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

Stofdocument deel A

CAS-nr: 460-19-5 **Dicyaan** **NC-CN** **VN-nr: 1026**
GEVI: 263

Synoniemen: cyanogeen, oxalonitril, ethaandinitril (Engels: cyanogen)

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	**VRW (mg/m^3)**	5,4	5,4	4,3	3,4	2,7	2,2
Alarmeringsgrenswaarden	**AGW (mg/m^3)**	110	36	18	9,0	9,0	9,0
Levensbedreigende waarden	**LBW (mg/m^3)**	320	110	54	27	27	27
Datum vaststelling: November 2015				1 mg/m^3 = 0,462 ppm; 1 ppm = 2,16 mg/m^3			

Explosiegrens:
LEL: 6,6% ≈ 143.000 mg/m^3

Geur: Stekende, amandelachtige geur
LOA: niet afgeleid

Fysisch-chemische eigenschappen

Uiterlijk: kleurloos gas
Brand: zeer brandgevaarlijk

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,8

Molecuulmassa: 52,03 g/mol
Zuurgraad: Geen data
LogKow: 0,07
Wateroplosbaarheid: 0,97 g/100 ml
Verzadigde dampdruk: 5.730 mbar

Overige informatie

Publieke grenswaarde:
Voor cyaniden geldt:
1 mg/m^3 (TGG 8 uur),
10 mg/m^3 (TGG 15 min)
MAK: 11 mg/m^3, H notatie
TLV-TWA: 21.6 mg/m^3

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW: lichte irritatie van ogen en neus

VRW → AGW: matige irritatie van ogen en neus, hoofdpijn

AGW → LBW: hoesten, ernstige irritatie, misselijkheid, braken, duizeligheid, spierzwakte, verwardheid

Boven LBW: convulsies, ademnood, coma, ademstilstand, hartstilstand, sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- De stof reageert met zuren tot de vorming van cyaanwaterstof.
- Cyanide blokkeert de ademhalingsketen in de cel. Hierdoor wordt de energiehuishouding verstoord en kan uiteindelijk lactaatacidose ontstaan.
- Primaire systemische doelorganen zijn het centrale zenuwstelsel en het cardiovasculaire systeem.
- De stof werkt irriterend op de ogen, en de luchtwegen.
- Snelle verdamping kan bevriezingsverschijnselen veroorzaken.

Effecten bij blootstelling aan vloeistof

Huidcontact: *vloeistof*: bevriezingsletsel

Oogcontact: *gas*: roodheid en pijn, *vloeistof*: bevriezingsletsel

Carcinogeniteit

IARC classificatie: Niet geclassificeerd
CRP: Niet afgeleid

Beknopte medische informatie

Ontsmetting gas

algemeen: frisse lucht, rust, halfzittende houding, GEEN mond-op-mondbeademing, 100% zuurstof, specifieke behandeling en direct spoedeisende medische hulp inzetten.

Ontsmetting vloeistof

huid: verontreinigde kleding uittrekken, specifieke behandeling, *in geval van bevriezingswonden*: aan de huid vastgevroren kleding NIET lostrekken, eerst spoelen met veel water, dan pas kleding uittrekken, daarna weer spoelen, en direct spoedeisende medische hulp inzetten.

ogen: *in geval van bevriezingswonden*: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.

inslikken: n.v.t. (gas)

Specifieke behandeling en materialen: Bij vergiftiging is specifieke eerste hulp noodzakelijk; specifieke antidota (zoals 100% zuurstof, natriumthiosulfaat en hydroxocobalamine) moeten met gebruiksaanwijzing ter plekke beschikbaar zijn.

Neem contact op met het NVIC (tel: +31 (0)30 –274 8888) voor verdere 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: 460-19-5 **Cyanogen** **NC-CN** **UN-nr: 1026**

Basis for the Dutch Intervention Values

VRW: AEGL value is adopted, 2h value added

AGW: Same rationale for AEGL (one-third of LBW), 2h value added

LBW: AEGL value is adopted, 2h value added using different rationale (time-scaling based on 1-hour LBW value)

Date: November 2015	AEGL document: Final, 2014

Dutch Intervention Values (mg/m^3)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	5.4	5.4	4.3	3.4	2.7	2.2	VRW values for hydrogen cyanide were adopted; mild headache in humans.
AGW	110	36	18	9.0	9.0	9.0	One-third of the LBW values
LBW	320	110	54	27	27	27	Lethality threshold in rats.

Derivation of the Dutch Intervention Values

VRW: Because no human exposure data for cyanogen for durations longer than 8 min were available and because the cyanide metabolite has the potential to cause the systemic effects reported for cyanogen, the VRW values for hydrogen cyanide were adopted as VRW values for cyanogen.
The VRW levels for hydrogen cyanide were based on data from monitoring studies in workers. Although the exposures were of chronic duration, they represent the best available human data. Exposure in a cyanide-salt production facility (exposure duration 1-40 years) to a geometric mean concentration of 0.03-0.96 ppm (0.034- 1.08 mg/m^3) (+ possible excursions up to 6 ppm (6.7 mg/m^3)) in 63 male workers did not result in exposure-related health effects as compared to 100 referent workers. As point of departure, an 8 hour exposure to 1 ppm (1.123 mg/m^3) hydrogen cyanide was used. Mild headache was considered a suitable critical endpoint. Using this point of departure no intraspecies uncertainty factor was used because it is the lowest NOAEL observed. The data were scaled across time using the relationship $C^n \times t = k$, with default values n=3 when extrapolating to shorter exposure durations.

The approach is supported by a study with cyanogen in which seven human subjects were exposed to cyanogen in three separate tests. These tests resulted in a NOEL for irritation in humans of 8 ppm (17.3 mg/m^3) for 6 min. Ocular and nasal irritation was reported at the next highest concentration tested, namely 16 ppm for 6 min (34.6 mg/m^3). Applying the default uncertainty factor of 3 to account for intraspecies differences, would result in a threshold for irritation of 2.7 ppm (5.8 mg/m^3). To ensure that the VRW values based on hydrogen cyanide are all protective of both irritation and potential systemic cyanide effects, the 10 min value was set equal to the 30 min value in order to stay below the cyanogen irritation threshold of 2.7 ppm (5.8 mg/m^3).

AGW: No appropriate data for derivation of AGW values are found for cyanogen. The AGW values were derived by dividing the LBW values for cyanogen by a factor of 3. That approach is justified by the steep concentration-response curve for cyanogen, e.g. mortality in rats:
- 0/6 at 1,000 ppm (2,164 mg/m^3) for 15 min versus 6/6 at 1,000 ppm for 30 min
- 0/6 at 500 ppm (1,082 mg/m^3) for 30 min versus 6/6 at 500 ppm for 45 min
- 0/6 at 400 ppm (866 mg/m^3) for 45 min versus 6/6 at 400 ppm for 60 min
- 3/6 at 4,000 ppm (8640 mg/m^3) for 7.5 min versus 6/6 at 4,000 ppm for 15 min
- 0/6 at 2,000 ppm (4320 mg/m^3) for 7.5 min versus 6/6 at 2,000 ppm for 15 min

LBW: Experimental concentrations causing no deaths in rats were used as points of departure for the 10-min, 30-min, and 1-h LBW values. The 30-min exposure at 500 ppm (1,082 mg/m^3) was used as the point of departure for the 10-min and 30-min LBW values, and the 1-h exposure at 250 ppm (541 mg/m^3) was used as the point of departure for the 1-h LBW value. The default total uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences. The 2-h LBW value was based on the 1-h LBW value using the equation $C^n \times t = k$, with a default value of n = 1. The 4- and 8-h LBW values were set equal to the 2-h LBW value. That approach was used because time scaling using the equation $C^n \times t = k$, with a default value of n = 1, yielded possible 4- and 8-h

LBW values of 6.3 and 3.2 ppm (13.5 and 6.8 mg/m^3), respectively. Those values are inconsistent with the repeated-exposure data in both monkey and rat studies. Rats experienced only decreased body weight, and monkeys similarly exposed showed only marginal behavioral effects. No effects were noted in either species exposed at 11 ppm (23.8 mg/m^3).

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

The mechanism of toxicity of cyanogen is similar to that of hydrogen cyanide. Hydrogen cyanide acts on the central nervous system. It interrupts cellular respiration by inhibiting cytochrome oxidase, thus blocking electron transfer to oxygen. Tissue oxygen concentrations rise, resulting in increased tissue oxygen tension and a decreased unloading for oxyhemoglobin. As a consequence, oxidative metabolism may slow to a point where it cannot meet metabolic demands. That is particularly critical in the brainstem nuclei where lack of an energy source results in central respiratory arrest and death. Cyanide can inhibit many other enzymes, particularly those that contain iron or copper, but cytochrome oxidase appears to be the most sensitive enzyme. Cyanide also stimulates the chemoreceptors of the carotid and aortic bodies to produce a brief period of hyperpnea. Cardiac irregularities may occur, but death is due to respiratory arrest. Brain lesions have been associated with exposure of animals to hydrogen cyanide at high concentrations.

The substance is also irritating to the eyes and the respiratory tract. Rapid evaporation of the liquid may cause frostbite.

No reproductive or developmental data were located for cyanogen. For hydrogen cyanide, no information on the reproductive or developmental toxicity via the inhalation route is available. The teratogenic potential of hydrogen cyanide was studied by infusing sodium cyanide to hamsters. Based on the results of this study and the results of studies with sodium cyanide, aliphatic nitriles and cyanogenic glycosides it can be concluded that the teratogenic activities can be attributed to the cyanide released through metabolism of the parent compounds: in each case, developmental toxicity was observed only at dose levels also inducing signs of maternal cyanide intoxication.

H330: Fatal if inhaled; H319: Causes serious eye irritation; H335: May cause respiratory irritation.

Carcinogenicity and derivation of the CRP value

IARC classification: Not classified.

No carcinogenic risk potency (CRP) was derived

Odour and derivation of the LOA value

Odour: pungent, penetrating, almond-like odour

Odour threshold: 509 mg/m^3 [Ruth, 1986]

No LOA was derived (due to lack of reliable data)

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

VRW level **4.3**	*AEGL-1* 4.3	*ERPG-1* Not Derived		*IDLH: Not Derived*
AGW level **18**	*AEGL-2* 18	*ERPG-2* Not Derived		
LBW level **54**	*AEGL-3* 54	*ERPG-3* Not Derived		