

# 1-NITROPROPANE

**CAS number:** 108-03-2

**Synonyms:** 1-NP

**Chemical formula:**  $C_3H_7NO_2$

**Structural formula:** —

## Workplace exposure standard (interim)

**TWA:** 25 ppm (91 mg/m<sup>3</sup>)

**STEL:** —

**Peak limitation:** —

**Notations:** —

**IDLH:** 1,000 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 25 ppm (91 mg/m<sup>3</sup>) is recommended to protect for eye and respiratory tract irritation in exposed workers.

Given the limited human 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

1-Nitropropane is used as a solvent, fuel additive and rocket propellant.

Critical effects of exposure are irritation of the eyes as reported in volunteers (ACGIH, 2018; DFG, 2017). Respiratory tract irritation is observed in animals following exposure (DFG, 2017).

No excesses of disease or cancer mortality are reported in a study of production workers exposed to nitroalkane mixtures; however, exposures were not measured (DFG, 2017). Irritation of the eyes but not the respiratory tract, is reported at concentrations above 150 ppm in an acute inhalation study in volunteers (ACGIH, 2018; DFG, 2017). Nasal epithelial degeneration and signs of respiratory tract irritation were observed at 24 ppm in a sub-chronic inhalation study in rats (DFG, 2017). No adverse histopathological or haematological effects were reported at 101 ppm in a chronic rat inhalation study (ACGIH, 2018). However, examinations of the respiratory tract were not carried out in this study (DFG, 2017).

From the available data, exposure at 100 ppm is tolerable without effects in volunteers (ACGIH, 2018; DFG, 2017). However, it is unclear if respiratory tract irritation is a critical effect in humans due to the short duration of the reported human study.

In the absence of long-term human exposure data, the current TWA of 25 ppm is recommended in the interim and is expected to be protective of irritation effects.

An examination of additional data sources is recommended during subsequent reviews to further assess the effects of long-term exposure in humans, including respiratory tract irritation.

### **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.

There are insufficient data to recommend a skin notation.

DRAFT

## APPENDIX

### Primary sources with reports

Source	Year set	Standard
<b>SWA</b>	<b>1991</b>	<b>TWA: 25 ppm (91 mg/m<sup>3</sup>)</b>
<b>ACGIH</b>	<b>2001</b>	<b>TLV-TWA: 25 ppm (91 mg/m<sup>3</sup>)</b>
<p>TLV-TWA intended to protect for irritation to the eyes and respiratory tract and potential liver damage. Not classifiable as a human carcinogen (A4) based on chronic animal exposure studies and negative mutagenicity results.</p> <p>Summary of data:</p> <p>Based on human and animal inhalation data, TLV-TWA of 25 ppm is considered protective. TLV-TWA derivation not discussed. Agency notes that the isomer 2-nitropropane is classified as carcinogenic, but that no evidence for carcinogenicity of 1-nitropropane is available.</p> <p>Human data:</p> <ul style="list-style-type: none"> <li>• Eye irritation in volunteers at &gt;100 ppm (inhalation study, brief duration, not specified, no further details provided)</li> </ul> <p>Animal data:</p> <ul style="list-style-type: none"> <li>• More toxic to liver than nitromethane and nitroethane</li> <li>• Lethal dose: 250–500 mg/kg (rabbits, oral)</li> <li>• Lethal at 5,000 ppm (rabbits, 3 h); non-lethal at 10,000 ppm (rabbits, 1 h) <ul style="list-style-type: none"> <li>◦ eye irritation, lachrymation, depressed respiration with rales and ataxia observed</li> </ul> </li> <li>• No significant gross or microscopic liver tissue changes or changes in liver, kidney and brain weights and haematology at 101 ppm (rats, 7 h/d, 5 d/wk, up to 21.5 mo)</li> <li>• Non-mutagenic <i>in vitro</i> in <i>S. typhimurium</i> strains with or without metabolic activation</li> <li>• No ADME data presented.</li> </ul> <p>Insufficient data to recommend a TLV-STEL or notations for skin absorption or sensitisation.</p>		
<b>DFG</b>	<b>2016</b>	<b>MAK: 2 ppm (7.4 mg/m<sup>3</sup>)</b>
<p>Summary of additional data:</p> <ul style="list-style-type: none"> <li>• Previous 1963 MAK of 25 ppm withdrawn due to short duration of volunteer inhalation study upon which it was based</li> <li>• Current MAK based on NOAEC of 24 ppm (females) and 48 ppm (males) for irritation reported in sub-chronic inhalation study in rats; a systemic NOAEC of 48 ppm was reported for both sexes: <ul style="list-style-type: none"> <li>◦ the lowest NOAEC of 24 ppm is adjusted with factors of 3 to account for anatomical differences in the nasal cavity of rats, 4 to account for potential cumulative irritational effects and 7/5 to account for translation from continuous exposure to workplace exposure and rounded up to derive a MAK of 2 ppm</li> </ul> </li> <li>• No evidence for carcinogenicity in the available studies and therefore, not classified as a carcinogen</li> <li>• Skin notation recommended based on <i>in vitro</i> data that suggests dermal uptake contributes significantly to overall exposure</li> <li>• Low liver toxicity relative to 2-nitropropane likely due to rapid absorption, metabolism and elimination.</li> </ul> <p>Human data:</p>		



Source	Year set	Standard
<ul style="list-style-type: none"> <li>Irritation of eyes, but not nose or throat, at 150 ppm in acute volunteer inhalation study published in 1946 (males/females, n=12/sex, 15 min); agency considered 100 ppm as tolerable dose (also cited in ACGIH, 2018)</li> <li>No evidence for increased diseases/cancer mortality in production plant workers (n=1,481); however, mixed exposures to other nitroalkanes confounded results</li> <li><i>In vitro</i> dermal penetration rate of human skin at steady state: 180 µg/cm<sup>2</sup>/h: <ul style="list-style-type: none"> <li>modelled penetration rates from saturated aqueous solutions calculated as 28, 44 and 236 µg/cm<sup>2</sup>/h in 3 separate studies.</li> </ul> </li> </ul> <p>Animal data:</p> <ul style="list-style-type: none"> <li>Dermal LD<sub>50</sub>: &gt;2,000 mg/kg (rabbits, non-occlusive, 4 h)</li> <li>Mortality, organ congestion, pulmonary oedema, signs of respiratory tract irritation and liver damage at 9,800 ppm reported in acute inhalation study (rabbits, guinea pigs, 3 h, also cited in ACGIH, 2018); mortality and liver damage reported at 5,000 ppm: <ul style="list-style-type: none"> <li>from these results, 1-nitropropane concluded to be more acutely toxic than nitromethane and nitroethane</li> </ul> </li> <li>Degeneration of olfactory epithelium (females) at 48 ppm and 96 ppm (males) in OECD-compliant inhalation reproductive study with exposure groups 0, 24, 48 and 96 ppm (rats, 6 h/d, 7 d/wk, females: 47 d, males: 28 d): <ul style="list-style-type: none"> <li>NOAEC: 24 ppm (females), 48 ppm (males)</li> </ul> </li> <li>Agency notes chronic 21.5-mo inhalation study in rats with exposure at 101 ppm (also cited in ACGIH, 2018) does not provide information on examinations of respiratory tract.</li> </ul> <p>Insufficient data to recommend a sensitiser notation.</p>		
<b>SCOEL</b>	<b>NA</b>	<b>NA</b>
No report.		
<b>OARS/AIHA</b>	<b>NA</b>	<b>NA</b>
No report.		
<b>HCOTN</b>	<b>NA</b>	<b>NA</b>
No report.		

## Secondary source reports relied upon

Source	Year	Additional information
ECHA	✓ 2019	<ul style="list-style-type: none"> <li>Results of OECD-compliant inhalation study (rats, 6 h/d, 7 d/wk, females: 47 d, males: 28 d, also cited in DFG, 2017) used as basis for DNEL: <ul style="list-style-type: none"> <li>overall assessment factor of 18 applied to NOAEC of 24 ppm to derive a long-term local DNEL of 1 ppm</li> </ul> </li> <li>Non-mutagenic <i>in vitro</i> based on 8 studies with bacteria and mammalian cells or <i>in vivo</i> based on 3 studies mice and rats.</li> </ul>



Source	Year	Additional information
OECD	✓ 2010	<ul style="list-style-type: none"> <li>Grouped assessment with nitromethane and nitroethane</li> <li>Nasal tissue degeneration at 48 ppm in controlled inhalation reproductive study with exposure groups 24, 48, 96 ppm (rats, 6 h/d, 7 d/wk, 28 d, also cited by DFG, 2017):               <ul style="list-style-type: none"> <li>NOAEC for local irritation/lesions: 24 ppm</li> <li>NOAEC for systemic effects: 96 ppm (highest dose)</li> </ul> </li> <li>Nitromethane carcinogenic above 188 ppm (mice, rats); nitroethane and 1-nitropropane non-carcinogenic at 200 and 100 ppm (rats, no further details provided)</li> <li>Non-mutagenic in mouse or rat bone marrow <i>in vivo</i>, but positive for micronuclei in rat liver cells <i>in vivo</i>:               <ul style="list-style-type: none"> <li>chemicals in grouped assessment are non-genotoxic <i>in vitro</i> based on studies with all chemicals in group but may be genotoxic <i>in vivo</i> based on studies with 1-nitropropane.</li> </ul> </li> </ul>
US NIOSH	✓ 1994	<ul style="list-style-type: none"> <li>IDLH based on acute inhalation toxicity data in animals.</li> </ul>

## 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	—
HCIS	—
NICNAS	NA
EU Annex	—
ECHA	—
ACGIH	Carcinogenicity – A4
DFG	H (skin)
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<sub>50</sub> ≤ 1000 mg/kg: no

Dermal repeat-dose NOAEL ≤ 200 mg/kg:

Dermal LD<sub>50</sub>/Inhalation LD<sub>50</sub> < 10:

*In vivo* dermal absorption rate > 10%:

Estimated dermal exposure at WES > 10%: yes

insufficient data to assign a skin notation

## IDLH

Is there a suitable IDLH value available? Yes

## Additional information

Molecular weight: 89.09

Conversion factors at 25°C and 101.3 kPa: 1 ppm = 3.64 mg/m<sup>3</sup>; 1 mg/m<sup>3</sup> = 0.275 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
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[Click here to enter year](#)

## References

American Conference of Industrial Hygienists (ACGIH®) (2018) TLVs® and BEIs® with 7<sup>th</sup> 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) (2017) 1-Nitropropane – MAK value documentation.

European Chemicals Agency (ECHA) (2019) 1-Nitropropane – REACH assessment.

Organisation for Economic Cooperation and Development (OECD) (2010) SIDS Final assessment profile –Nitroparaffins.

US National Institute for Occupational Safety and Health (NIOSH) (1994) Immediately dangerous to life or health concentrations – 1-nitropropane.