
Ketene

(CAS reg no: 463-51-4)

Health-based Reassessment of Administrative
Occupational Exposure Limits

Committee on Updating of Occupational Exposure Limits,
a committee of the Health Council of the Netherlands

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1 Introduction

The present document contains the assessment of the health hazard of ketene by the Committee on Updating of Occupational Exposure Limits, a committee of the Health Council of the Netherlands. The first draft of this document was prepared by H Stouten, M.Sc. (TNO Nutrition and Food Research, Zeist, the Netherlands).

The evaluation of the toxicity of ketene has been based on the review by the American Conference of Governmental Industrial Hygienists (ACG99). Where relevant, the original publications were reviewed and evaluated as will be indicated in the text. In addition, literature was retrieved from the online data bases Medline, Toxline, and Chemical Abstracts covering the period 1966 until 26 April 1999 (19990426/UP), 1965 until 29 January 1999 (19990129/ED), and 1967 until 24 April 1999 (19990424/ED; vol 130, iss 18), respectively, and using the following key words: ketene, carbomethene, and 463-51-4. HSDB and RTECS, data bases available from CD-ROM, were consulted as well (NIO99, NLM99). The final literature search has been carried out in April 1999.

In April 2001, the President of the Health Council released a draft of the document for public review. The committee received no comments.

2 Identity

name	:	ketene
synonyms	:	carbomethene; ethenone; keto-ethylene
molecular formula	:	C ₂ H ₂ O
structural formula	:	H ₂ C=C=O
CAS reg no	:	463-51-4

Data from ACG99, NLM99.

3 Physical and chemical properties

molecular weight	:	42.02
boiling point	:	-56°C
melting point	:	-151°C
flash point	:	-
vapour pressure	:	at 25°C: 1.4×10^3 kPa ('calculated from experimentally derived coefficients')
solubility in water	:	reacts forming acetic acid
log P _{octanol/water}	:	-0.52 (estimated)
conversion factors (20°C, 101.3 kPa)	:	1 ppm = 1.8 mg/m ³ 1 mg/m ³ = 0.57 ppm

Data from ACG99, NLM99, <http://esc.syres.com>.

Ketene is a colourless gas with a sharp, penetrating odour. It is an unstable, readily polymerising compound, and cannot be stored in the gaseous state.

4 Uses

Ketene is used as an acetylating agent in chemical synthesis, especially of acetic acid and acetate esters (ACG99).

5 Biotransformation and kinetics

The committee did not find data on the kinetics of ketene.

6 Effects and mechanism of action

Human data

Ketene was one out of 21 chemicals selected as a suspect chemical in a nested case-control study of non-Hodgkin's lymphoma (52 cases), multiple myeloma (20 cases), and lymphocytic and nonlymphocytic leukaemias (18 and 39 cases, resp) among a cohort of approximately 29,000 men employed at two chemical manufacturing facilities and one research and developmental centre. Based on only one case each, odds ratios of 1.3, 2.6, and 1.7 were calculated for

non-Hodgkin's lymphoma, multiple myeloma, and nonlymphocytic leukaemia, respectively. However, due to this limited number of cases and potential exposure to other compounds, no conclusions can be drawn with respect to an aetiological role of ketene (Ott89).

The committee did not find other data on workers occupationally exposed to ketene.

Animal data

Single exposure

For male mice, a 10-minute inhalation LC₅₀ of 30 mg/m³ (16.5 ppm) has been estimated (observation time: 10 days) (Men59).

Generally, higher inhalation concentrations were found to induce mortality in experiments conducted in the thirties and forties, probably because analytical measurement methods were less accurate (Men59) or even not available (Tre49) in those days. All mice (number not reported) exposed by inhalation to 180 mg/m³ (100 ppm), for 5 minutes, died within 1 to 4 hours. Five-minute exposures to 360-540 mg/m³ (200-300 ppm) killed all mice, rats, and guinea pigs (numbers not reported), within *ca.* 1/2-1, 2, and 2-4 hours, respectively (Cam37). When exposed for 10 minutes, inhalation concentrations of 210 and 430 mg/m³ (120, 245 ppm) were lethal to 0/4 and 4/4 rats, respectively (observation time: 10 days). In mice, mortality rates were 20/20 and 18/20 following exposures to 120 and 210 mg/m³ (68, 120 ppm), respectively; in guinea pigs, these rates were 3/4 and 4/4 at 630 and 1070 mg/m³ (359, 610 ppm), respectively (observation time: 3 days) (Woo47). Using exposure periods of 10 minutes as well, Treon *et al.* found inhalation concentrations of 45, 90, 450, 675, 360, and 1350 mg/m³ (25, 50, 250, 375, 200, 750 ppm) to be non-lethal in mice (n=10), monkeys (n=1), rats (n=2), guinea pigs (n=2), cats (n=1), and rabbits (n=2), respectively; corresponding minimum lethal concentrations were 90, 360, 675, 900, 1350, and 1800 mg/m³ (50, 200, 375, 500, 750, 1000 ppm), respectively (Tre49).

Generally, there were only minor signs of irritation, and - mostly after a latency period of variable duration - laboured breathing, jerky clonic movements, and coma were seen; the animals died from respiratory failure with intense pulmonary oedema and marked capillary ingestion (Cam37, Tre49, Woo47).

Pre-exposure to non-lethal levels of ketene (in excess of 9 mg/m³ or 5 ppm) for 10 minutes or to ozone protected mice against otherwise lethal concentrations of ketene or ozone at exposure 3 to 14 days later (Men59).

Repeated exposure

Following two 4-hour inhalation exposures to 41 mg/m³ (23 ppm) mortality rates were 0/2, 0/1, 10/10, 2/2, and 4/4 in rats, monkeys, mice, guinea pigs, and rabbits, respectively, while two 6.5-hour exposures to this level were lethal to 2/2 rats and 2/4 rabbits (other species not tested). When exposed to 22 mg/m³ (12 ppm), 6 hours/day (except for day 1 and 2 with 4.5 and 5.5 hours, resp), 5 days/week, for 3 weeks, 4/7 mice, 1/2 rats, and 4/4 rabbits died. Rats (n=2/group), guinea pigs (n=2/group), and monkeys (n=1/group) survived exposure to 1.8 mg/m³ (1 ppm), 7 hours/day, 5 days/week, for 14 or 55 days. In mice, survival rates were 9/10 each for both exposure periods, and in rabbits, 4/4 and 2/5 for the 14- and 55-day period, respectively. No apparent injury was observed in the surviving animals (Tre49). In view of the limited number of animals exposed and the statement of the authors that they did not have an analytical method at their disposal to determine actual concentrations, the significance of the results of these experiments cannot be assessed.

Mutagenicity and genotoxicity

Ketene did not induce back-mutations in *Neurospora* (Jen52).

Referring to a paper published in 1947, ketene was stated to produce positive results when tested in *Drosophila* (no details presented) (Jen52).

No data on carcinogenicity or reproduction toxicity of ketene have been found.

7 Existing guidelines

The current administrative occupational exposure limit (MAC) for ketene in the Netherlands is 0.9 mg/m³ (0.5 ppm), 8-hour TWA.

Existing occupational exposure limits for ketene in some European countries and in the USA are summarised in the annex.

8 Assessment of health hazard

From acute inhalation data from animal experiments (10-min LC₅₀ in mice: 30 mg/m³ or 16.5 ppm), the committee concludes that ketene is a very toxic compound. Acute exposures caused respiratory tract irritation and animals died from respiratory failure with severe pulmonary oedema.

Ketene was found to be negative in an *in vitro* mutagenicity test in fungi and positive in a *Drosophila*-test.

The committee did not find data from valid repeated exposure toxicity studies (including the potential carcinogenicity and reproduction toxicity) or from genotoxicity tests in bacterial and mammalian cell systems *in vitro* or in mammals *in vivo*.

The committee considers the toxicological data base on ketene too poor to justify recommendation of a health-based occupational exposure limit.

The committee concludes that in view of the acute toxicity data the present MAC-value of 0.9 mg/m³ (0.5 ppm), as an 8-hour TWA, for ketene is too high.

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Annex

Occupational exposure limits for ketene in various countries.

country -organisation	occupational exposure limit		time-weighted average	type of exposure limit	note ^a	lit ref ^b
	ppm	mg/m ³				
The Netherlands - Ministry	-	0.9	8 h	administrative		SZW01
Germany - AGS	0.5	0.9	8 h			TRG00
- DFG MAK-Kom.	0.5	0.9	15 min			DFG01
-	-	- ^c				
Great Britain - HSE	0.5	0.87	8 h	OES		HSE01
	1.5	2.6	15 min			
Sweden	-	-				Arb00b
Denmark	0.5	0.9	8 h			Arb00a
USA - ACGIH	0.5	-	8 h	TLV		ACG01
	1.5	-	15 min	STEL		
- OSHA	0.5	0.9	8 h	PEL		ACG00
- NIOSH	0.5	0.9	10 h	REL		ACG00
	1.5	3	15 min	STEL		
European Union - SCOEL	-	-				CEC00

^a S = skin notation, which means that skin absorption may contribute considerably to body burden; sens = substance can cause sensitisation

^b Reference to the most recent official publication of occupational exposure limits

^c Listed among substances for which studies of the effects in man or in experimental animals have yielded insufficient information for the establishment of MAK values