# Di-sec-octyl phthalate

| CAS number: | 117-81-7 |
| --- | --- |
| Synonyms: | DOP, Di (2-ethylhexyl) phthalate,  bis(2-ethylhexyl) phthalate, DEHP, phthalic acid |
| Chemical formula: | C24H38O4 |
| Structural formula: | — |

Workplace exposure standard (amended)

| TWA: | **2 mg/m3** |
| --- | --- |
| STEL: | **—** |
| Peak limitation: | **—** |
| Notations: | **Carc. 1B** |
| IDLH: | **5,000 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 2 mg/m3 is recommended to protect for developmental effects in the progeny of exposed workers and to protect for potential carcinogenic effects in exposed workers.

A STEL is not recommended as the TWA is considered sufficiently low to protect for short-term exposures.

## Discussion and conclusions

Di-sec-octyl phthalate (DEHP) is used as a plasticiser for polyvinyl chloride (PVC) resins and vinyl chloride copolymer resins.

The critical effects of exposure include developmental and fertility toxicity and a risk of cancer. DEHP is not considered genotoxic (NICNAS, 2014; USEPA, 1987). A NOAEC of 50 mg/m3 is reported in rats for developmental and maternal toxicity. The NOAEL from oral developmental studies are 3.7 mg/kg/day for testicular toxicity in rats and 20 mg/kg/day for fetotoxicity in mice. Extrapolation of these NOAELs results in equivalent human inhalation concentrations of 6 mg/m3 and 13 mg/m3, respectively (DFG, 2014). No carcinogenic effects were observed in a lifetime inhalation study in hamsters exposed to approximately 15 mg/m3 for 23 hours per day (ACGIH, 2018).

A TWA of 2 mg/m3 is recommended as assigned by the DFG (2014) based on the lowest observed NOAEL in animals (3.7 mg/kg/day for testicular toxicity in rats). This TWA is reported to be protective of developmental and fertility effects. There is also a sufficiently large margin between the recommended TWA and the concentration associated with no increase in tumour incidence in animals. The current STEL is recommended to be removed as the TWA is considered protective of acute exposures.

## 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 recommended based on the available evidence.

# Appendix

### Primary sources with reports

| Source Year set Standard |
| --- |
| SWA 1991 TWA: 5 mg/m3; STEL: 10 mg/m3 | |
|  |
| ACGIH 2001 TLV-TWA: 5 mg/m3 |
| TLV-TWA recommended to minimise the potential for irritation and possible neurotoxicity.  Summary of data:  Human data:   * A study in workers reported no significant association with exposure ≤0.7 mg/m3 and presence of symptoms and signs from the peripheral nervous system; no reported obstructive lung disease; no further details * One case report of occupational asthma due to exposure * No evidence of dermal irritation, systemic toxicity or sensitisation in a 7-d skin application test in 23 volunteers * Worker complaints of pain, numbness and spasms in the upper and lower extremities after 6 yr ambient air concentrations of 1.7–66 mg/m3 for range of related plasticisers * co-exposure to tri-o-cresyl phosphate (TOCP) was likely; TOCP is a known potent cause of human peripheral neuropathy * Evidence of poor dermal absorption reported.   Animal data:   * No irritant response from dermal application or sensitising potential reported * LD50:24,750 mg/kg (rabbits, dermal) * Lung and liver weight increase in female rats exposed at 1,000 mg/m3 for 4 wk * resolved after 8 wk of no exposure * thickened alveolar septum accompanied by diffuse foam cell proliferation in male rats reported at same exposure * 103-wk feeding study reported increased incidence of hepatocellular carcinomas in female rats and in male and female mice and an increased incidence of either hepatocellular carcinomas or neoplastic nodules in male rats; doses of 6,000 or 12,000 mg/kg/d in mice; 3,000 or 6,000 mg/kg/d in rats * No evidence for increased tumour incidence in hamsters exposed for lifetime by inhalation for 23 h/d at 15 ± 5 mg/m3 * DEHP not a reproductive or developmental toxin by either dermal contact or inhalation routes; developmental effects at massive oral doses.   Negative results in mutagenicity tests in bacteria and eukaryotic cells.  Insufficient data to recommend Skin or SEN notations or a TLV-STEL. |
| DFG 2014 MAK: 2 mg/m3 |
| Summary of additional data:  The critical effects include developmental toxicity, liver carcinogenicity and effects on fertility and the lungs and possibly on the larynx in rodents.   * NOAEC of 50 mg/m3 reported in rats based on prenatal development and maternal toxicity; reported in an inhalation study with exposure on GD 6–15 at concentrations of 0, 10, 50 or 300 mg/m3; significantly increased incidence of litters with retardation; maternal toxicity in high exposure group * 300 mg/m3 resulted in retardations in the foetuses together with maternal toxicity; exposures at GD 6–15 * NOAEL in mice extrapolated ≡ human 8 h inhalation concentrations using species correction of 1/7, 50% oral absorption, 70 kg human bw, 10 m3 respiratory volume in 8 h, 75% absorption by inhalation: * oral diet study; 7 days before mating, 98 days during cohabitation and 21 days afterwards; 0, 20, 200, 600 mg/kg/d; NOAEL 20 mg/k/d for fetotoxicity = 13 mg/m3 * NOAEL in rats extrapolated ≡ human 8 h inhalation concentrations using species correction of 1/4, 50% oral absorption, 70 kg human bw, 10 m3 respiratory volume in 8 h, 75% absorption by inhalation: * MAK derivation: 13 wk oral study in rats reported a NOAEL of 3.7 mg/kg/d based on testicular toxicity (slight vacuolation of Sertoli cells) = 6 mg/m3; value is based on animal studies a MAK value of 2 mg/m3 is recommended (half the extrapolated value and then rounded down) * Calculation: NOAEL x (7/5) x (70/10) × (1/4 or 1/7) × 0.5 (oral absorption by animals) / 0.75 (inhalation absorption by humans). |
| SCOEL NA NA |
| No report. |
| OARS/AIHA NA NA |
| No report. |
| HCOTN NA NA |
| No report. |

### Secondary source reports relied upon

| Source |  | Year | Additional information |
| --- | --- | --- | --- |
| NICNAS |  | 2013 | * Regarded as non-genotoxic * Critical effects to human health are reproductive and developmental toxicity, with a potential endocrine disruption mechanism and carcinogenicity. |
| US EPA |  | 1987 | * Not a direct acting mutagen * Inadequate human carcinogenicity data * 103 wk diet study: statistically significant increase in the incidence of hepatocellular carcinomas and combined incidence of carcinomas and adenoma were observed in female rats and both sexes of mice. |

### 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 | Carcinogenicity – category 1B |
| NICNAS | Carc. Cat 2 |
| EU Annex | NA |
| ECHA | NA |
| ACGIH | Carcinogenicity – A3 |
| DFG | Carcinogenicity – 4, H (skin) |
| SCOEL | NA |
| 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: |  |  |  | | Dermal LD50 ≤1000 mg/kg: |  |  |  | | Dermal repeat-dose NOAEL ≤200 mg/kg: | no | -3.00 |  | | Dermal LD50/Inhalation LD50 <10: |  |  |  | | *In vivo* dermal absorption rate >10%: |  |  |  | | Estimated dermal exposure at WES >10%: |  |  |  | |  |  | -3 | **a skin notation is not warranted** | |

### IDLH

| Is there a suitable IDLH value available? | Yes |
| --- | --- |

## Additional information

| Molecular weight: | 390.6 |
| --- | --- |
| Conversion factors at 25°C and 101.3 kPa: | 1 ppm = 15.99 mg/m3; 1 mg/m3 = 0.06 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) (2016) Di(2‐ethylhexyl) phthalate (DEHP) – MAK value documentation.

International Agency for Research on Cancer (IARC) (2013) Di(2-ethylhexyl)phthalate. IARC Monographs on the evaluation of the carcinogenic risk to humans.

National Industrial Chemicals Notification and Assessment Scheme (NICNAS) (2013) 1,2-Benzenedicarboxylic acid, bis(2-ethylhexyl) ester: Human health tier II assessment – IMAP report.

US Environmental Protection Authority (US EPA) (1987) Integrated Risk Information System (IRIS) Chemical Assessment Summary – Di(2-ethylhexyl)phthalate (DEHP).

US National Institute for Occupational Safety and Health (NIOSH) (1994) Immediately dangerous to life or health concentrations – Di-sec octyl phthalate.