M-PHENYLENEDIAMINE

CAS number: 108-45-2

Synonyms: 1,3-Benzenediamine, *m*-diaminobenzene

Chemical formula: $C_6H_8N_2$

Structural formula: —

Workplace exposure standard (retained)

TWA: **0.1 mg/m^3**

STEL: **—**

Peak limitation: **—**

Notations: **Sk., 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 0.1 mg/m^3 is recommended to protect for potential liver effects and skin irritation in exposed workers.

Discussion and conclusions

m-Phenylenediamine is used in permanent hair dye preparations. It is also used in dyes for textiles and other materials and as a component of photographic developing.

Critical effects of exposure are potential liver injury, skin irritation and dermatitis.

No inhalation data are available. *m*-Phenylenediamine produced a slight burning and itching of the skin when applied topically to humans. It also produced allergic reaction in workers exposed during production of the chemical. A NOAEL of 6 mg/kg/day for effects on the liver reported in a 90-day rat study by gavage. A 10% alcoholic m-phenylenediamine solution applied to the skin of rabbits caused local, moderate dermatitis but no sign of systemic toxicity (ACGIH, 2018).

Given the limited available data, the SWA TWA of 0.1 mg/m^3, the same as the TLV-TWA by ACGIH (2018) is recommended to limit any liver and irritant effects.

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 recommended based on evidence of systemic effects following dermal exposure in humans.

APPENDIX

Primary sources with reports

Source	Year set	Standard
SWA	***1991***	***TWA: 0.1 mg/m³***
ACGIH	***2001***	***TLV-TWA: 0.1 mg/m³***

TLV-TWA recommended to minimise the potential for possible liver injury, skin irritation and dermatitis.

Summary of data:

- Shares same toxicity profile as *p*-phenylenediamine
  - TLV-TWA of 0.1 mg/m^3 to minimise potential for respiratory and skin sensitisation
  - protection from eye and skin irritation, dermatitis and blood dyscrasia.

Human data:

- Application of 10% alcoholic solution directly to 1–5 cm^2 of intact skin and left uncovered produced a slight burning and itching sensation; no further details
- No local or systemic effects reported for dermal exposure of *o*- and *m*-phenylenediamine applied to ≈4 cm^2 of clean forearm skin left uncovered for 24 h
- 8% of workers potentially exposed for 5–10 yr to *m*-phenylenediamine during production returned positive result for the scratch test (with *m*-phenylenediamine allergen):
  - caused dysuria (painful urination) in 13.4 % of workers.

Animal data:

- LD_{50}: 650 mg/kg (rats, oral)
- 10% alcoholic solution applied to the skin of rabbits caused no sign of systemic toxicity and produced a local, moderate dermatitis
- 90-d oral gavage study in rats; 0, 2, 6 or 18 mg/kg/d; significant increase of the absolute and relative liver weights and an abundance of degenerative lesions with a significant increase in the numbers of pyknotic hepatocytes in the livers in both males and females at 18 mg/kg/d:
  - NOAEL of 6 mg/kg/d
- Not carcinogenic in rats and mice when administered orally or topically
- Evidence of mutagenicity *in vitro* and not *in vivo*
- A commercially available hair-dye preparation, containing 1.5% produced no evidence of embryotoxicity or teratogenicity following topical application to 20 pregnant rats throughout gestation.

Derivation of TLV-TWA:

- Starting with the NOAEL of 6 mg/kg/d and assuming a 70 kg worker inhales 10 m^3 of air over an 8-h working day arrives at ≈1 mg/m^3; it appears an UF of 10 is applied to arrive at a TWA of 0.1 mg/m^3; no further details.

Insufficient data to recommend a sensitiser or skin notation or TLV-STEL.

Source	Year set	Standard
DFG	***2009***	***Not assigned***
Due to the lack of information as to the effects in humans and particularly sensitising potential of the substance, a MAK value cannot be established; no further information.		
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	• Induced skin sensitisation in patch tests in 8/38 workers with dermatitis • A scratch test in workers showed adverse reactions; no further details • Induced mild sensitisation in guinea pigs • Considers critical health effects are mutagenicity, skin sensitisation, acute toxicity and eye irritation.

Carcinogenicity — non-threshold based genotoxic carcinogens

Is the chemical mutagenic?	Insufficient data
Is the chemical carcinogenic with a mutagenic mechanism of action?	No

The chemical is not a non-threshold based genotoxic carcinogen.

Notations

Source	Notations
SWA	—
HCIS	Skin sensitisation – category 1
NICNAS	—
EU Annex	Skin sensitisation – category 1
ECHA	NA
ACGIH	Carcinogenicity – A4
DFG	Carcinogenicity – 3B, H (skin), Sh (dermal sensitiser)
SCOEL	NA

Source	Notations
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:	yes
Dermal LD_{50} ≤1000 mg/kg:	
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 warranted

IDLH

Is there a suitable IDLH value available?	No

Additional information

Molecular weight:	108.15
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.

Deutsche Forschungsgemeinschaft (DFG) (2009) m-Phenylenediamine – MAK value documentation.

International Agency for Research on Cancer (IARC) (1978) Volume 16, Some aromatic amines and related nitro compounds—Hair Dyes, Colouring Agents and Miscellaneous Industrial Chemicals. IARC Monographs on the evaluation of the carcinogenic risk to humans.

National Industrial Chemicals Notification and Assessment Scheme (NICNAS) (2013) 1,3-Benzenediamine: Human health tier II assessment – IMAP report.

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).