 1,000 ppm was lethal after 4 h (species not disclosed) o all species survived single exposure to 777 ppm for 7 h, but guinea pigs and rabbits died during second exposure • Sub-chronic inhalation study 40 exposures at 600 ppm (guinea pigs, rabbits, 7 h/d, 5 d/wk 8 wk duration) o all rabbits and half the guinea pigs died at the 20th exposure o no changes in blood cells following exposure o observed corneal cloudiness caused by superficial contact with the substance.		
DFG	***NA***	***NA***
No report.		
SCOEL	***NA***	***NA***
No report.		
OARS/AIHA	***NA***	***NA***
No report.		

Source	Year set	Standard
HCOTN	***2003***	***TWA: 5 ppm (20 mg/m^3)***

Summary of additional data:

A revised TWA of 1.2 ppm (5 mg/m^3) is recommended based on a sub-chronic repeat inhalation study with rats. An overall uncertainty factor of 27 is applied to the LOAEL of 100 mg/m^3 to account for the absence of a NOAEL, and intra- and interspecies variability (individual uncertainty factors were not specific). This result is rounded up to TWA of 5 mg/m^3. No data on potential carcinogenicity or reproductive toxicity available in this source

Human data:

- Several cases of visual disturbance, nausea and headaches reported in accidental exposures at distillation plant
    - visual distress occurred in 2–3 h of exposure and lasted for 2 h
    - mean atmospheric concentrations in the plant were 25–50 ppm with peak concentrations of 180 ppm, which lasted for ≈5–10 min 3 times a day
- Used as an intravenous anti-hypersensitive agent in clinical pharmacology to reduce blood pressure (25–200 mg as hydrochloride salt).

Animal data:

- LC_{50}: 1,140 ppm (rats, 2 h), 1,000 ppm (mice, 2 h); clinical observations included laboured breathing, high pitched respiratory sounds, closed eyelids, nasal and ocular discharges, ocular opacity and tremors
- Repeat inhalation study with 24, 144, and 480 ppm concentrations (rats, 15/sex/group, 6 h/d, 5 d/wk, 1 mo):
    - 3 rats in 480 ppm group died; additional effects in this group included respiratory difficulties, mucous membrane irritation, body weight reduction, and increased weight of adrenals, kidneys, and heart
    - dose-dependent incidence of corneal lesions (13, 75, 100% in low, mid, to high exposure groups, respectively)
    - all treated rats (144–480 ppm) showed mucosal inflammation and erosion; necrosis/dissolution of nasal cartilage/bone
    - LOAEL of 24 ppm because it caused reduced immune cell count, and corneal and nasal lesions
- LD_{50}: 2,900 mg/kg (rabbits, dermal)
- Median respiratory depression (RD_{50}): 161 ppm (mice, oronasal, 15 min), 102 ppm (mice, intratracheal, 2 h); concluded that substance is a lower respiratory tract irritant
- Severe eye irritation in rabbits (using 5%, 15%, and 100% solutions)
- Moderate to severe skin irritation in dermal application study, treatment range: 150, 450, 2,000 mg/kg/d (rats, 5 d); no irritation in 150 mg/kg/d group
- Non-sensitising in patch test with 0.3 mL of 10% solution (rabbits, 6 h/d, 3 d/wk, 3 wk induction phase, insult after 2 wk with 5% solution)
- Mutation tests with *S. typhimurium* are equivocal and DNA repair tests with rat hepatocytes were negative.

Secondary source reports relied upon

Source		Year	Additional information
HSE	✓	2002	TWA: 5 ppm (21 mg/m^3).

Source		Year	Additional information
OECD	✓	2013	• Grouped with other secondary alkyl amines, but may be metabolised differently due to isopropyl substituents • Not considered mutagenic by analogy to other alkyl amines examined in assessment • Negative carcinogenicity results in chronic inhalation study with 0.32 mg/L dimethyl amine or 0.37 mg/L diethyl amine (rats, 2 yr).
US NIOSH	✓	1994	IDLH based on acute inhalation toxicity data in workers.

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	Skin
HCIS	—
NICNAS	NA
EU Annex	—
ECHA	NA
ACGIH	Skin
DFG	NA
SCOEL	NA
HCOTN	Skin
IARC	NA
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:	
Dermal LD_{50}/Inhalation LD_{50} <10:	
In vivo dermal absorption rate >10%:	
Estimated dermal exposure at WES >10%:	
	a skin notation is not warranted

IDLH

Is there a suitable IDLH value available?	Yes

Additional information

Molecular weight:	101.19
Conversion factors at 25°C and 101.3 kPa:	1 ppm = 4.13 mg/m^3; 1 mg/m^3 = 0.242 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.

Health Council of the Netherlands (HCOTN) (2003) Diisopropylamine. Health-based calculated occupational cancer risk values. The Hague: Health Council of the Netherlands; publication no. 2000/15OSH/080.

Organisation for Economic Cooperation and Development (OECD) (2013) SIDS initial assessment profile – Aliphatic Secondary Amines.

Tenth Adaptation to Technical Progress Commission Regulation (EU Annex) No 2017/776 amending, for the purposes of its adaptation to technical and scientific progress, Regulation (EC) No 1272/2008 of the European Parliament and of the Council on classification, labelling and packaging of substances and mixtures (the CLP Regulation).

UK Health and Safety Executive (HSE) (2002) EH40/2005 Workplace exposure limits.

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