# p-nitrochlorobenzene

| CAS number: | 100-00-5 |
| --- | --- |
| Synonyms: | p-Chloronitrobenzene, PCNB, PNCB, 4-chloronitrobenzene, 4-chloro-1-nitrobenzene |
| Chemical formula: | NO2C6H4Cl |
| Structural formula: | — |

Workplace exposure standard (retained)

| TWA: | **0.1 ppm (0.64 mg/m3)** |
| --- | --- |
| STEL: | **—** |
| Peak limitation: | **—** |
| Notations: | **Carc. 2, Sk.** |
| IDLH: | **100 mg/m3** |
| 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 ppm (0.64 mg/m3) is recommended to protect for methaemoglobinaemia in exposed workers.

## Discussion and conclusions

*p*-Nitrochlorobenzene (PNCB) has been used as an intermediate in the manufacture of dyes, rubber and agricultural chemicals.

The critical effects from exposure is an increase of methaemoglobin and resulting methaemoglobinaemia.

It is reported to be absorbed through the lungs and skin to contribute to methaemoglobinaemia in humans and animals. There are case reports of dermal and inhalation exposure in humans resulting in headache and weakness accompanied with cyanosis. No chronic intoxication but increased methaemoglobin, the appearance of Heinz bodies, headache, vertigo and cases of eczema are reported in exposed workers following exposures at 3.6 mg/m3 and greater concentrations. No further details were provided. Data from a two-week, head only exposure study in rats was used to extrapolate a threshold concentration of 0.15 ppm (0.97 mg/m3) for no increase in methaemoglobin (ACGIH, 2018). NICNAS (2016) reported a LOAEC of 5 mg/m3 after four weeksand 9.81 mg/m3 after thirteen weeks (based on methaemoglobinaemia) from a four and thirteen week repeat dose inhalation toxicity study in rats.

Given the available data, the SWA TWA of 0.1 ppm (0.64 mg/m3) is recommended to be retained to protect for methaemoglobinaemia in exposed workers, as assigned by ACGIH (2018).

## Recommendation for notations

Classified as a carcinogen category 2 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 systemic effects following dermal exposure in humans.

# Appendix

### Primary sources with reports

| Source Year set Standard |
| --- |
| SWA 1991 TWA: 0.1 ppm (0.64 mg/m3) | |
|  |
| ACGIH 2001 TLV-TWA: 0.1 ppm (0.64 mg/m3) |
| TLV-TWA recommended to minimise the potential for methaemoglobinaemia and resulting anoxia and cyanosis.  Summary of data:  No specific derivation provided; based on threshold concentration for increase of methaemoglobin of 0.15 ppm in rats.  Human data:   * Absorbed through lungs and skin to contribute to methaemoglobinaemia * Case reports of dermal and inhalation exposure resulting in headache and weakness accompanied the cyanosis * Study in workers exposed at average of 8.6, 19.6, and 22.3 mg/m3 and mixed PCNB and nitrophenetole 3.6 mg/m3: * no chronic intoxication at 3.6 mg/m3 exposure concentration; no further details * increased methaemoglobin, the appearance of Heinz bodies, headache, vertigo, and cases of eczema * unable to determine if effects were due primarily to dermal or respiratory uptake.   Animal studies   * LD50: 3,040 mg/kg (rabbits, dermal) * Absorbed through the skin producing methaemoglobinaemia * 2-wk head-only inhalation study in rats; 6 h/d, 5 d/wk at 0, 8.2, 45 or 99 ppm; methaemoglobinaemia and increased spleen weight observed at all concentrations: * threshold concentration of 0.15 ppm (0.97 mg/m3) extrapolated for which no increase in methaemoglobin would be produced; no further information * 4-wk whole-body inhalation study in rats; 6 h/d, 5 d/wk at 0, 0.82, 2.5, or 7.5 ppm; dose-related increases in blood methemoglobin levels and decreases in haemoglobin, haematocrit, and RBC count values; statistically significant in the mid- and high-exposure groups after 2 wk and 4 wk * Feeding study in rats and mice; male and female mice showed an increase in vascular tumours at highest dose of 5 mg/kg/d; an increase in liver tumours at the lowest dose of 0.1 mg/kg/d reported for male mice.   Insufficient data to recommend a sensitiser notation or TLV-STEL. |
| DFG 1992 Not assigned |
| MAK not assigned due to carcinogenetic potential as demonstrated in animals.  No additional data. |
| SCOEL NA NA |
| No report. |
| OARS/AIHA NA NA |
| No report. |
| HCOTN 2002 Not assigned |
| Evaluation of the carcinogenicity and genotoxicity.  Insufficient information to classify as either carcinogen or genotoxic. |

### Secondary source reports relied upon

| Source |  | Year | Additional information |
| --- | --- | --- | --- |
| NICNAS |  | 2016 | * Positive respiratory reactions observed in a study where rats exposed at a concentration of 0.008 mg/m3 for 5 mo * 4 and 13 week repeated dose inhalation toxicity study in rats; LOAEC of 5 mg/m3 (~0.8 ppm) 4-wk exposure; LOAEC of 9.81 mg/m3 (~1.5 ppm) based on methaemoglobinaemia. |

### 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 | Carcinogenicity – category 2 |
| NICNAS | Carc. Cat. 3 |
| EU Annex | Carc 2 |
| ECHA | NA |
| ACGIH | A3, Skin |
| DFG | H (skin) |
| SCOEL | NA |
| HCOTN | — |
| IARC | 2B |
| 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 | 4.00 |  | | Dermal LD50 ≤1000 mg/kg: | no |  |  | | Dermal repeat-dose NOAEL ≤200 mg/kg: |  |  |  | | Dermal LD50/Inhalation LD50 <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? | Yes |
| --- | --- |

## Additional information

| Molecular weight: | 157.56 |
| --- | --- |
| Conversion factors at 25°C and 101.3 kPa: | 1 ppm = Number mg/m3; 1 mg/m3 = 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*](http://www.acgih.org/tlv-bei-guidelines/policies-procedures-presentations) on the ACGIH website.

Deutsche Forschungsgemeinschaft (DFG) (1992) p-Chloronitrobenzene – MAK value documentation.

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).

Health Council of the Netherlands (HCOTN) (2002) p-Chloronitrobenzene. Evaluation of the carcinogenicity and genotoxicity. The Hague: Health Council of the Netherlands; publication no. 2002/03OSH.

International Agency for Research on Cancer (IARC) (2012) Arsenic, Metals, Fibres and Dust. IARC Monographs on the evaluation of the carcinogenic risk to humans.

National Industrial Chemicals Notification and Assessment Scheme (NICNAS) (2016) Benzene, 1-chloro-4-nitro: Human health tier II assessment – IMAP report.

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