

Stofdocument deel A

CAS-nr: 108-24-7

Azijnzuuranhydride (CH₃CO)₂O

VN-nr: 1715

GEVI: 83

Synoniemen: acetyloxide, azijnzuuroxide (Engels: acetic anhydride)

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	2,1	2,1	2,1	2,1	2,1	2,1
Alarmeringsgrenswaarden	AGW (mg/m³)	34	23	19	15	12	7,6
Levensbedreigende waarden	LBW (mg/m³)	290	200	160	120	99	65
Datum vaststelling: 31-10-2017		1 mg/m ³ = 0,235 ppm; 1 ppm = 4,247 mg/m ³					
Explosiegrens: LEL = 2,0 vol% ≈ 84 939 mg/m ³ (boven 49°C damp met lucht explosief)		Geur: stekende geur LOA: 8,0 mg/m ³					
Fysisch-chemische eigenschappen				Overige informatie			
Uiterlijk: kleurloze vloeistof Brand: brandgevaarlijk		Molecuulmassa: 102,1 g/mol Zuurgraad: ≈ 3 bij 1g/100ml LogKow: -0,3		Publieke grenswaarde: Niet afgeleid MAK: 21 mg/m ³ TLV-TWA: 4,3 mg/m ³			
Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,01		Wateroplosbaarheid: reactie Verzadigde dampdruk: 5,1 mbar					
Toxicologische eigenschappen							
Effecten bij inhalatoire blootstelling <u>Onder VRW:</u> lichte irritatie van neus <u>VRW → AGW:</u> irritatie slijmvliezen, pijn achter borstbeen <u>AGW → LBW:</u> keelpijn en hoest, tranen, branderig gevoel, benauwdheid <u>Boven LBW:</u> larynx- en glottisoedeem, ademnood, sterfte				Toxiciteit bij eenmalige, inhalatoire blootstelling <ul style="list-style-type: none"> Azijnzuuranhydride werkt irriterend tot bijtend op de ogen, de huid en de luchtwegen. Blootstelling aan azijnzuuranhydride kan longontsteking, longoedeem en een astmatische reactie veroorzaken. De verschijnselen hiervan kunnen vertraagd optreden en versterkt worden door lichamelijke inspanning. In ernstige gevallen kans op verstikking door zwellingen in de keel. Personen met verminderende longfunctie en (chronische) obstructieve luchtwegaandoening zijn mogelijk gevoeliger voor de effecten van azijnzuuranhydride. 			
Effecten bij blootstelling aan vloeistof <i>Huidcontact:</i> bijtend, prikkeling, roodheid, blaren, pijn, brandwonden <i>Oogcontact:</i> tranenvloed, bijtend, hoornvliesbeschadiging, ernstige brandwonden, verlies van gezichtsvermogen				Carcinogeniteit IARC classificatie: niet geclassificeerd CRP: niet afgeleid			
Beknopte medische informatie							
Ontsmetting damp <i>algemeen:</i> frisse lucht, rust, halfzittende houding, direct spoedeisende medische hulp inzetten							
Ontsmetting vloeistof <i>huid:</i> bij verbranding aan de huid vastgeplakte kleding NIET lostrekken, spoelen met veel water / kleding verwijderen, direct spoedeisende medische hulp inzetten. <i>ogen:</i> minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer. <i>inslikken:</i> mond laten spoelen (uitspugen!), GEEN braken opwekken, direct spoedeisende medische hulp inzetten.							
Specifieke behandeling en materialen: geen. Neem contact op met het NVIC (Tel:+31 (0)30 274 8888) voor informatie met betrekking tot medisch handelen							

Stofdocument deel B

CAS-nr: 108-24-7

Acetic anhydride

(CH₃CO)₂O

UN-nr: 1715

Basis for the Dutch Intervention Values

VRW: Based on information as described in ERPG-document, other time-points added

AGW: Based on information as described in ERPG-document, different values are derived, other time-points added.

LBW: Based on information as described in ERPG-document, different values are derived, other time-points added.

Date: 31-10-2017

ERPG, 2008

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	2.1	2.1	2.1	2.1	2.1	2.1	Mild respiratory irritation
AGW	34	23	19	15	12	7.6	Reversible irritation of the eye and respiratory tract
LBW	290	200	160	120	99	65	Threshold for rat lethality

Derivation of the Dutch Intervention Values

VRW: In the absence of suitable single exposure data, the VRW is based on data from a subchronic inhalation study. Rats (10/sex/concentration) were exposed to concentrations of 0.98, 4.96 and 20 ppm (4.2, 21 and 85 mg/m³, respectively) for 6 hours per day, 5 days per week for 13 weeks. One third of each group was retained for a 13-week recovery period. At 85 mg/m³, rats had partially closed eyes after the first two exposures, followed by noisy breathing (indicative of mild effects on the respiratory tract) which progressively diminished in the recovery period. Because noisy breathing was only occasionally observed at 21 mg/m³, this was selected as a PoD for the VRW derivation. The default uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences. Time scaling was not applied as respiratory irritation is considered to be concentration-dependent rather than exposure duration-dependent.

AGW: In the absence of suitable single exposure data, the AGW is based on data from a subacute inhalation study as described in the ERPG document. Rats (5/sex/concentration) were exposed to concentrations of 24, 103 (males)/104 (females), and 407 (males only) ppm (corresponding to 102, 437/442 and 1729 mg/m³, respectively) for 6 hours/day, 5 days/week for various periods of time: for 2 weeks for the 102 mg/m³ group, only for 6 days (exposure was terminated due to treatment-related effects) for the 437/442 mg/m³ group and for 1 day for the 1729 mg/m³ group (due to mortality within 24 hours). Females were not treated with 1729 mg/m³ due to the mortality observed in males. Rats exposed to 437 and 1729 mg/m³ showed lachrymation, gasping, noisy respiration and half-closed eyes. At 1729 mg/m³, severe degenerative changes were seen in nasal passages, larynx, trachea and lungs. At 437 and 102 mg/m³, less severe degenerative changes were seen in nasal passages, larynx, trachea and lungs. At 102 mg/m³, half-closed eyes in females was the only clinical abnormality seen during the first day of exposure and there were no clinical signs in males and no effects on bodyweight after the first exposure. For these reasons, 24 ppm (102 mg/m³) was selected as the PoD for the AGW derivation. These findings are supported by a 13-week study (see VRW) which showed that at 85 mg/m³, rats had partially closed eyes after the first two exposures, followed by noisy breathing. All changes regressed in this study during the recovery period, indicating the effects were reversible. The default uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences. Time scaling was applied using the equation $C^n \times t = k$ with the default values of n=1 and n=3 when extrapolating to longer and shorter time points, respectively.

LBW: In the absence of suitable single exposure data, the LBW is based on the same subacute inhalation toxicity study in rats as used for the AGW. Rats were exposed to 24, 103 (males)/104 (females), and 407 (males only) ppm (102, 437/442 and 1729 mg/m³, respectively) for 6 hours/day for 1 day to 2 weeks. For exposure details see AGW rationale. At 1729 mg/m³, 2/5 males died within 24 hours after one treatment and the remaining 3 males were killed due to clinical conditions (all had gasping

respiration and 2 were lethargic). Females were not exposed to these concentrations due to severity of effects observed in male rats. No animals (males or females) died after repeated exposure to 102 mg/m³ for 2 weeks or to 437 mg/m³ for 6 days. The concentration of 1729 mg/m³ in a 6-hour sub-acute inhalation toxicity study with rats was used as PoD for the derivation of the LBW. This exposure level is considered an assumed LC₅₀ as 2 out of 5 male rats died. A modifying factor was applied to extrapolate this value to an LC₀₁ value. Given the steep concentration-response curve a MF of 2 was considered sufficient. The default uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences. Time scaling was applied using the equation $C^n \times t = k$ with the default values of n=1 and n=3 when extrapolating to longer and shorter time points, respectively.

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

Susceptible populations include individuals with impaired pulmonary function, especially those with obstructive airway disease.

The available data indicate that acetic anhydride is not teratogenic or toxic for reproduction after inhalation.

H332: harmful if inhaled; H314: Causes severe burns and eye damage; H302: harmful if swallowed.

Carcinogenicity and derivation of the CRP value

IARC classification: not classified
Derivation of the carcinogenic risk potency (CRP):
No carcinogenic risk potency (CRP) was derived

Odour and derivation of the LOA value

Odour: pungent
OT: 0.56 mg/m³ [Ruth, 1986]
LOA = 11.8 * 0.56 * 1.33 = 7.8 mg/m³
(The concentration Level leading to distinct Odour Awareness (I=3) is calculated using the formula: $I = 2.33 * \log(C/OT) + 0.5$. A correction factor of 1.33 is applied to this value)
The LOA lies below the AGW and LBW values, and above the VRW.

Other standards and guidelines (1h values in mg/m³, unless otherwise indicated)^a

VRW level 2.1	AEGL-1 -	ERPG-1 2.1		IDLH: -
AGW level 19	AEGL-2 -	ERPG-2 63		
LBW level 160	AEGL-3 -	ERPG-3 420		

^a Note that the ERPG values as presented here (in mg/m³) are derived using the conversion factors of the ERPG