ACETIC ANHYDRIDE

CAS number:	108-24-7
Synonyms:	Ethanoic anhydride
Chemical formula:	$C_4H_6O_3$
Structural formula:	

Workplace exposure standard (amended)

TWA:	**0.5 ppm (2.1 mg/m^3)**
STEL:	**1 ppm (4.2 mg/m^3)**
Peak limitation:	**—**
Notations:	**—**
IDLH:	**200 ppm**
Sampling and analysis:	The recommended value is readily quantifiable through currently available sampling and analysis techniques.

Recommendation and basis for workplace exposure standard

A TWA of 0.5 ppm (2.1 mg/m^3) and STEL of 1 ppm (4.2 mg/m^3) are recommended to protect for irritation of the respiratory tract and eyes in exposed workers.

Discussion and conclusions

Data in humans is inconclusive. Irritation of the upper respiratory tract and eyes is reported at concentrations above 5 ppm. However, symptoms of eye irritation such as conjunctival irritation, reddening and lacrimation were also reported at concentrations below 5 ppm (ACGIH, 2018).

A NOAEC of 1 ppm was established based on a 90-d inhalation study in rats (ACGIH, 2018; DFG, 2018). The DFG (2018) used this point of departure to derive the recommended MAK of 0.1 ppm.

The recommended TWA applies an uncertainty factor of 2 to the NOAEC in rats of 1 ppm to account for the deficiency of the database and lack of clearly defined data in humans. Based on the evidence of acute irritant effects associated with short-term exposures to 5 ppm in humans and the NOAEC of 1 ppm in rats, a STEL of 1 ppm (4.2 mg/m^3) is recommended to protect for these effects.

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.

A skin notation is not warranted as there is no indication of systemic effects resulting from skin absorption.

APPENDIX

Primary sources with reports

Source	Year set	Standard
SWA	Year	***Peak limitation: 5 ppm (21 mg/m³)***
ACGIH	***2011***	***TLV- TWA: 1 ppm (4.2 mg/m³); TWA-STEL 3 ppm (13 mg/m³)***
TLV-TWA and TLV-STEL recommended to reduce upper respiratory tract and eye irritation in exposed workers. Summary of data: Human data: • Irritating to eyes, mucous membranes and skin • Vapour concentrations >5 ppm result in immediate, acute irritation of the eyes and upper respiratory tract. • Reports of conjunctival irritation, reddening of the eye and lacrimation at <5 ppm • Odour threshold reported between 0.13–0.81 ppm. Animal data: • NOAEL: 1 ppm; with irritation threshold at 1–5 ppm (rats, inhalation, 90 d) • LD_{50}: 4,000–4,320 mg/kg (rabbits, dermal) • No evidence of mutagenic effects in bacterial reverse mutation assays. Not classifiable as a human carcinogen. Limited data available to assign a Skin notation as acetic anhydride rapidly hydrolyses at site of contact to acetic acid and is not distributed systemically. Insufficient data available to assign a Sensitiser notation.		
DFG	***2018***	***MAK: 0.1 ppm (0.42 mg/m³)***

MAK value recommended to prevent irritation of mucous membranes and inflammation in humans.
Summary of data:
• PoD based on NOAEC of 1 ppm (90-d inhalation rats as per ACGIH) with application of uncertainty factor:
  ○ 3 for extrapolating animal data
  ○ 2 for chronic exposure considerations
  ○ rounded to 0.1 ppm using the DFG Preferred Value Approach
• Absorption via the skin is unlikely
• Not genotoxic.		

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
HSE	✓	2018	• TWA of 0.5 ppm and STEL of 2 ppm • Information on reasoning not identified.
NICNAS	✓	2018	• Limited information.
OECD	✓	1997	• Suggested revision of OEL based on NOAEC from 90 d inhalation study in rats (1 ppm) • LC_{50}: 1,680 mg/m^3 (≈402 ppm) (rat, inhalation study, 6 h) • Same study used by DFG (2018) in the derivation of the MAK and noted by ACGIH (2011).
US NIOSH	✓	1994	• IDLH: 200 ppm based on acute inhalation toxicity data.

Carcinogenicity — non-threshold based genotoxic carcinogens

Is the chemical mutagenic?	No

Notations

Source	Notations
SWA	NA
HCIS	NA
NICNAS	NA
EU Annex	NA
ECHA	NA
ACGIH	Carcinogenicity – A4
DFG	NA
SCOEL	NA
HCOTN	NA
IARC	NA
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? Yes

Additional information

Molecular weight:	102.09
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) (2018) Acetic Anhydride [MAK value documentation, 2018].

National Industrial Chemicals Notification and Assessment Scheme (NICNAS) (2018). Acetic anhydride: Human health tier I assessment – IMAP report.

Organisation for Economic Cooperation and Development (OECD) (1997). Acetic anhydride: SIDS Initial Assessment Report for 6th SIAM.

UK Health and Safety Executive (HSE) (2018) acetic anhydride – EH40/2005 Workplace exposure limits.

US National institute for Occupational Safety and Health (NIOSH) (1994) Immediately dangerous to life and health concentrations – acetic anhydride.