

DIMETHYL ACETAMIDE

CAS number: 127-19-5

Synonyms: DMAC, N,N-Dimethylacetamide, acetdimethylamide, EINECS, 204-826-4, U-5954, SK 7176, N,N-dimethylethanamide, dimethylamide acetate

Chemical formula: C₄H₉NO

Workplace exposure standard (retained)

TWA: 10 ppm (36 mg/m³)

STEL: —

Peak limitation: —

Notations: Carc. 2, Sk.

IDLH: 300 ppm

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 ppm (36 mg/m³) is recommended to protect for effects in liver and kidneys, on reproduction and the central nervous system (CNS) in exposed workers, and to minimise potential effects in developing foetuses.

Discussion and conclusions

Dimethyl acetamide (DMAC) is widely used as a solvent for many organic reactions and in pharmaceutical preparations for parenteral administration (ACGIH, 2018).

Dermal exposure is a significant factor in overall absorption and toxicity. Studies in animals and humans have demonstrated that exposure can cause effects in liver, kidneys and reproductive effects, among other complications. An increase in liver injury was reported in two studies involving workers in a manufacturing setting (no exposure data provided). Liver and kidney toxicity are reported in chronic inhalation studies in rats and mice, with a NOAEC of 25 ppm reported. A NOAEC of 57 ppm for developmental effects was reported in an inhalation study in pregnant rabbits (ACGIH, 2018). Carcinogenicity studies indicated increased incidence of hepatocarcinomas following lifetime inhalation exposure for rats and mice. Despite confirmed carcinogenicity in animals, human data remains inconclusive.

The current TWA of 10 ppm is recommended to be retained based on the weight of evidence presented and it is considered protective for the critical effects reported in animals.

Recommendation for notations

Classified as a category 2 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 as evidence indicates significant absorption through the skin in the workplace.

APPENDIX

Primary sources with reports

Source	Year set	Standard
SWA	1991	TWA: 10 ppm (36 mg/m³)
ACGIH	2018	TLV-TWA: 10 ppm (36 mg/m³)
<p>Summary of data:</p> <p>TLV-TWA recommended to protect for potential hepatic, renal, developmental and reproductive and CNS effects reported in human and animal studies.</p> <p>Chronic inhalation studies in rodents result in a NOAEL of 25 ppm for hepatic and renal toxicity. Strong link between chronic inhalation exposure and hepatocarcinomas in animals. Not a genotoxic carcinogen based on weight of evidence.</p> <p>Skin notation recommended as dermal absorption is a significant contributor to overall toxicity. Information on the derivation of TLV-TWA not provided.</p> <p>Human data:</p> <ul style="list-style-type: none"> Repeated exposures at 20–25 ppm resulted in jaundice due to dermal absorption: <ul style="list-style-type: none"> 14/41 workers exposed for 2–10 yr) were found to have hepatomegaly and abnormal liver function (exposure concentrations unknown) Workers exposed to concentrations 0–2 ppm (with sporadic increases between 11–34 ppm) experienced dizziness, lethargy and weakness <ul style="list-style-type: none"> a concentration-dependent correlation between DMAC and its primary urinary metabolite monomethylacetamide (MMAC) was reported in 1 study on airborne concentrations (10 ppm of urinary MMAC for 1 ppm of DMAC inhaled) indicating airborne DMAC accounted for the greatest amount of urinary MMAC Limiting skin exposure by showering or changing clothes significantly reduced MMAC urinary levels in another study, confirming the importance of a skin notation Exposure resulted in a higher incidence of hepatic injury (observed 2–6 mo following exposure) in two studies involving workers in a manufacturing setting <ul style="list-style-type: none"> the incidence rate of hepatic injury was 7–10 times higher for workers exposed to higher concentrations (>20 mg MMAC/g creatinine) in one of the studies. <p>Animal data:</p> <ul style="list-style-type: none"> Oral LD₅₀: 5,809 mg/kg (rats, male), 4,930 mg/kg (rats, female) Dermal exposures caused severe skin irritation, discomfort and weight loss, followed by death under increased concentrations (2,000 mg/kg in rabbits) LC₅₀: ≥2,475 ppm (rats, 1 h inhalation) Studies investigating chronic exposures and carcinogenicity reported rats and mice exposed to 100 and 350 ppm (6 h/d, 5 d/wk, for 18 or 24 mo): <ul style="list-style-type: none"> increased liver weight, hepatic focal cystic degeneration (rats) and lipofuscin/haemosiderin accumulation in Kupffer cells (mice), among other complications increased incidence of hepatocellular adenomas (300 ppm, 6 h/d, 5 d/wk for 104 wk) in mice male rats had an increased incidence of liver tumours at 450 ppm 		



Source	Year set	Standard
<ul style="list-style-type: none"> ○ NOAEL reported at 25 ppm (rats, mice). • Developmental studies determined fetotoxic and teratogenic in several animal species; • NOAEL of 57 ppm in rabbits for developmental effects (increased skeletal variations); inhalation study 6 h/d from days 7–19 of gestation • Multiple genotoxicity studies demonstrated not a genotoxic carcinogen. 		
DFG	2009	MAK: 10 mL/m³; 36 mg/m³
Summary of additional data:		
Additional human data:		
<ul style="list-style-type: none"> • Exposure at 2 ppm (12 h mean value) or short-term exposure at 6.7 ppm resulted in no hepatotoxicity • 12 volunteers exposed to 6.1 ppm for 4 h determined ≈40% skin absorption. 		
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	<ul style="list-style-type: none"> • Repeated exposure can cause hepatitis in humans • Dermal LD₅₀: >2,000 mg/kg (mice, rats and rabbits); dermal repeat NOAELs of 500 and 1,000 mg/kg for male and female rats respectively • Dermal application on hamsters did not result in carcinogenicity, on the contrary, DCAM showed antitumor properties (lowered incidence of tumours).
NTP	✓ 2019	<ul style="list-style-type: none"> • Negative results for <i>K.Salmonella</i> mutagenicity test.
OECD	✓ 2001	<ul style="list-style-type: none"> • A cytogenic assay on human lymphocytes from 20 workers did not reveal an increase in chromosomal aberration.
US NIOSH	✓ 2014	<ul style="list-style-type: none"> • IDLH of 300 ppm based on acute inhalation toxicity animal data.

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	Skin
HCIS	—
NICNAS	Skin
EU Annex	NA
ECHA	NA
ACGIH	Carcinogenicity – A3, Skin
DFG	H (skin)
SCOEL	NA
HCOTN	NA
IARC	NA
US NIOSH	—

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:	No
Dermal repeat-dose NOAEL ≤ 200 mg/kg:	yes
Dermal LD ₅₀ /Inhalation LD ₅₀ < 10:	yes
<i>In vivo</i> dermal absorption rate > 10%:	yes
Estimated dermal exposure at WES > 10%:	No data
A skin notation is warranted	

IDLH

Is there a suitable IDLH value available?

Yes

Additional information

Molecular weight:	87.12
Conversion factors at 25°C and 101.3 kPa:	1 ppm = 3.56 mg/m ³ ; 1 mg/m ³ = 0.28 ppm
This chemical is used as a pesticide:	<input type="checkbox"/>
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 checked="" type="checkbox"/> ACGIH <input checked="" type="checkbox"/> DFG <input type="checkbox"/> SCOEL

Workplace exposure standard history

Year	Standard
1991	TWA: 10 ppm; 36 mg/m ³

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). N,N-Dimethyl acetamide – MAK value documentation.

National Industrial Chemicals Notification and Assessment Scheme (NICNAS). (2013). Acetamide, N,N-dimethyl-: Human health tier II assessment – IMAP report.

National Toxicology Program (NTP). (2019). Testing Status: N,N-Dimethylacetamine 10822-A.

Organisation for Economic Cooperation and Development (OECD) (2001) SIDS initial assessment profile – Dimethyl acetamide

US National Institute for Occupational Safety and Health (NIOSH) (2014) Immediately dangerous to life or health concentrations – Dimethyl acetamide.