4-METHOXYPHENOL

CAS number: 150-76-5

Synonyms: Hydroquinone monomethyl ether, hydroxyanisole, mequinol

Chemical formula: $C_7H_8O_2$

Structural formula: —

Workplace exposure standard (retained)

TWA: **5 mg/m^3**

STEL: **—**

Peak limitation: **—**

Notations: **DSEN**

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 5 mg/m^3 is recommended to protect for skin and eye irritation and skin depigmentation 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

4-Methoxyphenol is primarily used as a chemical inhibitor, stabiliser and intermediate.

Critical effects of exposure are skin and eye irritation and skin depigmentation. There are limited data from both human and animal studies. As such, ACGIH (2018) base their TWA by analogy to more toxic hydroquinone in combination with dermal and ocular symptoms reported in animals. The lowest NOAEL identified for 4-methoxyphenol is 50 mg/kg/day in a sub-chronic oral study in rats for minor systemic effects (NICNAS 2017).

Given the limited available data, the TWA of 5 mg/m^3 is recommended to be retained to limit irritant effects based on the recommendation by ACGIH (2018). An examination of additional sources should be prioritised during subsequent reviews as no reliable long-term exposure data are available for this evaluation.

Recommendation for notations

Not classified as a carcinogen according to the Globally Harmonized System of Classification and Labelling of Chemicals (GHS).

Classified as a skin sensitiser and not a 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/m^3***
ACGIH	***2001***	***TLV-TWA: 5 mg/m^3***
TLV-TWA recommended to minimise the risk of skin and eye irritation and skin depigmentation in exposed workers. Summary of data: Human data: • Occupational exposure resulted in skin depigmentation. Animal data: • LD_{50}: 1,600 mg/kg (rats, oral) • LD_{50}: 720–970 mg/kg (rabbits, IP) • Direct exposure to rabbit eyes caused moderate corneal damage • Reported as 2–4 times less toxic than hydroquinone • Dermal studies on rabbits resulted in skin depigmentation, necrosis and chemical burns • Dogs exposed to 12 g/d (oral) resulted in bw loss, no effects at 6 g/d. TLV-TWA recommended partially by analogy to hydroquinone. Insufficient data to recommend a skin, sensitiser or carcinogen notation.		
DFG	***NA***	***NA***
No report.		
SCOEL	***NA***	***NA***
No report.		
OARS/AIHA	***NA***	***NA***
No report.		
HCOTN	***2011***	***Not assigned***
Available data insufficient to evaluate the carcinogenic properties of 4-methoxyphenol. • Pre-neoplastic and neoplastic abnormalities in carcinogenic study (oral, rat) not considered relevant to humans • Negative results in mutagenic assay.		

Secondary source reports relied upon

Source		Year	Additional information
NICNAS	✓	2017	• LD_{50}: 621 mg/kg (mice, oral) • LD_{50}: >2,000 mg/kg (rats and rabbits, dermal) • Positive results in 2 sensitisation studies in guinea pigs • Repeat dose NOAEL: 125 mg/kg/d (rats, 1 yr, oral) for body weight decrease, increases in liver and kidney weights and hyperplasia in the forestomach • NOAEL: 50 mg/kg/d (rats, 5–7 wk, oral) for body weight decrease • Positive in gene mutation assay in mammalian cells (MLTK assay) • Chromosomal aberrations induced in Chinese hamster ovary cells • DNA denaturation observed in T4 bacteriophage • Positive in mammalian cell gene mutation assay in L5178Y mouse lymphoma cells • Negative results in *in vivo* genotoxicity assays.
ECHA	✓	2011	• No additional information.

Carcinogenicity — non-threshold based genotoxic carcinogens

Is the chemical mutagenic?	Yes
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	Sen
HCIS	Skin sensitisation – category 1
NICNAS	Skin sensitisation
EU Annex	NA
ECHA	Skin Sens. 1
ACGIH	NA
DFG	NA
SCOEL	NA
HCOTN	NA
IARC	NA

Source	Notations
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 LD_{50} ≤1000 mg/kg:	no
Dermal repeat-dose NOAEL ≤200 mg/kg:	
Dermal LD_{50}/Inhalation LD_{50} <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:	124.14
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:	☐
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* 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).

Health Council of the Netherlands (HCOTN) (2011) 4-Methoxyphenol. Evaluation of the carcinogenicity and genotoxicity. Health Council of the Netherlands; publication no. 2011/28.

National Industrial Chemicals Notification and Assessment Scheme (NICNAS) (2017) Phenol, 4-methoxy: Human health tier II assessment – IMAP report.