

NITROGEN DIOXIDE

CAS number: 10102-44-0

Synonyms: Nitrogen peroxide, nitrito

Chemical formula: NO₂

Structural formula: —

Workplace exposure standard (amended)

TWA: 0.2 ppm (0.38 mg/m³)

STEL: —

Peak limitation: —

Notations: —

IDLH: 20 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 0.2 ppm (0.38 mg/m³) is recommended to protect for adverse effects in the lower respiratory tract in exposed workers. The recommended TWA is also considered to protect for the effects of acute exposure.

Discussion and conclusions

Nitrogen dioxide (NO₂) is found in ambient air as a product of natural as well as human activities. Occupational exposure to NO₂ can occur from exhaust from combustion engines, during gas welding, in agriculture, mining explosives, fertiliser production and power plants.

NO₂ can penetrate to the lower respiratory zone of the lungs. Critical effects of exposure include lower respiratory tract irritation and tissue damage.

No effect on airway resistance or methacholine reactivity were observed in a controlled human exposure study where non-asthmatics and mild asthmatics exposed (at rest) for 1 hour at 0.1 ppm. No statistically significant increase in bronchial reactivity was seen in asthmatics exposed at 0.2 ppm undertaking light intermittent exercise. Mild asthmatics exposed at 0.4 ppm for 3 hours had increased airway reactivity to inhalation challenge with dust mite allergen. In mild asthmatics, subclinical effects on bronchoalveolar lavage cells could be seen after exposure at 0.26 ppm for half an hour (ACGIH, 2018). A NOAEC of 0.5 ppm was reported based on lung function effects under chronic occupational exposures from an epidemiological study in hard coal miners (SCOEL, 2014). A NOAEC of 0.2 ppm is reported for treatment related changes in lung morphology, lung function and pulmonary host defence in mice continuously exposed for up to 12 months (HCOTN, 2004).

A TWA of 0.2 ppm (0.38 mg/m³) by ACGIH (2018) is recommended based on the weight of evidence presented. This TWA is considered protective of adverse effects in the lower respiratory tract as reported in humans and animals. Additionally, the recommended TWA is considered sufficiently low to adequately protect for any short-term excursions in exposure.

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 or respiratory sensitiser according to the GHS.

There are insufficient data to recommend a skin notation.

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APPENDIX

Primary sources with reports

Source	Year set	Standard
SWA	1991	TWA: 3 ppm (5.6 mg/m³); STEL: 5 ppm (9.4mg/m³)
ACGIH	2012	TLV-TWA: 0.2 ppm (0.38 mg/m³)
<p>TLV-TWA recommended to minimise lower respiratory tract irritation. Should protect both non-asthmatic and asthmatic workers from respiratory system effects.</p> <p>Summary of data:</p> <p>Human data:</p> <ul style="list-style-type: none"> • Asthmatics experience airway irritant effects at concentrations lower than those that produce the same effects in non-asthmatics • Relatively insoluble and can penetrate past nasal passages and upper respiratory tract to reach small respiratory zone even at small doses • Exercise and activity increase the delivered dose of NO₂ to the smaller, more peripheral airways • Controlled exposure studies provide the key evidence informing the TWA: <ul style="list-style-type: none"> ○ no effect on airway resistance or methacholine reactivity in non-asthmatics and mild asthmatics exposed for 1 h at 0.1 ppm at rest ○ no statistically significant increase in bronchial reactivity in asthmatics exposed for 2 h at 0.2 ppm with light intermittent exercise ○ mild asthmatics exposed for 0.5 h at rest at 0.26 ppm; allergen challenge 4 h after exposure; subclinical effects increased bronchoalveolar lavage percent neutrophils and eosinophilic cationic protein after NO₂ plus allergen challenge ○ no symptoms or lung function effects in mild asthmatics after 75 min of exposure at 0.6 ppm with intermittent exercise ○ mild asthmatics exposed at 0.4 ppm for 3 h with dust mite allergen challenge had increased airway reactivity ○ non-asthmatics exposed at rest for 1 h at 2 ppm had an increased methacholine airway reactivity • Background exposure to NO₂; a common ambient air pollutant with daily exposure at variable levels impacting the general population; recent studies indicate impact from NO₂ on cardiac arrhythmias in adults with underlying heart disease; occupational exposures relevant to adults return to the workplace with pacemakers and defibrillators implanted in the chest following serious heart disease. <p>Animal data:</p> <ul style="list-style-type: none"> • Animal data not important to the TLV basis because acute short-term effects have been demonstrated at lower levels in human exposure • Chronic respiratory tract effects of inhaled NO₂ are strongly dose related, reversible biochemical abnormalities, subclinical lung injury, chronic lung disease and subsequent premature death • Evidence of airway histologic injury becomes more widespread through the respiratory tree and the degree of injury more severe becomes more apparent. <p>No clear evidence in humans or animals to suspect carcinogenic effects.</p> <p>Limited evidence of genotoxicity in bacteria.</p>		

Source	Year set	Standard
Insufficient evidence to recommend a skin or sensitiser notation or TLV-STEL.		
DFG	2010	MAK: 0.5 ppm (0.95 mg/m³)
MAK recommended to prevent damage to tissue in the lower respiratory tract.		
Summary of additional data:		
<ul style="list-style-type: none"> MAK based on the following evidence: <ul style="list-style-type: none"> 21 volunteers exposed at 0, 0.6 and 1.5 ppm during intermittent physical exercise at 1-wk intervals; changes in bronchoalveolar lavage fluid and initial signs of inflammatory reactions at 1.5 ppm (and noted from other study at 2 ppm; no further detail); no effects at 0.6 ppm (cited by ACGIH, 2018); rats exposed on 5 d for 6h/d at 0, 0.5, 5 or 20 ppm; LOAEC of 5 ppm; histopathological changes in the lungs (bronchoalveolar hyperplasia, infiltration of mononuclear cells and alveolar histocytes) and in the trachea (diffuse hyperplasia of the tracheal epithelium) and cell proliferation was found in the large and medium bronchi, terminal bronchioles and alveoli NOAEC of 2.15 ppm in rats; based on changes in bronchoalveolar lavage fluid; 13 wk inhalation study, 5 d/wk for 6 h/d; dose 0.008, 0.25, 0.82 or 2.15 ppm. 		
SCOEL	2014	TWA: 0.5 ppm (0.955 mg/m³); STEL: 1 ppm (1.91 mg/m³)
TWA and STEL recommended to protect for effects in the deep respiratory tract.		
Summary of additional data:		
<ul style="list-style-type: none"> NO₂ is often found in ambient air with nitrogen monoxide (NO); oxidation of NO to NO₂ occurs easily in some circumstances Basis for TWA: Epidemiological study in hard coal miners; long-term longitudinal study considering number of shifts underground, the exposure to coal mine dust, quartz dust, NO, NO₂, smoking behaviours and the lung function parameters FVC, FEV1 and FEV1/FVC <ul style="list-style-type: none"> 1,369 miners worked on average 3,017 shifts underground per person total mean concentrations of 0.007 ppm NO₂ and 0.58 ppm NO exposure in defined subgroups was consistently higher mean 8-h shift concentrations: Diesel engine drivers, 1.35 ppm NO and 0.21 ppm NO₂; Diesel train drivers, 1.35 ppm NO and 0.52 ppm NO₂; blasting specialists, 0.84 ppm NO and 0.014 ppm NO₂ concluded exposures to nitrogen oxides, including those in the subgroups, showed no adverse influence on lung function concluded a NOAEC of 0.5 ppm regarding lung function under chronic occupational exposures LOAEC of 5 ppm and NOAEC of 2.15 ppm in rats (cited by DFG, 2010); animal studies supporting TWA Basis for STEL: Changes in the BALF were observed in volunteers after a 3-h exposure to NO₂ ≥ 1.5 ppm (cited by DFG, 2010). 		
OARS/AIHA	NA	NA
No report.		
HCOTN	2004	TWA: 0.2 ppm (0.4 mg/m³); STEL: 0.5 ppm (1.0 mg/m³)
TWA and STEL recommended to protect for local effects on the respiratory system.		



Source	Year set	Standard
Summary of additional data:		
<ul style="list-style-type: none">• Considers epidemiological data insufficient to inform the derivation of a TWA due to co-exposures with other substances• NOAEC of 0.04 ppm (0.08 mg/m³) and LOAEC of 0.4 ppm (0.76 mg/m³) in rats; continuous exposure for 9, 18 and 27 mo; concentrations 0.04, 0.4 or 4 ppm<ul style="list-style-type: none">○ after 9 mo: 4 ppm hypertrophy and hyperplasia of bronchial mucosa and thickening of walls through the bronchopulmonary junction of alveolar duct with cell infiltration and increase in Clara cells; no changes at other concentrations○ after 18 mo: no changes at 0.04 ppm; epithelial changes and interstitial oedema of alveolar wall at 0.4 ppm○ after 27 mo: interstitial fibrosis and hyperplasia of epithelium progressed steadily at 4 ppm; definite alteration of the epithelium became evident at 0.4 ppm; no lung morphology changes at 0.04 ppm○ considers gap of 10-fold between NOAEL and LOAEL too large; the "real" NOAEL may be higher• No treatment related changes in lung morphology, lung function and pulmonary host defence in mice, continuously exposed at 0.2 ppm (0.38 mg/m³) for up to 12 mo; considered the NOAEC for derivation of the TWA• Clinical studies on healthy volunteers showed toxicological significant effects on lung function or respiratory resistance from exposure ≥2 ppm (3.8 mg/m³)• Considered a NOAEL of 0.5 ppm (1 mg/m³) based on human volunteer studies; no further information; basis for STEL.		

Secondary source reports relied upon

NIL.

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	Carcinogenicity – A4
DFG	Carcinogenicity – 3B
SCOEL	NA



Source	Notations
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:	40.01
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:	<input type="checkbox"/>
This chemical is a biological product:	<input type="checkbox"/>
This chemical is a by-product of a process:	<input checked="" 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

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) (2010) Nitrogen dioxide – MAK value documentation.

EU Scientific Committee on Occupational Exposure Limits (SCOEL) (2014) Recommendation from the Scientific Committee on Occupational Exposure Limits for nitrogen dioxide. SCOEL/SUM/53.

Health Council of the Netherlands (HCOTN) (2004) Nitrogen dioxide. Health-based recommended occupational exposure limit. The Hague: Health Council of the Netherlands; publication no. 2004/01OSH.

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

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