

PIPERIDINE

CAS number: 110-89-4

Synonyms: —

Chemical formula: $(\text{CH}_2)_5\text{NH}$

Structural formula: —

Workplace exposure standard (retained)

TWA: 1 ppm (3.5 mg/m³)

STEL: —

Peak limitation: —

Notations: Sk.

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 1 ppm (3.5 mg/m³) is recommended to protect for decreased motor activity and eye and upper respiratory tract irritation in exposed workers.

Discussion and conclusions

Piperidine is used as a solvent and an ingredient in fuels and oils. It is also used as a curing agent for rubber and epoxy resins.

Critical effects of exposure include decreased motor activity, blanching, upper respiratory tract irritation and nasal secretions.

Very limited human toxicological data are available. An irritation threshold of 26 ppm is established from a volunteer study and odour is considered intolerable at between 2 and 5 ppm (HSE, 1993; OARS, 1996). Animal eye and dermal studies show piperidine to be severely irritating with permanent corneal injury, necrosis, oedema reported. Altered brain electrical activity, effects on the cardiovascular system and sperm generation and some loss of function in the liver and kidneys following exposure at 2.9 ppm for four months is reported in inhalation studies in animals (species not stated). A NOAEC of 20 ppm (70 mg/m³) is identified in a 28-day inhalation study in rats for slightly decreased body weight gain in males and increased liver weight in females (NICNAS, 2016; ECHA, 2019). This NOAEC is used as a point of departure by ECHA (2019) to calculate a derived no effect level (DNEL) of 7.05 mg/m³ (approximately 2 ppm).

Based on the reported intolerable odour at a concentration as low as 2 ppm, adverse systemic effects in animals at 2.9 ppm in a sub-chronic study and the DNEL of 2 ppm, the SWA TWA of 1 ppm (3.5 mg/m³) derived by OARS/AIHA (1996) is recommended to be retained. The recommended TWA is expected to protect for irritant effects in exposed workers and minimise the potential for adverse effects on the CNS.

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.

DRAFT

APPENDIX

Primary sources with reports

Source	Year set	Standard
SWA	1991	TWA: 1 ppm (3.5 mg/m³)
Adopted from UK HSE.		
ACGIH	NA	NA
No report.		
DFG	NA	NA
No report.		
SCOEL	NA	NA
No report.		
OARS/AIHA	1996	TWA: 1 ppm (3.5 mg/m³)
Summary of data: TWA derived on analogy to 2-aminopyridine and ACGIH TLV of 0.5 ppm. Not considered as acutely toxic as 2-aminopyridine. Given irritation and odour thresholds, a WEEL (TWA) of 1 ppm is considered adequate. No derivation or further information provided.		
Human Data:		
<ul style="list-style-type: none"> • Respiratory irritation at 26 ppm • Odour intolerable at 2–5 ppm • Skin exposure to liquid for <3 min caused severe epithelial damage. 		
Animal Data:		
<ul style="list-style-type: none"> • Oral LD₅₀: 133 mg/kg (female rats); 200 mg/kg (male rats), acute haemorrhage of stomach, necrosis, ulceration and congestion of kidneys • Oral LD₅₀: 145 mg/kg (rabbits); 30 mg/kg (mice) • Severe skin irritant to rats, mice, guinea pigs (no further information) • Dermal LD₅₀: 275 mg/kg (rats); 320 mg/kg (rabbits) • In rabbits, necrosis of skin following application to uncovered belly • Instillation in rabbit eye caused severe injury and permanent corneal damage • 4 h exposure at 4,000 mg/m³ in rats was lethal to 6/6 animals: <ul style="list-style-type: none"> ○ acute toxic response included increased blood pressure and heart rate, nausea, vomiting, salivation, respiratory distress, ataxia, muscular weakness, paralysis and convulsions • IP LD₅₀: <50 mg/kg (rats); 50 mg/kg (mice) • Negative results in <i>S. typhimurium</i> in Ames test and host-mediated assay: <ul style="list-style-type: none"> ○ in mouse lymphoma assay DNA strand breaks only occurred at a significant level when incubated with S9 fraction. 		
HCOTN	NA	NA
No report.		

Secondary source reports relied upon

Source	Year	Additional information
HSE	1993	<ul style="list-style-type: none"> Irritation threshold of 26 ppm established in a volunteer study In animal studies (species not disclosed), inhalation exposure at 2.9 ppm for 4 h/d for 4 mo resulted in: <ul style="list-style-type: none"> altered brain electrical activity, effects on the cardiovascular system and sperm generation and some loss of function in the liver and kidneys at 0.6 ppm decreased blood pressure and neuromuscular irritability were reported
NICNAS	✓ 2016	<ul style="list-style-type: none"> Caused death in laboratory animals following absorption through skin LD₅₀: 133–740 mg/kg (rats, duration not stated), sublethal effects were decreased motor activity, tremors, blanching, piloerection, lethargy and respiratory effects LD₅₀: ≈ 275 mg/kg (rabbits, dermal, applied to shaved trunk) 4 h LC₅₀: 4.8 mg/L (4,800 mg/m³) (rats, inhalation, whole body), concentration range 1–7 mg/L (1,000–7,000 mg/m³) Corrosive to rabbit skin after 3 min exposure: <ul style="list-style-type: none"> severely irritating to skin of rats and mice (no further information) 0.5 mL undiluted applied to shaved back of rabbits (occlusive conditions) for 3 min, 1 h and 4 h caused necrosis and oedema; not reversible Not considered a skin sensitiser Whole body exposure at 2 mg/m³ and 10 mg/m³ (4 h/d, 5 d/wk, 4 mo duration) in rats and rabbits: <ul style="list-style-type: none"> LOAEC = 10 mg/m³ based on reduced and impaired kidney function effects fully reversible study not according to OECD Whole body exposure at 5 ppm, 20 ppm and 100 ppm (6 h/d, 5 d/wk, 28 d duration) in rats: <ul style="list-style-type: none"> at 100 ppm, slight decreased body weight gain in males and increased liver weight in females no adverse effects described at 20 ppm study in accordance with OECD Positive result in <i>in vitro</i> mammalian cell forward mutation assay; genotoxicity not observed in all other <i>in vitro</i> studies Negative results for carcinogenicity. NOAEC: 3 mg/m³ (exposure at 3, 15 or 100 mg/m³ until GD 21) and 71 mg/m³ (exposure at 17, 71 and 280 mg/m³, 6 h/d, during GD 6–15), for developmental and/or maternal toxicity in rats.
ECHA	✓ 2019	<ul style="list-style-type: none"> No skin sensitisation observed in workers handling the chemical and no allergic reactions to the chemical amongst 448 patients tested; 2 patch-tested patients found to be hypersensitive following case of allergic contact dermatitis from wearing rubber gloves confirmed to contain piperidine

Source	Year	Additional information
		<ul style="list-style-type: none"> Rats exposed at 50–200 ppm for 6 h experienced upper respiratory tract irritation/nasal secretions, eye irritation; no effects at 20 ppm Not sensitising to male and female guinea pigs in dermal sensitisation study NOAEL: 80 mg/kg/d (male and female rats, 90 d feeding study), based on reduced body weight, doses at 0, 80, 160 and 310 mg/kg/d NOAEC of 20 ppm (70 mg/m³) from 28 d rat study (cited in NICNAS, 2016) selected as POD for derivation of DNEL; resulting DNEL following application of AFs was 7.05 mg/m³ Not mutagenic in <i>in vivo</i> studies.

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
HCIS	—
NICNAS	Skin
EU Annex	NA
ECHA	—
ACGIH	NA
DFG	NA
SCOEL	NA
HCOTN	NA
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:
Dermal LD ₅₀ ≤ 1000 mg/kg: yes



Dermal repeat-dose NOAEL ≤ 200 mg/kg:

Dermal LD₅₀/Inhalation LD₅₀ <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? No

Additional information

Molecular weight:	85.15
Conversion factors at 25°C and 101.3 kPa:	1 ppm = Number mg/m ³ ; 1 mg/m ³ = Number 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
Click here to enter year	

References

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

National Industrial Chemicals Notification and Assessment Scheme (NICNAS) (2016) Piperidine: Human health tier II assessment – IMAF report.

Occupational Alliance for Risk Science (OARS) / American Industrial Hygiene Association (AIHA) (1996) Workplace environmental exposure level – Piperidine.

UK Health and Safety Executive (HSE) (2003) Piperidine – EH64: Summary criteria for occupational exposure limits.