FORMALDEHYDE

CAS number: 50-00-0

Synonyms: Methanal; methyl aldehyde

Chemical formula: H_2CO

Structural formula: HCOH

Workplace exposure standard (amended)

TWA: **0.1 ppm (0.12 mg/m^3)**

STEL: **0.3 ppm (0.37 mg/m^3)**

Peak limitation: **—**

Notations: **Carc. 1A; DSEN**

IDLH: **20 ppm**

Recommendation and basis for workplace exposure standard

A TWA of 0.1 ppm (0.12 mg/m^3) is recommended to protect for irritation of the eyes and upper respiratory tract and subsequently nasal cancer in exposed workers.

A STEL of 0.3 ppm (0.37 mg/m^3) is recommended to avoid significant sensory irritation and subsequent nasal pathologies.

Discussion and conclusions

Effects from inhalation exposure to formaldehyde are primarily localised, manifesting as sensory irritation and cellular changes that may lead to cancer. The LOAEL for irritation following inhalation identified in humans are reported at 0.25 and 0.3 ppm (ACGIH, 2018; HCOTN, 2003). Evidence in humans suggests that the prevention of irritation effects will protect against nasal cancers with results of a 40 year study indicating that exposure to 0.3 ppm formaldehyde for 40 years produces very low additional cancer risks (DFG, 2000). This is supported by evidence in animals with a NOAEL for nasal cancer in rats reported at 2 ppm and 1 ppm for nasal effects in rats and monkeys, respectively (ACGIH 2018; SCOEL, 2017). Consequently, the recommended TWA of 0.1 ppm is considered sufficient to protect against sensory irritation and therefore nasal cancer in all workers.

Data from human studies indicate short term exposure to concentrations of approximately 1 ppm results in slight eye irritation (ACGIH, 2018; HCOTN, 2003). Therefore, the recommended STEL of 0.3 ppm is considered protective.

Recommendation for notations

Classified as a carcinogen according to the Globally Harmonized System of Classification and Labelling of Chemicals (GHS). Recent re-classifications by ACGIH and IARC support a change to the carcinogenicity notation to the equivalent of 1A. It is therefore recommended that a review of the GHS classification for this endpoint is undertaken.

Classified as a skin sensitiser and not a respiratory sensitiser according to the GHS. However, the available evidence in humans is limited. Some investigation reports indicate the potential for formaldehyde to cause occupational asthma and ACGIH considers formaldehyde a respiratory sensitiser (RSEN). A further review of the literature is recommended to establish a RSEN notation.

Local effects predominate in human studies and limited animal data was presented regarding dermal absorption and systemic effects. Overall, there are insufficient data to recommend a skin notation.

APPENDIX

PRIMARY SOURCES WITH REPORTS

Source	Year set	Standard
SWA	***1986***	***TWA: 1 ppm (1.2 mg/m^3); STEL: 2 ppm (2.5 mg/m^3)***
ACGIH	***2017***	***TLV-TWA: 0.1 ppm (0.12 mg/m^3); TLV-C: 0.3 ppm (0.37 mg/m^3)***

TLV-TWA TLV-C recommended to protect for sensory irritation (eye and upper respiratory tract).

Summary of data:

- Highly irritating to both humans and animals
- Immunologic effects (allergic reactions and sensitisation) noted in human studies
- Hepatotoxicity reported in sub chronic studies in humans and animals.

Human data:

- Eye, nose, throat and lung irritation reported at <1–3 ppm
- Intolerance for prolonged exposure at 4–5 ppm
- Severe symptoms such as difficulty breathing at 10–20 ppm
- Respiratory tract injury at >50 ppm
- Chamber study (volunteers exposed for 4 h/d, 5 d/wk for 10 wk) reported:
  - LOAEL for eye irritation at 0.5 ppm (short-term peaks 1.0 ppm)
  - LOAEL for eye and nose irritation at 0.3 ppm
- Worker cross sectional study reported eye and respiratory tract irritation at 0.3 ppm (as 8 h TWA)
- Study of exposed pathologists observed an increase in M1dG adducts only at levels >0.53 ppm (no duration provided)
- Confirmed human carcinogen (A1) notation recommended based on:
  - elevated risk of nasopharyngeal cancer from epidemiologic studies
  - tumourigenic responses in short and long term inhalation studies on rats
  - consistency in site and cell type in animal experimental studies of nasopharyngeal cancer and human epidemiology observations
  - significant increase in cell proliferation in nasal epithelium of rats and rhesus monkeys
  - evidence of genotoxicity in rats, rhesus monkeys and humans exposed to formaldehyde
- Significant increases in deaths from nasopharyngeal cancer in workers exposed to an average of >1 ppm
- Occupational registry study reported 12/230 patients sensitised (respiratory)
- Reported that respiratory sensitisation is rare
- 0.2 ppm may increase susceptibility to respiratory hypersensitivity via activation the immune system.

Animal data:

- A rat exposure study of up to 14 d noted significant inhibition of mucociliary activity at 15 ppm and no effects at 0.5 ppm

Source	Year set	Standard

• NOAEL of 2 ppm for squamous cell nasal cancer in rat inhalation study
• *In vitro* studies suggest formaldehyde is a relatively weak mutagen:
  ○ genetic alterations (Drosophila larvae, fungi, bacteria)
  ○ negative and positive results in dominant lethal tests
• Studies evaluating DNA adducts in rats and macaques (6 h/d for 1 and 2 d) noted formation of endogenous DNA was higher in macaques.
• Lethality reported at 700 ppm in cats and mice (8 and 2 h); 15–16 ppm in mice and rabbits (>10 h)
• LC_{50}: 81 ppm (rats; total exposure not provided)
• No *in vitro* or animal data on dermal absorption
• Not teratogenic to animals; insufficient data about reproductive and developmental toxicity.		

DFG	***2000 & 2014***	***MAK: 0.3 ppm (0.37 mg/m³); MomV: 1 ppm (1.42 mg/m³)***

MAK recommended to protect for irritant effects on the eye.
Summary of additional data:
• In the low dose range, which does not lead to an increase in cell proliferation, it is considered that formaldehyde genotoxicity plays a minor part in carcinogenic potential:
  ○ supported by the results of a risk assessment which, for workers exposed to concentrations of 0.3 ppm for 40 yr, yielded a very low additional cancer risk for smokers and non-smokers
• Skin sensitisation confirmed through case reports and patch testing. 0.025–0.05% considered the threshold for eliciting a patch test reaction:
  ○ supported in animal study outcomes (guinea pigs and mice)
• Respiratory sensitisation reported in several human case reports
• Systemic reactions including anaphylaxis reported after skin contact
• No *in vitro* or animal data on dermal absorption.		

SCOEL	***2016***	***TWA: 0.3 ppm (0.369 mg/m³); STEL 0.6 ppm (0.738 mg/m³)***
TWA recommended to protect for sensory irritation and therefore, nasal cancer. Summary of additional data: • Genotoxic carcinogen with identified threshold; genotoxicity plays minor role in carcinogenic effects at low concentrations (0.7 ppm lowest dose tested in monkeys) • NOAEC of 1 ppm in rats and monkeys for nasal effects (6 to 22 h/d) • LOAEL from four long term of 6 ppm for rats (nasal cancer) (no further information) • Local carcinogenicity effects (inhalational studies in animals) relevant to humans • Prevention of irritation will prevent nasal cancer at low concentrations (<1 ppm) • Skin notation not assigned as local effects predominate • Dermal sensitisation notation assigned based on human results • Respiratory sensitisation notation not warranted as only rarely reported.		
OARS/AIHA	***NA***	***NA***
No report.		

Source	Year set	Standard
HCOTN	***2003***	***TWA: 0.12 ppm (0.15 mg/m^3), STEL: 0.42 ppm (0.5 mg/m^3)***

TWA assigned to protect for sensory irritation and cellular changes in the nose that lead to nasal cancer.

Summary of additional data:

- TWA is based on a LOAEL of 0.25 ppm (sensory irritation) with a factor of 2 applied to compensate for extrapolation to a NOAEL
- TWA sufficient to protect workers against cytotoxicity-induced hyperproliferation of the nasal respiratory epithelium and consequently the risk of nasal cancer
- RD_{50}: 3 ppm (mice, 10 min)
- No convincing evidence of respiratory sensitisation
- Skin sensitiser at concentrations >2%
- High incidence of nasal cancer reported in rats at >10 ppm (no further details)
- Long term chronic inhalational studies in animals report non-neoplastic adverse effects at >2 ppm (no further details)
- Positive genotoxic results in variety of experimental systems
- Reported a steep non-linear dose-response curve for nasal tumours
- Not found to affect reproduction in animal inhalational studies.

Secondary source reports relied upon

Source		Year	Additional information
NICNAS	✓	2006	• A LOEL of 0.5 ppm reported for sensory irritation in humans • LD_{50}: 270 mg/kg (rabbits, dermal) • LC_{50}: 414 ppm (497 mg/m^3) (mice, 4 h) • Strong skin sensitiser • The available human and animal data indicate gaseous formaldehyde is unlikely to induce respiratory sensitisation • No systemic toxicity was observed following repeated exposure to formaldehyde in animals and humans • Recommends that the current Australian workplace exposure standard be set at TWA of 0.3 ppm and STEL of 0.6 ppm (no evidence to support).

Carcinogenicity — non-threshold based genotoxic carcinogens

Is the chemical mutagenic?	No

Notations

Source	Notations
SWA	Carc. 2; SK:SEN
HCIS	Carcinogenicity – category 1B; Skin sensitisation – category 1
NICNAS	Carcinogen – category 2
EU Annex	Carcinogenicity – category 1B; Skin sensitisation – category 1

Source	Notations
ECHA	Carcinogenicity – category 1B
ACGIH	Carcinogen A1; DSEN; RSEN
DFG	Carcinogenicity category 4; Sh
SCOEL	Carcinogenicity – C; Sensitisation (Dermal)
HCOTN	—
IARC	Carcinogenicity – Group 1
US NIOSH	SK:SEN

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:	yes
Dermal repeat-dose NOAEL ≤200 mg/kg:	
Dermal LD_{50}/Inhalation LD_{50} <10:	yes
In vivo dermal absorption rate >10%:	
Estimated dermal exposure at WES >10%:	
	consider assigning a skin notation

IDLH

Is there a suitable IDLH value available? Yes

Additional information

Molecular weight:	92.53
Conversion factors at 25°C and 101.3 kPa:	1 ppm = 3.80 mg/m^3; 1 mg/m^3 = 0.263 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
1991	Peak limitation: 1 ppm (3.8 mg/m³)

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.

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