NITRIC OXIDE

CAS number: 10102-43-9

Synonyms: Nitrogen monoxide, nitrogen oxide, nitric oxide, mononitrogen monoxide

Chemical formula: NO

Workplace exposure standard (amended)

TWA: **2 ppm (2.5 mg/m^3)**

STEL: **—**

Peak limitation: **—**

Notations: **—**

IDLH: **100 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 2 ppm (2.5 mg/m^3) is recommended to protect for respiratory tract irritation and lung damage effects in exposed workers.

Discussion and conclusions

Nitric oxide (NO) is used in the production of nitric acid for nitrate fertilisers, nitrosyl carbonyl preparation and an intermediate in preparation of nitric acid. It is also used in hospitals as a respiratory stimulant and is produced as a part of exhaust of internal combustion engine (ACGIH, 2018; SCOEL, 2014).

Critical effects of exposure are respiratory tract irritation and lung damage.

A NOAEC of 2.5 ppm based on effects on lung function is reported in a longitudinal study in workers. Possibility of lung function impairment identified after long exposure periods to concentrations as low as 1.7 ppm in a study of mine workers. However, this study could not dissociate the effects of NO from those of other variables (SCOEL, 2014). Lung function parameters were unaffected at exposures up to 1.36 ppm in a cohort study of coal miners. However, some uncertainties are noted in the study, undermining its suitability (DFG, 2009). Dogs exposed at 1.6 ppm for 16 hours per day over 68 months developed effects in the alveoli, indicative of emphysema-like changes. Potential for pro-inflammatory or detrimental changes in lungs associated with continuous exposure at 2 to 6 ppm over a few weeks in rats (SCOEL, 2014).

The evidence presented indicates that the current TWA of 25 ppm is not adequately protective of workers. A TWA of 2 ppm (2.5 mg/m^3) derived by SCOEL (2014) is recommended to be adopted. The TWA is based on the NOAEC of 2.5 ppm reported in humans and supported by the evidence in animals. The recommended TWA is expected to be protective of adverse lung effects.

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.

APPENDIX

Primary sources with reports

Source	Year set	Standard
SWA	***1991***	***TWA: 25 ppm (31 mg/m^3)***
ACGIH	***2001***	***TLV-TWA: 25 ppm (31 mg/m^3)***

TLV-TWA recommended to minimise occupational worker's potential for respiratory tract irritation, hypoxia and cyanosis.

Summary of data:

No derivation provided; based on analogy to the substantially more toxic NO_2 (2018 TLV-TWA 0.2 ppm (0.38 mg/m^3)) for lower respiratory tract irritation.

Human Data:

- Intoxication of 2 individuals when used as anaesthetic; 75% NO in O_2; both showed cyanosis and MetHb
  - 1 died from cardiac arrest; other made full recovery.

Animal Data:

- LC_{50}: 320 ppm (mice, inhalation)
- Albino mice exposed at 5,000 ppm for 6–8 min died; death from exposure at 2,500 ppm for 12 min with cyanosis occurring after a few minutes:
  - red eyegrounds became grey-blue and then dyspnoea commenced with paralysis and convulsions
  - indicates NO ≈1/5 acutely toxic as NO_2
- Dogs exposed at 5,000 ppm for 24 min; arterial oxygen declined, methaemoglobin concentrations increased, circulating CO_2 increased:
  - death within 7–120 min
  - dogs inhaling 20,000 ppm died within 15–50 min accompanied by acute pulmonary oedema.

Insufficient data available for notations of Skin, SEN or carcinogenicity or a TLV-STEL.

DFG	***2009***	***MAK: 0.5 ppm (0.625 mg/m^3)***

Provisional MAK based on MAK for NO_2 of 0.5 ppm.

Additional Data:

- Volunteers exposed at ≈0.1 ppm for 2 h showed significant reduction in specific airway conductance; not considered adverse; no further information
- Cohort study of coal miners; lung function parameters unaffected at 0.84–1.36 ppm:
  - uncertainties in the study and not considered suitable for OEL derivation
- Continuous exposure in rats at 0.5–2 ppm for several weeks and dogs at 1.6 ppm for 68 mo resulted in lung changes in the alveolar region
- No evaluations specifically of persons exposed at higher concentrations and therefore difficult to assess whether effects resulting from long-term exposure at higher concentrations can be ruled out with certainty
- No animal studies with workplace-relevant (intermittent) exposure periods

Source	Year set	Standard
SCOEL	***2014***	***TWA: 2 ppm (2.5 mg/m^3)***
TWA recommended to protect for lung damage from long term repeated exposure. Additional Data: • Single exposures of human volunteers at 40 ppm for 10 min or 1 ppm for 2 h did not lead to adverse changes in lung function tests • Non-irritant upon acute exposure; acute effects are vasodilatory effects and, at high concentrations, MetHb formation; no requirement for a STEL • NOAEC of 2.5 ppm based on lung function with chronic exposure reported in a longitudinal study in diesel locomotive and diesel train drivers; discrimination of effects of nitrogen oxides was performed using General Estimation Equation models: ○ underground miners exposed at mean NO concentrations of 0.58 ppm (NO_2: 0.007 ppm) ○ diesel train and engine drivers exposed at mean exposures were 1.35 ppm NO (NO_2: 0.21 and 0.52 ppm) ○ no adverse influence on lung function from these NO_x exposures • In an earlier study of workers in 2 mines the possibility of lung function impairment in miners exposed for long periods of time was reported by the authors; mean exposures: ○ 1.7 ppm NO (0.4 ppm NO_2) in the 1st mine ○ 1.4 ppm NO (0.5 ppm NO_2) in the 2nd mine ○ this study could not dissociate the effects of NO_x from those of other variables (dust, diesel exhaust etc.) • Studies in rats suggest potential for pro-inflammatory or detrimental changes in lungs following continuous exposure at 2–6 ppm over a few weeks • Dogs exposed at 0 or 1.6 ppm (with 0.14 ppm NO_2), 16 h/d, 68 mo; maintained exposure-free for 3 yr; lung histopathology revealed alveolar air space enlargement, destruction of alveolar septa and an increase in alveolar pores: ○ observations indicative of emphysema-like changes ○ not attributed to NO_2. TWA based primarily on NOAEC of 2.5 ppm as identified in human field studies supported by data in animals.		
OARS/AIHA	***NA***	***NA***
No report.		
HCOTN	***NA***	***NA***
No report.		

Secondary source reports relied upon

Source		Year	Additional information
NICNAS	✓	ND	• IMAP – Tier I Human Health Assessment.

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	NA
HCIS	NA
NICNAS	NA
EU Annex	NA
ECHA	NA
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
Insufficient data to assign a skin notation.

IDLH

Is there a suitable IDLH value available?	Yes

Additional information

Molecular weight:	30.01
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:	☐
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.

Deutsche Forschungsgemeinschaft (DFG) (2014) Nitrogen monoxide – MAK value documentation.

EU Scientific Committee on Occupational Exposure Limits (SCOEL) (2014) Recommendation from the Scientific Committee on Occupational Exposure Limits for nitrogen monoxide. SCOEL/SUM/89.

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