DINITROTOLUENE

CAS number: 25321-14-6

Synonyms: Dinitrotoluol, DNT

Chemical formula: $C_7H_6N_2O_4$

Structural formula: —

Workplace exposure standard (amended)

TWA: **0.5 µg/m³ (1.1 ppb)**

STEL: **—**

Peak limitation: **—**

Notations: **Carc 1B, Sk.**

IDLH: **—**

Sampling and analysis: The recommended value is likely to be below the current limit of detection for standard sampling and analysis techniques.

Recommendation and basis for workplace exposure standard

A TWA of 0.5 µg/m³ (1.1 ppb) is recommended to minimise the potential for cancer in exposed workers.

Discussion and conclusions

Dinitrotoluene (DNT) is used in the production of toluene diisocyanate and toluene diamine, which are intermediates in the making of polyurethane foams and polymers.

Critical effects include heart disease, reproductive effects and cancer. Based on evidence in animals, it is characterised a non-threshold based genotoxic carcinogen (ACGIH, 2018; NICNAS, 2014; US EPA, 1990). Carcinogenicity is demonstrated to act *via* a mutagenic mode of action.

The recommended TWA of 0.5 µg/m³ (rounded) has been derived at a minimal cancer risk level by applying an oral slope factor. This value is based on a study reporting significant increases in the incidence of malignant tumour types at multiple sites in rats (two strains) and malignant renal tumours in male mice (US EPA, 1990).

Recommendation for notations

Classified as a category 1B 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 of dermal absorption and systemic effects in humans.

APPENDIX

Primary sources with reports

Source	Year set	Standard
SWA	***1991***	***TWA: 1.5 mg/m^3***
ACGIH	***2001***	***TLV-TWA: 0.2 mg/m^3***

TLV-TWA recommended to minimise the potential for heart disease and possible reproductive effects.

Summary of data:

Used in the production of toluene diisocyanate and toluene diamine, which are intermediates in the making of polyurethane foams and polymers.

Human data:

- Toxic effects similar in character to those of other aromatic nitro compounds
- Acute effects driven by production of methaemoglobin, resulting in cyanosis accompanied by headache, irritability, dizziness, weakness, nausea, vomiting, dyspnoea, drowsiness, unconsciousness, and possible death
- Study in workers concluded skin exposure is a major route of absorption during the study; established urinary concentrations of the metabolite 2,4-dinitrobenzoic acid (2,4-DNBA) appropriate to determine exposure
- A study in workers determined the proportion of metabolites in humans substantially different to F-344 rats; large proportion of uptake from skin absorption
- Study in chemical plant with technical grade DNT with personal and area concentrations from not detectable to 0.49 mg/m^3 reported decreased sperm counts and a reduction in the number of large morphologic sperm forms
- Excess mortality from ischaemic disease reported in a cohort study; no exposure concentrations provided.

Animal data:

- LD_{50}: 27 mg/kg (cats, oral)
- Local irritating effect on skin of rabbits following Draize procedure
- Hepatotoxic effects in rats fed 14 or 35 mg/kg/d for 26 wk
- Hepatocellular carcinomas in 18/20 male rats fed 7 mg/kg/d for 26 wk; 19/19 rats fed 14 mg/kg/d developed hepatocellular carcinomas after 52 wk
- Hepatocellular carcinomas and other cancers in rats and mice exposed to technical grade in other chronic feeding studies
- Dietary doses >5 mg/kg/d required to induce low-grade anaemia and neuromuscular, hepatic, renal, and reproductive effects in mice, rats, or dogs.

Mutagenicity

- 6 isomers of DNT weakly mutagenic in *S. typhimurium*
- 2,6-dinitrobenzaldehyde, a metabolite, found to be a direct-acting mutagen
- Technical grade DNT and the purified 2,6-DNT isomer were potent inducers of DNA repair in rat mutagenicity tests.

Insufficient data to recommend sensitiser notation or a TLV-STEL.

Source	Year set	Standard
DFG	***1985***	***Not assigned***
No MAK recommended due to potential carcinogenicity. • Long-term feeding studies mice and rats shown to be a carcinogen in both species • Numerous short-term tests for genotoxic effects have yielded positive results (no further detail provided).		
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	✓	2014	• Considered low potential for sensitisation • DNA adduct formation observed in several organs, mainly the liver, in rats • Mutagenic in several strains of *S. typhimurium* • Recommended that SWA consider whether current controls adequately minimise the cancer risk to workers.
US EPA	✓	2014	• Oral slope factor based on a study reporting multiple benign and malignant tumour types at multiple sites in both sexes of rats (2 strains) and malignant renal tumours in male mice • Supported by evidence of mutagenicity.

Carcinogenicity — non-threshold based genotoxic carcinogens

Is the chemical mutagenic?	Yes
Is the chemical carcinogenic with a mutagenic mechanism of action?	Yes
The chemical is a non-threshold based genotoxic carcinogen.	
Is a cancer slope factor or inhalation unit risk value available?	Yes
Cancer slope factor (1/(mg/kg/day))	6.8×10^{-1}
Calculated TWA value (µg/m^3)	0.822

Notations

Source	Notations
SWA	Carc. 1B, Skin

Source	Notations
HCIS	Carcinogenicity – category 1B
NICNAS	Carc. Cat 2, Skin
EU Annex	Carcinogenicity – category 1B
ECHA	Carc. 1B
ACGIH	Carcinogenicity – A3, Skin
DFG	Carcinogenicity – 2, H (skin)
SCOEL	NA
HCOTN	NA
IARC	NA
US NIOSH	SK:SYS

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, the chemical is a genotoxic carcinogen

Additional information

Molecular weight:	182.13
Conversion factors at 25°C and 101.3 kPa:	1 ppm = 7.45 mg/m^3; 1 mg/m^3 = 0.134 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 (ECHA) (2019) Dinitrotoluene – REACH assessment.

Deutsche Forschungsgemeinschaft (DFG) (1993) Dinitrotoluenes (mixtures of isomers) – MAK value documentation.

National Industrial Chemicals Notification and Assessment Scheme (NICNAS) (2015) Benzene, methyldinitro: Human health tier II assessment – IMAP report.

Tenth Adaptation to Technical Progress Commission Regulation (EU) 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).

US National Institute for Occupational Safety and Health (NIOSH) (2011) NIOSH Skin Notation Profiles: Dinitrotoluene; 2,4-Dinitrotoluene (2,4-DNT); 2,6-Dinitrotoluene (2,6-DNT).

US Environmental Protection Authority (US EPA) (2014) Integrated Risk Information System (IRIS) Chemical Assessment Summary – Dinitrotoluene.