# Hexamethyl phosphoramide

| CAS number: | 680-31-9 |
| --- | --- |
| Synonyms: | Hempa, hexametapol, hexamethylphosphoric triamide, HMPA, tris(dimethylamino)-phosphine oxide |
| Chemical formula: | C6H18N3OP |
| Structural formula: | — |

Workplace exposure standard (new)

| TWA: | **—** |
| --- | --- |
| STEL: | **—** |
| Peak limitation: | **—** |
| Notations: | **Carc 1B.** |
| 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

There is insufficient evidence to establish a TWA. Given the limited data available in the sources, it is recommended that a review of additional sources be conducted at the next scheduled review to resolve uncertainties about its potential carcinogenicity.

## Discussion and conclusions

Hexamethyl phosphoramide (HMPA) is used as a solvent for polymers, a selective solvent for gases and a thermal and ultraviolet radiation degradation stabiliser in various polymers.

Limited toxicological data are available. There is some evidence of a potential for carcinogenicity in animals. Relevance of carcinogenicity in humans is unknown due to lack of data availability (ACGIH, 2018; SCOEL, 2010; NICNAS, 2015). Nasal tumours were reported after 12 months exposure at 0.05 ppm in a two-year rat inhalation study. No tumours were observed in rats exposed at 0.01 ppm (SCOEL, 2010).

A TWA cannot be recommended due to the lack of suitable data. It is recommended that an investigation of additional data sources is undertaken as a priority.

## 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 not warranted based on the available information.

# Appendix

### Primary sources with reports

| Source Year set Standard |
| --- |
| SWA 1991 Not assigned | |
|  |
| ACGIH 2001 Not assigned |
| A numerical TLV is not recommended for occupational exposure to hexamethyl phosphoramide (HMPA) due to lack of toxicological data in humans or animals.  Summary of data:  No human data presented.  Animal data:   * LD50:2,600 mg/kg (rabbits, dermal) * Responses in animals include renal damage, significant respiratory tract effects and testicular atrophy * Squamous cell carcinoma of the nasal cavity in rats exposed by inhalation at 0.05 ppm;  6–9 mo exposure.   Positive mutagenicity in mouse lymphoma test. |
| DFG NA NA |
| No report. |
| SCOEL 2010 Not assigned |
| Summary of additional data:   * No data concerning toxicity or carcinogenicity in humans * Described as ‘very powerful animal carcinogen’; likely carcinogenic to humans * Inhalation study in rats; 6 h/d, 5 d/wk, 9 mo to 2 yr: * nasal tumours at 400 ppb (0.4 ppm) 7 mo * nasal tumours at 50 ppb (0.05 ppm) 12 mo * no tumours were noted at 10 ppb (0.01 ppm) * Possible metabolism in the nasal tissue leads to production of formaldehyde, which then forms DNA-protein cross-links.   Mutagenicity data:   * Mutagenic to several strains of *S. typhimurium* with metabolic activation system; no further information * Mode of action uncertain; needs further support by experimentation and modelling; assigned as a genotoxic carcinogen * No health-based OEL can be deduced. |
| OARS/AIHA NA NA |
| No report. |
| HCOTN NA NA |
| No report. |

### Secondary source reports relied upon

| Source |  | Year | Additional information |
| --- | --- | --- | --- |
| NICNAS |  | 2016 | * Identified as having the potential to cause carcinogenic and mutagenic systemic long-term effects. |
| NTP |  | 2009 | * No additional data. |
| US EPA |  | 2012 | * Suggestive evidence of carcinogenic potential by the inhalation route of exposure; nasal tumours in rats * Negative mutagenicity results in *S. typhimurium* strains TA98, TA100, TA1535, TA1537, and TA1538 in the presence and absence of metabolic activation systems * Positive results for DNA-protein cross links in rat nasal epithelial cells and gene mutations in mouse lymphoma P388F and L5178Y cells * Study (as per SCOEL, 2010) provides extensive data on the carcinogenic response; the data from this study are not sufficient to support a quantitative cancer dose-response assessment. |

### Carcinogenicity — non-threshold based genotoxic carcinogens

| Is the chemical mutagenic? | Insufficient data |
| --- | --- |
| Is the chemical carcinogenic with a mutagenic mechanism of action? | Insufficient data |
| **Insufficient data are available to determine if the chemical is a non-threshold based genotoxic carcinogen.** |  |

## Notations

| Source | Notations |
| --- | --- |
| SWA | NA |
| HCIS | Carcinogenicity – category 1B |
| NICNAS | — |
| EU Annex | Carcinogenicity – category 1B |
| ECHA | Carcinogenicity – category 1B |
| ACGIH | Carcinogenicity – A3, Skin |
| DFG | NA |
| SCOEL | Carcinogenicity – B, Skin |
| HCOTN | NA |
| IARC | Carcinogenicity – Group 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: | no |  |  | | 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 not warranted** | |

### IDLH

| Is there a suitable IDLH value available? | No |
| --- | --- |

## Additional information

| Molecular weight: | 179.2 |
| --- | --- |
| 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.

European Chemicals Agency Regulation (ECHA) No 1907/2006 of the European Parliament and of the Council of 18 December 2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH).

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).

International Agency for Research on Cancer (IARC) (1999) Volume 71 re-evaluation of some organic chemicals, hydrazine and hydrogen peroxide. IARC Monographs on the evaluation of the carcinogenic risk to humans.

EU Scientific Committee on Occupational Exposure Limits (SCOEL) (2010) Recommendation from the Scientific Committee on Occupational Exposure Limits for hexamethylphosphoramide. SCOEL/SUM/156.

National Industrial Chemicals Notification and Assessment Scheme (NICNAS) (2016) CMR chemicals not registered under REACH: Human health tier II assessment – IMAP report.

National Toxicology Program (NTP) (2009) NTP-RoC: hexamethyl phosphoramide.

US Environmental Protection Authority (US EPA) (2012) Integrated Risk Information System (IRIS) Chemical Assessment Summary – hexamethyl phosphoramide.