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

Stofdocument deel A

CAS-nr: 75-86-5 **Acetoncyaanhydrine** **$(CH_3)_2$−C(OH)−CN** **VN-nr: 1541** **GEVI: 669**

Synoniemen: ACH, 2-cyano-2-propanol; 2-methylacetonitril; (Engels: acetone cyanohydrin)

Interventiewaarden		10 min.	30	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	**VRW (mg/m^3)**	13	8,8	7,0	5,6	4,4	3,5
Alarmeringsgrenswaarden	**AGW (mg/m^3)**	45	35	30	26	22	19
Levensbedreigende waarden	**LBW (mg/m^3)**	88	69	59	50	44	38
Datum vaststelling: 16-12-2010			1 mg/m^3 = 0,28 ppm; 1 ppm= 3,5 mg/m^3				

Explosiegrens: LEL=2,2 vol% ≈ 78.000 mg/m^3
Stof reageert heftig met oxidatiemiddelen, geconcentreerde zuren en sterke basen met kans op brand en explosie, waarbij stof ontleedt in cyaanwaterstof en aceton.

Geur: Een bittere amandelgeur als gevolg van het ontstaan van HCN bij het snel uiteenvallen van acetoncyaanhydrine. De stof zelf heeft geen geur. De geur kan niet als detectiemaat worden gehanteerd.

LOA: niet afgeleid

Fysisch-chemische eigenschappen

Uiterlijk: kleurloze tot gele vloeistof

Brand: brandbaar

Molecuulmassa:	85,1 g/mol
Zuurgraad:	Geen data
LogKow:	-0,5
Wateroplosbaarheid:	Volledig
Verzadigde dampdruk:	1,00 mbar

Overige informatie

Publieke grenswaarde:
Niet afgeleid
MAK: niet afgeleid
TLV-TWA: niet afgeleid

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW:	geen effecten te verwachten
VRW → AGW:	hoofdpijn, misselijkheid
AGW → LBW:	duizeligheid, verwardheid, braken, oogirritatie, amandel of bittere smaak, verlamming, snelle pols en rood worden van gezicht
Boven LBW:	depressie van CZS en ademhaling, hartritmestoornissen, hypotensie, convulsies, coma en sterfte; mogelijk voorafgegaan door korte periode van CZS stimulatie, hypertensie en hyperventilatie

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Acetoncyaanhydrine ontleedt zeer snel in aceton en cyaanwaterstof. De acute toxiciteit van aceton is vele malen lager dan de acute toxiciteit van cyaanwaterstof; de toxiciteit van acetoncyaanhydrine wordt bepaald door de vorming van cyaanwaterstof.
- Cyanide blokkeert de ademhalingsketen in de cel. Hierdoor wordt de energiehuishouding verstoord en kan lactaatacidose ontstaan.
- Primaire doelorganen zijn het centrale zenuwstelsel en het cardiovasculaire systeem.
- Sterfte is veelal het gevolg van ademhalingsdepressie.

Effecten bij blootstelling aan vloeistof

Huidcontact: roodheid en pijn
Stof kan door de huid worden opgenomen.

Oogcontact: roodheid en pijn

Carcinogeniteit

IARC classificatie: niet geclassificeerd
CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp
algemeen: 100% zuurstof, GEEN mond-op-mondbeademing, specifieke behandeling en direct spoedeisende medische hulp inzetten.

Ontsmetting vloeistof
huid: direct spoedeisende medische hulp en specifieke behandeling inzetten, ondertussen verontreinigde kleding uittrekken, *af*spoelen met veel water of douchen.
ogen: direct spoedeisende medische hulp inzetten, ondertussen *uit*spoelen met water (evt. contactlenzen verwijderen)
inslikken: mond laten spoelen (uitspugen!), specifieke behandeling (GEEN mond-op-mondbeademing, GEEN braken opwekken) en direct spoedeisende medische hulp inzetten.

Specifieke behandeling en materialen:
De benodigde middelen (100% zuurstof, specifieke antidota zoals o.a. hydroxocobalamine, of 4-DMAP, beide evt. gevolgd door natriumthiosulfaat) moeten met gebruiksaanwijzing ter plekke beschikbaar zijn.

Neem contact op met het NVIC (Tel: +31 (0)30 - 274 8888) voor informatie met betrekking tot medisch handelen

Stofdocument deel B

CAS-nr: 75-86-5 **Acetone cyanohydrin** **$(CH_3)_2$−C(OH)−CN** **VN-nr: 1541**

Dutch Intervention Values (mg/m^3)

VRW: Based on hydrogen cyanide values, in accordance with AEGL (except 10 min value for which time scaling was applied), 2h value added

AGW: Based on hydrogen cyanide values, same point of departure as for AEGL values but using different value for n, 2h value added

LBW: Based on hydrogen cyanide values, same point of departure as for AEGL values but using different value for n, 2h value added

Date 16-12-2010 | AEGL document: final, 2005

Proposal for the Dutch Intervention Values (mg/m^3)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	13	8.8	7.0	5.6	4.4	3.5	Analogy with hydrogen cyanide; no adverse effects in humans during occupational exposure
AGW	45	35	30	26	22	19	Analogy with hydrogen cyanide; slight CNS depression in monkeys
LBW	88	69	59	50	44	38	Analogy with hydrogen cyanide; Lethality rats

Derivation of the Dutch Intervention Values

VRW: The derivation of the VRW values was based upon the fact that acetone cyanohydrin decomposes spontaneously to hydrogen cyanide and acetone and that both local and systemic toxic effects of acetone cyanohydrin are due to free cyanide. Once absorbed, a dose of acetone cyanohydrin behaves in a manner identical to that of its molecular equivalent in absorbed free cyanide. It is appropriate to apply the intervention values (on a ppm basis) derived from hydrogen cyanide to acetone cyanohydrin.

Chronic exposure of 63 workers in a cyanide salt production plant to geometric mean concentrations up to approximately 1 ppm and possible excursions up to 6 ppm, hydrogen cyanide (exposure duration was considered to be 8h) during part of the year did not produce clear exposure related symptoms. The 8-h no effect mean geometric concentration of 1 ppm was used as point of departure for determining VRW levels for acetone cyanohydrin. This would correspond to 1 ppm (3.5 mg/m^3) acetone cyanohydrin. This value was time scaled to the other shorter exposure durations using $C^n xt=k$ with default values of n=3 when extrapolating to shorter exposure durations.

This derivation-procedure is supported by the fact that similar values would have been derived on the basis of available acetone cyanohydrin studies in rats (derivation basis would be exposure to 9.2 ppm (33 mg/m^3 acetone cyanohydrin) for 6 hours/day, 5 days/weeks for 4 weeks, which did not result in red nasal discharge) using the default time scaling procedure and a total uncertainty factor of 10.

AGW: The AGW values were based on hydrogen cyanide values using the same approach as the VRW.

Exposure of monkeys to 60 ppm hydrogen cyanide for 30 minutes resulted in slight central nervous system depression. Because the respiratory tracts of humans and monkeys are more similar than those of humans and rodents, because uptake is more rapid in the monkey than in humans, and because both species have been shown to be relatively insensitive to the incapacitative effects and lethalilty of HCN (but at the same time, species susceptibilities to lethal effects do not differ by more than a factor of 1.5), an interspecies uncertainty factor of 2 was applied. Human (adult) accidental and occupational exposures indicate that there are individual differences in sensitivity to HCN, as evidenced by symptoms following chronic exposures, but the magnitude of these differences does not appear to be great. These studies and the clinical use of nitroprusside solutions to control hypertension do not demonstrate a susceptible population. The detoxifying enzyme rhodanese is functional in all individuals, including newborns. Therefore, an uncertainty factor of 3 was applied to account for potential differences in human susceptibility. The 30-min exposure value of 60 ppm was divided by a total uncertainty factor of 6 and scaled across time using the $C^n \times t = k$, where n = 4.4 (based on lethality data, see LBW).

This derivation-procedure is supported by the fact that similar values would have been derived on the basis of

available acetone cyanohydrin studies in rats (derivation basis would be exposure to 19.9 ppm (70 mg/m^3 acetone cyanohydrin) for 6 hours/day, 5 days/week for 4 weeks, which caused signs of irritation, while the next higher concentration produced respiratory distress, prostration, convulsions and tremors) using the default time scaling procedure and an uncertainty factor of 10.

LBW: The LBW values were based on hydrogen cyanide values using the same approach as the VRW.

Groups of 10 male rats were exposed to hydrogen cyanide at 273-508 ppm for 5 min, 110-403 ppm for 15 min, 128-306 ppm for 30 min, or 76-222 ppm for 60 min. For all exposure durations, deaths occurred during exposures or within 1 d postexposure.
In contrary to the AEGL derivation, the LC_{01}values and the related time scaling factor were calculated using Doseresp instead of the regression analysis as applied in the AEGL document. Five minute inhalation values are generally considered to be less reliable than longer exposure periods. When excluding these data in Doseresp, the program calculates an n of 4.4 for time scaling. The LC_{01} values were used as point of departure. Lethal concentrations are very similar for various species, and study data show that man and the monkey are less sensitive to the effects of HCN than are the rat and dog. Relative to body weights, humans have a much lower respiratory rate and cardiac output than rodents. These are primary determinants of systemic uptake of volatile substances. Thus at similar exposure levels, rodents will absorb substantially more cyanide than primates. Lower detoxifying enzyme activity levels in primates will not be significant in high, acute HCN exposure levels. Based on this information, an interspecies uncertainty factor of 1 could be argued. However, in view of the high acute toxicity and the rapid action of HCN, an interspecies factor of 2 was applied. This factor was based on the species differences in LC_{50} values of less than 2. The available data do not demonstrate a susceptible population. The detoxifying enzyme is available in all humans, including newborns. Therefore, an intraspecies uncertainty factor of 3 was applied, leading to a total uncertainty factor of 6.

This procedure is supported by the close similarity of acetone cyanohydrin and hydrogen cyanide regarding death in rats: In a study with hydrogen cyanide, 3 out of 10 rats died after the first exposure to 68 ppm hydrogen cyanide for 6h, while subsequent two exposures on the following days caused no additional deaths. This finding closely resembles a study with acetone cyanohydrin reporting death of 3 out of 20 animals after the first exposure to 60 ppm (212 mg/m^3) acetone cyanohydrin for 6h, while no additional deaths were found in the 19 subsequent exposures.

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

No specific susceptible populations were identified. The detoxifying enzymes are present in all individuals, including newborns.

From two fertility studies with rats with repeated inhalation exposure demonstrated that exposure to 60 ppm acetone cyanohydrin did not result in any potential for reproductive toxicity in male rats, nor did demonstrate any adverse effects on the fertility in females.

H300: Fatal if swallowed; H310: Fatal in contact with skin; H330: Fatal if inhaled

Carcinogenicity and derivation of the CRP value

IARC classification: not classified

No carcinogenic risk potency (CRP) was derived.

10^{-4} risk level after inhalation: not applicable

No information regarding the carcinogenic potential of acetone cyanohydrin exposure was located in the available literature. Genotoxicity studies with cyanide salts were generally negative and no cancers were induced in rats in a two-year feeding study with HCN.

In test using different *Salmonella* strains, acetone cyanohydrin failed to yield a reproducible positive response. No mutagenic activity was observed *in vitro* using CHO gene mutation assay. No significant increase in the frequency of chromosome aberrations were observed in an *in vivo* the bone marrow test.

Odour and derivation of the LOA value

Acetone cyanohydrin itself has no smell. However, since it decomposes readily into cyanide and acetone it can have the characteristic bitter almond odour due to the presence of free hydrogen cyanide. The level of detection will therefore also depend on the level of decomposition of acetone cyanohydrin in the air. Detection of odour will provide no information on uncontrolled exposure concentrations.

OT_{50}: no data
LOA = not derived

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

VRW level **7.0**	*AEGL-1* 7.0	*ERPG-1* -		*IDLH: not derived*
AGW level **30**	*AEGL-2* 25	*ERPG-2* -		
LBW level **59**	*AEGL-3* 53	*ERPG-3* -		