# Methyl demeton

| CAS number: | 8022-00-2 |
| --- | --- |
| Synonyms: | Demeton-O-methyl plus demeton-S-methyl,  O,O-di-methyl-O-ethylthioethyl phosphorothioate mixed with O,O-dimethyl-S-ethylthioethyl phosphorothioate, Duratox, mercaptophos,  methyl systox |
| Chemical formula: | C6H15O3PS2 |
| Structural formula: | — |

Workplace exposure standard (interim)

| TWA: | **0.5 mg/m3** |
| --- | --- |
| STEL: | **—** |
| Peak limitation: | **—** |
| Notations: | **Sk.** |
| IDLH: | **—** |
| **Sampling and analysis:** The recommended value is quantifiable through available sampling and analysis techniques. | |

## Recommendation and basis for workplace exposure standard

A TWA of 0.5 mg/m3 is recommended to protect for neurotoxic cholinergic effects in exposed workers.

A priority review of the data for the chemical is recommended at the next scheduled review.

## Discussion and conclusions

Methyl demeton is used as a systemic and contact organophosphate insecticide.

Critical effects of exposure are adverse effects on cholinesterase activity. Acute poisoning symptoms include nausea, vomiting, headache, dizziness and hyperaemia of nasal mucosa (ACGIH, 2018).

Exposure at up to 1.9 mg/m3 of 30:70 mixture of S- and O-isomers over five days in human volunteers did not produce effects on red blood cell acetylcholinesterase or plasma cholinesterase (HCOTN, 2003). A NOAEL of 0.09 mg/kg/day with the more acutely toxic compound demeton was reported in humans. Repeat dose oral studies with demeton identified NOAEL of 0.025 mg/kg/day and 0.05 mg/kg/day in dogs and rats respectively, however no further information on these studies was provided (ACGIH, 2018). A NOAEL of 0.036 mg/kg/day from a one-year study in dogs and 0.05 mg/kg/day from a two-year study in rats, based on brain and red blood cell acetylcholinesterase inhibition from methyl-S-demeton also reported (HCOTN, 2003).

Given the limited toxicological data available for methyl demeton and some uncertainty in the reported data, the TWA of 0.5 mg/m3 is retained in the interim. It is considered sufficiently low to minimise the potential for neurotoxic cholinergic effects based on the evidence presented in humans. A priority evaluation of additional data sources is recommended at the next scheduled review.

## 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.

A skin notation is recommended based on accidental dermal exposure in humans resulting in cholinergic effects and adverse systemic effects reported in animals.

# Appendix

### Primary sources with reports

| Source Year set Standard |
| --- |
| SWA 1991 TWA: 0.5 mg/m3 | |
|  |
| ACGIH 2007 TLV-TWA: 0.005 ppm (0.05 mg/m3) |
| TLV-TWA recommended to protect against cholinergic effects.  Summary of data:   * No specific derivation of the TLV provided due to limited data * TLV based on analogy to the reportedly more acutely toxic compound demeton; cited as based on demeton NOAEL of 0.09 mg/kg/d in humans; NOAEL of 0.05 mg/kg/d in rats; and NOAEL of 0.025 mg/kg/d in dogs.   Human data:   * Acute poisoning symptoms include nausea, vomiting, headache, dizziness and hyperaemia of nasal mucosa * Occupational exposures causing inhibition of AChE appear to be due to respiratory and dermal absorption; dose unknown or inadequate * Single fatality reported: following ingestion of 15 mL (died 9 d following exposure from acute pulmonary embolism) and in another case 50–500 mg/kg (died 83 h following exposure from acute cardiovascular collapse) * For demeton, no effects in humans exposed at 0.09 mg/kg/d; no further information.   Animal studies:   * S-isomer of methyl demeton more toxic to rats than O-isomer * LD50: 62–80 mg/kg demeton-S-methyl (female rats, oral), 676 mg/kg demeton-O-methyl (female rats, oral) * LD50: 110 mg/kg (guinea pigs, oral) * LD50: 64.6 mg/kg demeton-S-methyl (rats, intravenous), 216 mg/kg demeton-O-methyl (rats, intravenous) * No acute inhalation toxicity data; suggested to be like that following intravenous injection * Dermal applications in rats (15 daily applications at 5 mg/kg/d) did not result in overt toxicity, but partial reversible degeneration and necrosis of the liver, and reversible ChE inhibition in brain and serum noted * No genotoxicity studies available * No adverse effects reported in studies using repeat oral doses of demeton at 0.05 mg/kg/d in rats and 0.025 mg/kg/d in dogs produced no effects; no further information.   A skin notation is assigned following repeated dermal exposure to a relatively low dose in rats eliciting cholinergic and liver response. Insufficient data to recommend SEN, carcinogenicity notation or TLV-STEL. |
| DFG 1958 MAK: 0.5 ppm (4.8 mg/m3) |
| * MAK justification not provided * No additional data. |
| SCOEL NA NA |
| No report. |
| OARS/AIHA NA NA |
| No report. |
| HCOTN 2003 TWA: 0.5 mg/m3 |
| Review is based on methyl-S-demeton and studies after 1957, since after 1957 methyl demeton (which used to contain 30:70 ratio of S- to O-isomer) did not contain O-isomer.  Summary of additional data:   * 2 groups of 2 volunteers applied 30:70 mixture (S- and O- isomers) up to 1.9 mg/m3 in greenhouses for 5 consecutive d, 5 h/d and no significant change in serum ChE or RBC AChE activity * Lethal suicidal intoxication reported following ingestion ≈5 g * LC50: 210–500 mg/m3 (rats, 4 h) * LD50: 250 mg/kg bw (male rats, dermal); 33-129 mg/kg bw (rats, oral) * NOAEL: 0.036 mg/kg/d (dogs, 1 yr); doses 0, 0.036, 0.36 or 3.6 mg/kg/d methyl-S-demeton (reduced to 1.8 mg/kg/d from wk 37); and 0.05 mg/kg/d (rats, 2 yr), doses 0, 0.05, 0.35 or 2.5 mg/kg/d methyl-S-demeton; brain and RBC AChE inhibition * NOAEL: 0.07 mg/kg/d for maternal and reproduction toxicity in 2-generational study of rats; doses 0, 0.07, 0.35 or 1.75 mg/kg/d methyl-S-demeton in diet * Positive results in *in vitro* test in bacteria and mouse lymphoma cells, however negative results in mammals (Chinese hamster). Carcinogenic effects not observed in rats and mice * High acute lethal dermal toxicity in rats; skin notation recommended.   Recommended revision to health-based OEL (HBROEL) derived from NOAEL of 0.05 mg/kg/d in continuous feeding study of rats. Multiplication of the NOAEL by 7/5 for conversion to 5 d exposure from 7 d continuous study, results in concentration of 0.07 mg/kg/d. A factor of 4 was applied for allometric scaling from rats to humans and an assessment factor of 9 for inter- and intraspecies variation, resulting into a value of 0.002 mg/kg/d. Assuming a 70 kg worker with a respiratory rate of 10 m3 per 8 h shift, a revised TWA of 0.01 mg/m3 was recommended. |

### Secondary source reports relied upon

| Source |  | Year | Additional information |
| --- | --- | --- | --- |
| ECHA |  | 2019 | * Only demeton-S-methyl data available; no additional information. |

### 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 | Skin |
| HCIS | NA |
| NICNAS | NA |
| EU Annex | NA |
| ECHA | NA |
| ACGIH | Skin |
| DFG | H (skin) |
| SCOEL | NA |
| HCOTN | — |
| 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 |
| --- |

|  |  |  |  |
| --- | --- | --- | --- |
|  |  |  |  |
| Adverse effects in human case study: | yes | 4.00 |  |
| Dermal LD50 ≤1000 mg/kg: | yes | 3.00 |  |
| Dermal repeat-dose NOAEL ≤200 mg/kg: |  |  |  |
| Dermal LD50/Inhalation LD50 <10: | no | -3.00 |  |
| *In vivo* dermal absorption rate >10%: |  |  |  |
| Estimated dermal exposure at WES >10%: |  |  |  |
|  |  | 0 | **a skin notation is warranted** |

### IDLH

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

## Additional information

| Molecular weight: | 230.28 |
| --- | --- |
| Conversion factors at 25°C and 101.3 kPa: | 1 ppm = 9.4 mg/m3; 1 mg/m3 = 0.1 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) (2002) Demetonmethyl – MAK value documentation.

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).

Health Council of the Netherlands (HCOTN) (2003) Methyl-S-demeton. Health-based Reassessment of Administrative Occupational Exposure Limits. The Hague: Health Council of the Netherlands; publication no. 2000/15OSH/072.