

METHOXYCHLOR

CAS number: 72-43-5

Synonyms: Marlate, p,p'-dimethoxydiphenyltrichloroethane, DMDT, methoxy-DDT, 1,1,1-trichloro-2,2-bis(p-methoxyphenyl) ethane

Chemical formula: $C_{16}H_{15}Cl_3O_2$

Structural formula: —

Workplace exposure standard (interim)

TWA: 10 mg/m³

STEL: —

Peak limitation: —

Notations: —

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 10 mg/m³ is recommended to protect for adverse effects on the liver, central nervous system (CNS) and developmental effects in the foetus and offspring in exposed workers.

Given the limited data available from the primary sources, it is recommended that a review of additional sources be conducted at the next scheduled review.

Discussion and conclusions

Methoxychlor is a chlorinated hydrocarbon insecticide used on fruits, vegetables, forage crops and livestock.

The critical effects of exposure are adverse effects in the liver and CNS and on the developing foetus.

No inhalation data are identified. In humans, no adverse effects are identified in volunteers ingesting up to 2 mg/kg/day for eight weeks (ACGIH, 2018). ACGIH (2018) recommend a TWA of 10 mg/m³, concluding that at this concentration a worker will absorb up to 1.4 mg/kg/day, which is less than the dose (2 mg/kg/day) shown to be without adverse health effects. A NOAEL of 0.9 mg/kg/day for prenatal developmental toxicity is identified from a two generational study in rats, with maternal and foetal toxicity occurring at 44 mg/kg/day and above. This NOAEL was used as the starting point by DFG to derive a MAK of 1 mg/m³ (DFG, 2014). The influence of maternal toxicity on foetal effects remains unclear due to some concerns regarding the quality of this study. The US EPA (1990) presented an oral reference dose of 0.005 mg/kg/day for environmental health exposure based on a NOEL of 5.01 mg/kg/day in rabbits for excessive loss of litters.

The current SWA TWA of 10 mg/m³ is recommended be retained in the interim. This TWA is expected to be protective for adverse effects in the liver and CNS and developmental toxicity. Some

uncertainties remain regarding the robustness of the reported two-generational study by DFG (2014). An evaluation of additional sources is recommended at the next 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.

There are insufficient data to recommend a skin notation.

DRAFT

APPENDIX

Primary sources with reports

Source	Year set	Standard
SWA	1991	TWA: 10 mg/m³
ACGIH	2001	TLV-TWA: 10 mg/m³
<p>TLV-TWA is recommended to minimise the potential for adverse effects on the liver and CNS demonstrated in limited studies with animals.</p> <p>Summary of data:</p> <p>TLV based on following:</p> <p>At 10 mg/m³ a worker could absorb up to 1.4 mg/kg/d (calculation not presented); this dose is less than the highest dose shown to be without adverse health effects in sub-chronic studies in humans.</p> <p>Human data:</p> <ul style="list-style-type: none"> • No adverse effects in volunteers ingesting ≤2.0 mg/kg/d for 7 d/wk for 8 wk; used to justify TLV-TWA; no derivation description • No confirmed case of human poisoning in the literature. <p>Animal data:</p> <ul style="list-style-type: none"> • Low acute oral toxicity • In dogs, weight loss when fed 1,000 mg/kg/d for 6 mo: <ul style="list-style-type: none"> ◦ 2,000 mg/kg/d resulted in convulsion at 6 wk, followed by death within additional 3 wk • Rabbits died after 4–15 doses of 200 mg/kg/d; mild liver damage and nephrosis • Dietary 100 ppm (≈350 mg/d [human]) produced no sign of intoxication in rats • Inconclusive evidence of carcinogenicity. <p>Insufficient data to recommend a skin or sensitiser notation or TLV-STEL.</p>		
DFG	2014	MAK: 1 mg/m³
<p>MAK established in 2013 and based on teratogenic effects in rats.</p> <p>Summary of additional data:</p> <ul style="list-style-type: none"> • No available valid human data • LOAEL of 20 mg/kg/d; rats dosed <i>via</i> gavage at 0, 20, 100, 500 mg/kg/d, 5 d/wk for 28 d; mammary acinar atrophy significant from 100 mg/kg/d in males and T4 elevation in male rats not significant at 500 mg/kg/d • In a 2-generation study in male and female rats dosed with 0, 10, 500 or 1500 mg/kg in feed 10 weeks before and 7 weeks after mating (female doses P generation: at 0; 0.9; 44 or 122 mg/kg/d; F1 generation: at 0; 0.9; 45 or 133 mg/kg/d): <ul style="list-style-type: none"> ◦ from 44 mg/kg/d, the number of implantations and the number of live offspring decreased in a dose-dependent manner, with maternal toxicity also occurring in form of body weight gain, feed consumption decrease and oestradiol concentration in serum reduced ◦ from 44 mg/kg/d there were postnatal effects on body weight development, on the absolute or relative thymus and uterine weights and on the sexual development of the offspring (premature vaginal opening, delayed preputial separation, prolonged oestrus cycle) 		



Source	Year set	Standard
<ul style="list-style-type: none"> from 122 mg/kg/d in parent group – uterine weight reduced, prolonged oestrus and fertility index reduced (45.5%) authors conclude a NOAEL 0.9 mg/kg/d for prenatal developmental toxicity effects MAK derivation: <ul style="list-style-type: none"> Starting point: NOAEL of 0.9 mg/kg/d 7:5 for the daily exposure of the animals to 5 d occupational exposure per week 1:4 for rat and human-specific species-specific correction value 100% assumed oral absorption 70 kg 10 m³ respiratory volume 100% assumed lung absorption halved due to NOAEL from animal study result concentration of 1 mg/m³. <p>Skin notation based on 22 µg/cm²/h in goats and structural similarity comparison to DDT.</p>		
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	✓ N.D.	<ul style="list-style-type: none"> Human health Tier 1 assessment; not considered to pose an unreasonable risk to the health of workers.
US EPA	✓ 1990	<ul style="list-style-type: none"> No reliable information is available on the effects in humans RfD of 5x10⁻³ mg/kg/d based on NOEL of 5.01 mg/kg/d in rabbits; excessive loss of litters.

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	NA
NICNAS	NA



Source	Notations
EU Annex	NA
ECHA	NA
ACGIH	Carcinogenicity – A4
DFG	H (skin)
SCOEL	NA
HCOTN	NA
IARC	Carcinogenicity – Group 3
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:

Dermal repeat-dose NOAEL ≤ 200
mg/kg:

Dermal LD₅₀/Inhalation LD₅₀ < 10:

In vivo dermal absorption rate > 10%:

Estimated dermal exposure at WES
> 10%: yes

insufficient data to assign a skin notation

IDLH

Is there a suitable IDLH value available? Yes

Additional information

Molecular weight:	345.65
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:	✓
This chemical is a biological product:	<input type="checkbox"/>
This chemical is a by-product of a process:	<input 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) (2014) Methoxychlor – MAK value documentation.

International Agency for Research on Cancer (IARC) Methoxychlor. IARC Monographs – 20.

National Industrial Chemicals Notification and Assessment Scheme (NICNAS) (N.D.) Benzene, 1,1'-(2,2,2-trichloroethylidene)bis[4-methoxy-: Human health tier II assessment – IMAP report.

US Environmental Protection Agency (US EPA) (1990) Integrated Risk Information System (IRIS) Chemical Assessment Summary – Methoxychlor.

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