Rijksinstituut voor Volksgezondheid en Milieu
Ministerie van Volksgezondheid, Welzijn en Sport

Stofdocument deel A

CAS-nr: 67-64-1 **Aceton** **CH_3-CO-CH_3** **VN-nr: 1090**
GEVI: 33

Synoniemen: dimethylketon, 2-propanon, DMK (Engels: dimethyl ketone)

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	**VRW (mg/m^3)**	480	480	480	480	480	480
Alarmeringsgrenswaarden	**AGW (mg/m^3)**	22.000*	12.000*	7.800*	5.200*	3.500	2.300
Levensbedreigende	**LBW (mg/m^3)**	40.000**	21.000*	14.000*	9.200*	6.100*	4.100
Datum vaststelling: 13-05-2009				1 mg/m^3 = 0,414 ppm; 1 ppm = 2,42 mg/m^3			

Explosiegrens: LEL= 2,1% ≈ 50.000 mg/m^3
* berekende interventiewaarde hoger dan 10% LEL
** berekende interventiewaarde hoger dan 50% LEL

Geur: Karakteristieke, fruitige geur
LOA: 390 mg/m^3

Fysisch-chemische eigenschappen

Uiterlijk: Kleurloze vloeistof.
Brand: De damp is zwaarder dan lucht en verspreidt zich over de grond met kans op ontsteking op afstand.
Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,2

Molecuulmassa: 58,1 g/mol
Zuurgraad: Geen data
LogKow: -0,2
Wateroplosbaarheid: volledig
Verzadigde dampdruk: 247 mbar

Overige informatie

Publieke grenswaarde:
1210 mg/m^3 (8 uur)
MAK: 1200 mg/m^3
TLV-TWA: 1810 mg/m^3

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW: Geen informatie

VRW → AGW: Lichte oog-, keel-, en neusirritatie, hoofdpijn, gevoel van zwakte

AGW → LBW: misselijkheid, braken, hoofdpijn, duizeligheid, verwardheid, bewustzijnsdaling

Boven LBW: coma, sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Aceton veroorzaakt irritatie van ogen, neus en keel.
- Aceton veroorzaakt depressie van het CZS.

Effecten bij blootstelling aan vloeistof

Huidcontact: prikkeling, droge huid, ruwe huid

Oogcontact: roodheid en pijn, tranenvloed

Carcinogeniteit

IARC classificatie: niet geclassificeerd
CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp

algemeen: frisse lucht, rust, halfzittende houding; arts raadplegen bij aanhoudende klachten (m.n. bewustzijnsverlaging)

ogen: desgewenst spoelen met water (evt. contactlenzen verwijderen)

Ontsmetting vloeistof

huid: verontreinigde kleding uittrekken, minimaal 20 min. spoelen met veel water of douchen

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen.

inslikken: mond laten spoelen (uitspugen!), GEEN braken opwekken en arts raadplegen

Specifieke behandeling en materialen*:…*

Neem contact op met het NVIC (Tel: 030 - 274 8888) voor informatie met betrekking tot medisch handelen

National Institute for Public Health and the Environment
Ministry of Health, Welfare and Sport

Stofdocument deel B

CAS-nr: 67-64-1 **Acetone** **CH_3-CO-CH_3** **UN-nr: 1090**

Basis for the Dutch Intervention Values

VRW: AEGL value is adopted, 2 h value added

AGW: AEGL value is adopted, 2 h value added

LBW: AEGL value is adopted, 2 h value added

Date: 13-05-2009 | AEGL document: Interim, 2005

Dutch Intervention Values (mg/m^3)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	480	480	480	480	480	480	NOAEL for slight irritation in humans
AGW	22,000*	12,000*	7,800*	5,200*	3,500	2,300	NOAEL for ataxia in rats
LBW	40,000**	21,000*	14,000*	9,200*	6,100*	4,100	No lethality in rats

* value higher than 10% of LEL; ** value higher than 50% of LEL

Derivation of the Dutch Intervention Values

VRW: The VRW derivation is based on observations in four studies with human volunteers exposed for 3-5 minutes, 2 hours, 6 hours and 7.5 hours. At 200 ppm (483 mg/m^3), subjective symptoms (eye/throat irritation) were not reported more often than in controls. At 250 ppm (604 mg/m^3) no irritative symptoms on mucous membranes or effects on the central nervous system (headache, fatigue, feeling of sickness, dizziness, intoxication) were observed in one study; in a second study, slight irritation and few complaints about subjective discomfort (feeling of tension, general weakness, heavy eyes, lacking in energy) were reported at 250 ppm (604 mg/m^3), and these subjective symptoms were felt by most volunteers at 500 ppm (1210 mg/m^3) and 1000 ppm (2420 mg/m^3). Slight irritation at 300 ppm (725 mg/m^3) and subjective irritation in the majority of exposed volunteers at 500 ppm (1210 mg/m^3) were reported in a further study. Therefore, 200 ppm (480 mg/m^3) was selected as point of departure to derive VRW values. However, the irritation effects at this concentration are probably influenced by the odour of acetone. Based on an extensive literature search by Arts *et al.* (2002), it was noted that subjective irritation is observed at acetone concentrations <1000 ppm (2420 mg/m^3) and objective irritation is observed >10,000 ppm acetone (24200 mg/m^3).

Because the concentration of the point of departure represents a NOAEL for local effects and effects at higher concentrations were weak, an intraspecies factor of 1 is applied. The value of 200 ppm (480 mg/m^3) was used for all timepoints since accommodation to slight irritation occurs and the complaints about subjective discomfort at higher concentrations were reported not to increase during 6 hour or 7.5 hour exposure.

AGW: The AGW is based on the NOAEL for ataxia in rats following exposure to 6000 ppm (14,500 mg/m^3) acetone for 4 hours. At the next higher concentration of 12,000 ppm (29,000 mg/m^3) reversible ataxia was observed. Reversible ataxia also was observed in another study at exposure of rats to 12,600 ppm (30,500 mg/m^3) for 3 hours, but a no-effect level was not determined in that study. An interspecies factor of 1 was used for the following reasons. First, toxicokinetic studies show that following inhalation the concentration of acetone in blood is similar or lower in humans than in rats. Furthermore, with respect to toxicodynamics, effects of substances such as acetone that are non-specific acute CNS-depressants in general do not show much variation between species. Finally, an interspecies factor of 3 would (together with an intraspecies factor of 4.2, see below) have resulted in AGW of 1150 mg/m^3 for 4 hours and of 765 mg/m^3 for 8 hours. These values are not supported by data from controlled human studies in which exposures up to 1000 - 1200 ppm (2420 – 2900 mg/m^3) for up to 7.5 hours resulted in irritation and slight headaches but no more severe effects. Furthermore, available toxicokinetic data for humans show that an exposure to 480 ppm (1160 mg/m^3) for 4 hours or 320 ppm (773 mg/m^3) for 8 hours would lead to acetone concentration in blood below 50 mg/L. Such concentrations are still in the physiological range which can be observed in healthy fasting humans. With respect to an intraspecies factor, it is observed in humans that newborns consistently are the most sensitive age group for volatile anesthetics in general. No human data for acetone were available allowing for the derivation of a substance-specific intraspecies factor. However, in a study with rats of different ages it was observed that the lethal dose (LD_{50} oral) of acetone was 4.2-fold lower in newborns than in adults. It is assumed that intraspecies differences between humans are also covered by this range. Therefore, an intraspecies uncertainty factor of 4.2 was applied to account for sensitive individuals. The data were scaled across time using $C^n \times t = k$ with n = 1.7 as outlined below for LBW.
It is noted that the reliability of the derived n-value is limited, however the n-value is derived from the same study and is expected to be better than the default values for n.

LBW: The LBW is based on a study in rats in which no deaths of animals occurred at exposure to 12,600 ppm (30,500 mg/m^3) for 3 hours. In that study, also no deaths were observed in animals exposed to 19,000 (45,900 mg/m^3) and 25,300 ppm (61,100 mg/m^3), but since 1 of 6 animals died at 16,000 ppm (38,700 mg/m^3) in another study, the findings at 12,600 ppm (30,500 mg/m^3) exposure for 3 hours were taken as point of departure for the derivation of LBW values. An interspecies uncertainty factor of 1 was applied because the same toxic effects (CNS depression) which are relevant for AGW are also relevant in case of LBW. Also, an interspecies factor of 3 (together with an intraspecies factor of 4.2, see below) would result in a 4 hour LBW of 840 ppm (2030 mg/m^3) and an 8 hour LBW of 560 ppm (1350 mg/m^3). These values are not supported by data from a controlled human study in which no life-threatening effects were observed at exposures up to 2110 ppm (5100mg/m^3) for 8 hours and a number of other studies in which no severe effects on the central nervous system were observed at exposures up to 1000 - 1200 ppm (2420 – 2900 mg/m^3) for 6 - 7.5 hours. A substance specific intraspecies uncertainty factor of 4.2 (see derivation of AGW above) was applied to account for sensitive individuals. The experimentally derived exposure values were scaled across time using $C^n \times t = k$ with n = 1.7 that was derived by extrapolation from 4-hour and 8-hour LC_{50} data.
It is noted that the reliability of the derived n-value is limited, however the n-value is derived from the same study and is expected to be better than the default values for n.

Additional toxicological information (including relevant results of a general literature search, if any)

The acute toxicity of acetone is low and no reports were located in which exposure of humans to acetone resulted in death. Following exposure to acetone, the primary effects in humans are irritation and effects on the central nervous system (CNS).

An extensive literature search was presented by Arts *et al.* (2002): An analysis of human response to the irritancy of acetone vapours. Crit. Rev. Toxicol. 32, 43-66. It was noted that subjective irritation is observed at acetone concentrations <1000 ppm (2420 mg/m^3) and objective irritation is observed >10,000 ppm acetone (24200 mg/m^3) and that subjective irritation is influenced by odour.

In a developmental/reproductive toxicity study with mice and rats, no maternal or fetal toxicity was observed at 2000 ppm (4800 mg/m^3). At 6,600 ppm (16,000 mg/m^3) in mice and 11,000 ppm (27,000 mg/m^3) in rats, maternal and fetal weight were reduced and the incidence of late resorptions in mice was slightly increased (however, the mean number of live fetuses per litter was not decreased). In rats exposed to 11,000 ppm (27,000 mg/m^3), the percent of litters with at least one pup exhibiting malformations and the diversity of malformations was higher compared to controls, but the incidence of fetal malformations was not significantly increased.

H319: Causes serious eye irritation; H336: may cause drowsiness or dizziness.

Carcinogenicity and derivation of the CRP value

IARC classification: not classified.

No carcinogenic risk potency (CRP) was derived.

Carcinogenicity studies are lacking.

Odour and derivation of the LOA value

Odour: sweetish, mildly pungent and fruity odor.

OT_{50}: 10.25 ppm (24.77 mg/m^3)[AEGL (2005); Wysocki et al. (1997)]
LOA = 11.8 * OT_{50} * 1.33 = 390 mg/m^3

(The concentration Level leading to distinct Odour Awareness (I=3) is calculated using the formula: I = 2.33 * log (C/OT_{50}) + 0.5. A correction factor of 1.33 is applied to this value)

The LOA is below the VRW, therefore subjects will be aware of the odour below the level where health effects may be expected.

Other standards and guidelines (1h values in mg/m^3, unless otherwise indicated)

VRW level **480**	*AEGL-1* 480	*ERPG-1* not derived		*IDLH*: 6,040 (30 minutes)
AGW level **7,800**	*AEGL-2* 7,700	*ERPG-2* not derived		
LBW level **14,000**	*AEGL-3* 14,000	*ERPG-3* not derived		