CYCLONITE

CAS number:	121-82-4
Synonyms:	Cyclotrimethylenetrinitramine, hexahydro-1,3,5-triazine, RDX
Chemical formula:	$C_3H_6N_6O_6$

Workplace exposure standard (amended)

TWA:	**0.1 mg/m^3**
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 0.1 mg/m^3 is recommended to protect for chronic system effects and acute central nervous system (CNS) effects in exposed workers.

Discussion and conclusions

Cyclonite is predominantly used as an explosive and also as a rodenticide.

Critical effects associated with exposure are seen in the liver, prostate, haematopoietic (blood) and CNS. Accidental ingestion by military personnel resulted in confusion, hyperirritability, myoclonic seizures and major motor seizures. A NOAEL of 1.5 mg/kg from a chronic feeding study is reported in rats for adverse systemic effects in liver and the hematopoietic and urogenital systems. A NOAEL of 0.3 mg/kg for effects on the spleen and the prostate is reported from an oral study in rats. A comparison of plasma levels in rodents and monkeys indicates that primates are more sensitive to acute CNS effects. Monkeys dosed with 10 mg/kg demonstrated some CNS effects including convulsions (ACGIH, 2018; HCOTN, 2004).

The TWA of 0.1 mg/m^3 is derived by converting the reported NOAEL of 0.3 mg/kg to an airborne concentration as per HCOTN 2004. Allowing for a five-day week, an allometric factor of four and a factor of nine for inter and intra species variation, the resulting value is rounded to 0.1 mg/m^3. On a weight of evidence, this TWA is considered protective for chronic system effects and acute central nervous 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.

A skin notation is recommended based on reports of adverse effects in humans.

APPENDIX

Primary sources with reports

Source	Year set	Standard
SWA	***1991***	***TWA: 1.5 mg/m^3***
ACGIH	***2001***	***TLV-TWA: 0.5 mg/m^3***
TLV-TWA recommended to minimise the potential for adverse hepatic, prostate and haematopoietic effects. It will also provide protection for acute CNS effects. Summary of data: Human data: • Accidental ingestion by military personnel resulted in confusion, hyperirritability, myoclonic seizures and major motor seizures (no further information) • Case report of epileptiform seizures in a child who ingested cyclonite pellets • Case report of possible skin absorption route in munition workers presenting epileptiform seizures and unconsciousness and at lesser exposures, irritability and insomnia. Animal data: • NOAEL of 1.5 mg/kg in rats; 6 and 12 mo feeding study, adverse systemic effects in liver and the hematopoietic and urogenital systems • Severe acute CNS effects in rats associated with plasma levels >5 µg/mL o subtle neurophysiological alterations at 2–3 µg/mL o no effects at 1 µg/mL related to ≤20 mg/kg • Monkeys dosed with 10 mg/kg demonstrated CNS toxicity; 2–3.7 µg/mL associated with convulsions o primates including humans expected to be more sensitive to acute CNS effects. No indications that chronic low-level exposure resulted in histopathological effects to the brain or CNS. Not carcinogenic in any chronic study, also not teratogenic or mutagenic. TWA is sufficiently low to minimise adverse systemic effects the liver and the hematopoietic and urogenital systems and the neurophysiological effects. No derivation provided.		
DFG	***NA***	***NA***
No report.		
SCOEL	***NA***	***NA***
No report.		
OARS/AIHA	***NA***	***NA***
No report.		
HCOTN	***2004***	***TWA: 0.1 mg/m^3***
A recommended TWA of 0.1 mg/m^3 to protect for long-term systemic effects. Summary of additional data: • Limited data indicated irritating to the skin of rabbits, but not a skin sensitiser		

Source	Year set	Standard
• Considers the compound as non-hazardous *via* the dermal route and toxic via the oral route • NOAEL of 0.3 mg/kg based on effects on the spleen and the prostate in rats used to derive TWA: o adjust NOAEL (7 d/wk) to get no-adverse-effect-level (NAEL) (5 d/wk): 0.3 mg/kg x (7/5) = 0.42 mg/kg o extrapolate to human NAEL using allometric factor of 4 for caloric demand and 9 for inter-and intraspecies variation: 0.42÷(4×9) mg/kg = 0.01 mg/kg o assuming a 70 kg worker inhales 10 m^3 of air per 8 h shift and rounding up the result of the calculation, a TWA 0.1 mg/m^3 is obtained.		

Secondary source reports relied upon

Source	Year	Additional information
NICNAS	✓	• Human health tier I assessment – not considered to pose an unreasonable risk to the health of workers based on the Tier I IMAP assessment.
ECHA	✓	• NOAEL of 0.1 mg/kg for neurotoxicity (no further information).

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	NA
NICNAS	NA
EU Annex	NA
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:	yes
Dermal LD_{50} ≤1000 mg/kg:	
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 warranted

IDLH

Is there a suitable IDLH value available?	No

Additional information

Molecular weight:	222.12
Conversion factors at 25°C and 101.3 kPa:	1 ppm = 9.09 mg/m^3; 1 mg/m^3 = 0.11 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.

European Chemicals Agency Regulation (ECHA) No 1907/2006 of the European Parliament and of the Council of 18 December 2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH).

Health Council of the Netherlands (HCOTN) (2004) Perhydro-1,3,5-trinitro-1,3,5-triazine. Health-based calculated occupational cancer risk values. The Hague: Health Council of the Netherlands; publication no. 2000/15OSH/108.

National Industrial Chemicals Notification and Assessment Scheme (NICNAS) (N.D.) 1,3,5-Triazine, hexahydro-1,3,5-trinitro: Human health tier I assessment – IMAP report.