KETENE

CAS number:	463-51-4
Synonyms:	Carbomethane, ethenone
Chemical formula:	C_2H_2O
Structural formula:	—

Workplace exposure standard (interim)

TWA:	**0.5 ppm (0.86 mg/m^3)**
STEL:	**—**
Peak limitation:	**1.5 ppm (2.6 mg/m^3)**
Notations:	**—**
IDLH:	**5 ppm**

Sampling and analysis: The recommended value is quantifiable through available sampling and analysis techniques.

Recommendation and basis for workplace exposure standard

An interim TWA of 0.5 ppm (0.86 mg/m^3) is recommended to protect for irritant effects in exposed workers.

A peak limitation of 1.5 ppm (2.6 mg/m^3) is recommended to protect for lung damage in acutely 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

Ketene is a gas under standard conditions that polymerises readily. It is used as an intermediate in chemical manufacture. Critical effects of exposure are respiratory tract and eye irritation, pulmonary oedema, and irreversible lung damage.

No human exposure data are currently available and occupational exposures are rare due to the instability of the compound (HCOTN, 2001). A repeat inhalation study in animals that reports a NOAEC of 1 ppm and a LOAEC of 5 ppm for pulmonary damage (ACGIH, 2018) is considered unreliable by DFG (2003).

Evidence for genotoxicity is limited to two equivocal studies (HCOTN, 2001). Increased risk for blood and lymph cancers in a small number of human case studies were insufficient to characterise carcinogenic potential (HCOTN, 2001).

Based on animal studies, an interim TWA of 0.5 ppm and a peak limitation of 1.5 ppm are recommended. The recommended TWA is expected to be protective of irritation and oedema observed in animals above 1 ppm. The peak limitation of 1.5 ppm is expected to protect for irreversible pulmonary damage observed in mice at 5 ppm (ACGIH, 2018).

A STEL is not recommended due to the severity of acute symptoms. Examination of additional chronic and human exposure data should be prioritised during subsequent reviews.

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.

There are insufficient data to recommend a skin notation.

APPENDIX

Primary sources with reports

Source	Year set	Standard
SWA	***1991***	***TWA: 0.5 ppm (0.86 mg/m^3); STEL: 1.5 ppm (2.6 mg/m^3)***
ACGIH	***2001***	***TLV-TWA: 0.5 ppm (0.86 mg/m^3); TLV-STEL: 1.5 ppm (2.6 mg/m^3)***

TLV-TWA and TLV-STEL intended to minimise potential respiratory tract irritation and pulmonary oedema. Insufficient data available to recommend notations for carcinogenicity, skin absorption, or sensitisation.

Summary of data:

Recommended TLV-TWA and TLV-STEL expected to be sufficiently low to protect for potential pulmonary oedema and respiratory tract irritation in workers. Thresholds derived from subchronic animal inhalation study that reported a NOAEL of 1 ppm for chronic lung injury, and by analogy to the similarly toxic phosgene.

Human data:

- No chemical specific data presented.
- By analogy to phosgene:
  - phosgene formerly used as chemical warfare agent
  - TLV-TWA: 0.1 ppm (0.40 mg/m^3) to protect for respiratory tract irritation and lung oedema
  - LC_{50}: 500 ppm (1 min), 3 ppm (170 min), 30 ppm (17 min).

Animal data:

- One of the most irritating gases to the respiratory tract with similar toxicity and mechanism of action to phosgene
- Minimum lethal concentration (LC_{LO}, 10 min) from acute inhalation study: 50 ppm (mice), 200 ppm (monkeys), 750 ppm (cats), 1,000 ppm (rabbits):
  - dyspnoea, cyanosis, and severe respiratory damage with variable latency after exposure; pathologic effects localised to lungs showed congestion and oedema
  - cross-tolerance to other oedema-producing agents noted in mice
  - LOAEL: 5 ppm for physiological responses may be associated with acquiring a tolerance
- NOAEL for chronic pulmonary injury at 1 ppm in inhalation study (several unspecified species, 6 h/d, 5 d/wk, 6 mo):
  - similar results in repeat exposure study (monkeys, 7 h/d, 55 exposures); however, analytical uncertainties of study make its conclusions tentative
- Fibrosis and emphysema may contribute to tolerance associated with chronic exposures
- No ADME or mutagenicity data presented.

TLV-TWA for phosgene derived from LOAEL of 0.2 ppm for pulmonary oedema and some pulmonary lesions in subchronic inhalation study (goats, cats, rabbits, guinea pigs, rats, mice, 5 h/d, 5 d); depressed ciliary function and higher incidence of severe lesions at 1 ppm.

DFG	***1999***	***Not assigned***

Summary of additional data:

Source	Year set	Standard

MAK not established due to absence of human exposure data and reliable repeat inhalation studies with animals. Genotoxicity and carcinogenicity have not been investigated. Insufficient data available to assign a skin or sensitiser notation. Toxicological information based on animal studies only.
Human data:
• Odour threshold: 12 ppm (no further information provided)
• Substance is typically processed in situ as an intermediate in closed systems; worker exposure would only occur in an accident or during cleaning works of the closed systems.
Animal data:
• Eye irritation, coughing, and lethargy at 23 ppm (monkey, n=1, 4 h)
• Mice are most sensitive to pathological lung effects:
  ○ LOAEL: 5.8 ppm (mice, 10 min); 3 h observation period
• Exposure-dependent damage to CNS and respiratory tract at 12–53 ppm in single-dose inhalation study (mice, rats, guinea pigs, cats, rabbits, monkey, 30 min–88 h)
• NOAEL of 1 ppm for pulmonary damage (cited in ACGIH, 2018) considered unreliable based on analytical uncertainties in maintenance of concentrations in test atmosphere
• Putative tolerance not affirmed in repeat inhalation study at 5–11.4 ppm on the first exposure and 18–39 ppm on second exposure after 1–14 d (mice, 10 min):
  ○ exposures of 6–7 ppm were already lethal at single doses
  ○ LC_{50}: 17 ppm (10 min) derived from overall results
• Chronic exposure/carcinogenicity studies are difficult to conduct due to high acute toxicity of the substance:
  ○ dimeric form (diketene) less toxic than ketene; lifetime exposures to diketene by ip injection at 4 mg or dermal application at 10 mg (in a 10% solution) did no elicit carcinogenicity (rats)
• No ADME data presented.		

SCOEL	***NA***	***NA***
No report.		
OARS/AIHA	***NA***	***NA***
No report.		
HCOTN	***2001***	***TWA: 0.5 ppm (0.9 mg/m³)***
Summary of additional information: Agency considers toxicological database too limited to make health-based TWA recommendation. Acute toxicity data suggest that the current administrative 8 h TWA is too high. Ketene polymerises rapidly and cannot be stored as a gas. Human data: • 1 case reported each for non-Hodgkin's lymphoma, multiple myeloma, and nonlymphocytic leukaemia with respective odds ratios of 1.3, 2.6 and 1.7 in extensive case-control study of two chemical manufacturing facilities (n=29,000): ○ study not used in agency's evaluation due to highly limited number of cases and potential exposure to other chemicals. Animal data: • 1 report of negative results for back-mutation *in vitro* in *Neurospora*; positive results in a mutagenicity test in *Drosophila* (no further information provided, article is not summarised)		

Source	Year set	Standard
• No *in vitro* bacterial or *in vivo* mammalian mutagenicity tests available for evaluation • No ADME data presented.		

Secondary source reports relied upon

Source		Year	Additional information
HSE	✓	2002	• TWA: 0.5 ppm (0.86 mg/m^3) • STEL: 1.5 ppm (2.6 mg/m^3).
US NIOSH	✓	1994	• IDLH based on acute inhalation toxicity data in humans and animals (based on same acute inhalation study cited in ACGIH, 2018 and DFG, 2003).

Carcinogenicity — non-threshold based genotoxic carcinogens

Is the chemical mutagenic?	Insufficient data
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	—
HCIS	NA
NICNAS	NA
EU Annex	NA
ECHA	NA
ACGIH	—
DFG	—
SCOEL	NA
HCOTN	—
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
Insufficient data to assign a skin notation

IDLH

Is there a suitable IDLH value available?	Yes

Additional information

Molecular weight:	42.04
Conversion factors at 25°C and 101.3 kPa:	1 ppm = 1.72 mg/m^3; 1 mg/m^3 = 0.582 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) (2003) Ketene – MAK value documentation.

Health Council of the Netherlands (HCOTN) (2001) Ketene. Health-based calculated occupational cancer risk values. The Hague: Health Council of the Netherlands; publication no. 2000/15OSH/024.

UK Health and Safety Executive (HSE) (2002) EH40/2005 Workplace exposure limits.

US National Institute for Occupational Safety and Health (NIOSH) (1994) Immediately dangerous to life or health concentrations – Ketene.