



# Grunnlag for fastsettelse av grenseverdi

Grunnlagsdokument for hydrogencyanid (HCN), kaliumcyanid (KCN) og natriumcyanid (NaCN)

Kommisjonsdirektiv 2017/164/EU

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kaliumcyanid (KCN) og natriumcyanid (NaCN).

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Denne rapporten omhandler det toksikologiske  
grunnlaget og vurderinger, samt tekniske og  
økonomiske hensyn for fastsettelse av  
grenseverdier for hydrogencyanid (HCN),  
kaliumcyanid (KCN) og natriumcyanid (NaCN).

# Innhold

Innhold	3
Forord	4
Innledning	5
1. Stoffets identitet	5
2. Fysikalske og kjemiske data	6
2.1 Forekomst og bruk	7
3. Grenseverdier	7
3.1 Nåværende grenseverdier	7
3.2. Grenseverdier fra EU	7
3.3. Grenseverdier fra andre land og organisasjoner	7
3.3.1 Grenseverdier for hydrogencyanid	7
3.3.2 Grenseverdier for kaliumcyanid	8
3.3.3 Grenseverdier for natriumcyanid	9
3.4. Stoffenes klassifisering	10
3.4.1 Klassifisering av hydrogencyanid	11
3.4.2 Klassifisering av kaliumcyanid og natriumcyanid	11
3.5. Biologisk overvåking	12
4. Toksikologiske data og helseeffekter	12
4.1. Anbefaling fra SCOEL	12
4.2. Kommentarer fra TEAN	13
5. Bruk og eksponering	14
5.1. Opplysning fra Produktregistret	14
5.2. Eksponering og måledokumentasjon	14
5.2.1 EXPO- data for hydrogencyanid	14
5.2.2 Prøvetakings- og analysemetode av hydrogencyanid	14
6. Vurdering	15
7. Konklusjon med forslag til ny grenseverdi	16
8. Nye grenseverdier	17
9. Referanser	18
Vedlegg SCOEL	19

# Forord

Grunnlagsdokumenter for fastsettelse av grenseverdier utarbeides av Arbeidstilsynet i samarbeid med Statens arbeidsmiljøinstitutt (STAMI) og partene i arbeidslivet (Næringslivets hovedorganisasjon/Norsk Industri og Landsorganisasjonen i Norge) i henhold til Strategi for utarbeidelse og fastsettelse av grenseverdier for forurensninger i arbeidsatmosfæren. Dette dokumentet er utarbeidet ved implementering av kommisjonsdirektiv 2017/164/EU fastsatt 31. januar 2017.

EU-rådets direktiv 98/24/EC (Vern av helse og sikkerhet til arbeidstakere mot risiko i forbindelse med kjemiske agenser på arbeidsplassen) av 7. april 1998 stiller krav om at EU- kommisjonen skal legge frem forslag til indikative grenseverdier for eksponering av visse kjemikalier som medlemslandene må innføre på nasjonalt nivå. De nasjonale grenseverdiene kan være høyere enn de som står oppført i direktivet, dersom et medlemsland mener at det er nødvendig av tekniske og/eller økonomiske hensyn, men landene bør nærme seg den indikative grenseverdien. Direktivet stiller krav om at indikative grenseverdier vedtas gjennom kommisjonsdirektiv.

I Norge ble de indikative grenseverdiene innført som veiledende administrative normer. Da nye Arbeidsmiljøforskrifter trådte i kraft 1.1.2013 ble de veiledende administrative normene forskriftsfestet i forskrift om tiltaks- og grenseverdier og fikk betegnelsen tiltaksverdier. I 2015 ble begrepet «grenseverdi» for kjemikalier presisert og begrepet «tiltaksverdi» for kjemikalier ble opphevet i forskrift om tiltaks- og grenseverdier. I vedlegg 1 til forskriften ble det innført en tydeliggjøring av anmerkningene.

Arbeidstilsynet har ansvaret for revisjonsprosessen og utarbeidelse av grunnlagsdokumenter for stoffene som blir vurdert. Det toksikologiske grunnlaget for stoffene i denne revisjonen baserer seg i hovedsak på kriteriedokumenter fra EUs vitenskapskomité for fastsettelse av grenseverdier, Scientific Committee for Occupational Exposure Limits (SCOEL). SCOEL utarbeider de vitenskapelige vurderingene som danner grunnlaget for anbefalinger til helsebaserte grenseverdier, og disse legges fram for kommisjonen.

Statens arbeidsmiljøinstitutt (STAMI) ved Toksikologisk ekspertgruppe for administrative normer (TEAN) bidrar med faglige vurderinger i dette arbeidet. TEAN vurderer og evaluerer de aktuelle SCOEL dokumentene, presiserer kritiske effekter og vurderer behov for korttidsverdier ut i fra den foreliggende dokumentasjonen. Videre søker og evaluerer TEAN nyere litteratur etter utgivelsen av dokumentet. TEAN bruker kriteriene gitt i SCOEL's metodedokument "Methodology for the derivation of occupational exposure limits: Key documentation (version 7, June 2013)". Dette er inkludert i TEANs Metodedokument del B (Prosedyre for utarbeidelse av toksikologiske vurderinger for stoffer som skal implementeres i det norske regelverket for grenseverdier etter direktiv fra EU-kommisjonen) utarbeidet for denne revisjonen.

Informasjon om bruk og eksponering i Norge innhentes fra Produktregisteret, EXPO databasen ved STAMI og eventuelle tilgjengelige måledata fra virksomheter/næringer. Beslutningsprosessen skjer gjennom drøftingsmøter der Arbeidstilsynet, Næringslivets hovedorganisasjon/Norsk Industri og Landsorganisasjonen i Norge deltar, samt orienteringsmøter og offentlig høring. Konklusjonene fra høringen med forskriftsendringer og nye grenseverdier forelegges Arbeids- og sosialdepartementet som tar den endelige beslutningen.

# Innledning

Dette grunnlagsdokumentet omhandler vurderingsgrunnlaget for fastsettelse av grenseverdier for hydrogencyanid (HCN), kaliumcyanid (KCN) og natriumcyanid (NaCN). Innholdet bygger spesielt på anbefalinger fra Scientific Committee on Occupational Exposure Limits (SCOEL) i EU for disse cyanidene, samt vurderinger og kommentarer fra Toksikologisk Ekspertgruppe for Administrative Normer (TEAN).

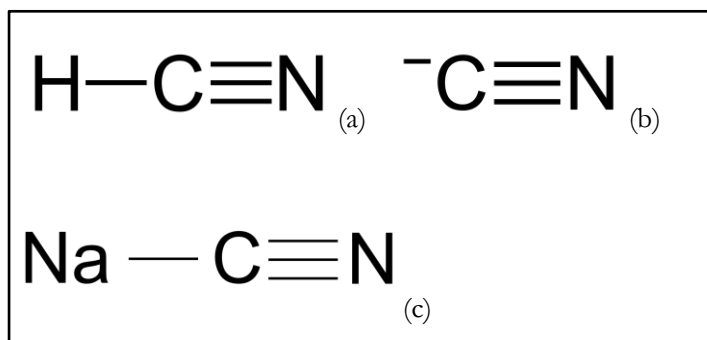
## 1. Stoffets identitet

Hydrogencyanid (HCN), kaliumcyanid (KCN) og natriumcyanid (NaCN) og deres molekylformler, synonymer av stoffenes navn, stoffenes identifikasjonsnumre i Chemical Abstract Service Registry number (CAS-nr.), European Inventory of Existing Commercial Chemical Substances (EINECS-numre og EC) er gitt i tabell 1. Strukturformler av stoffene er vist i figur 1.

Tabell 1. Stoffenes navn og identitet.

Kjemisk navn Molekylformel	Hydrogencyanid HCN	Kaliumcyanid* KCN	Natriumcyanid* NaCN
Synonymer	Blåsyre	Cyankalium Hydrogencyanidsyre av kalium	Hydrogencyanidsyre av natrium
CAS-nr.	74-90-8	151-50-8	143-33-9
EINECS-nr.	200-821-6	205-792-3	205-599-4
EC-nr.	006-006-00-X	006-007-00-5	006-007-00-5

\*Kaliumcyanid og natriumcyanid er salter av hydrogencyanid.



Figur 1. (a) Strukturformel av HCN (<https://commons.wikimedia.org/wiki/File:Hydrogen-cyanide-2D.svg>) og (b) anionet av cyanid (<https://commons.wikimedia.org/wiki/File:Cyanid-Ion.svg>). Når kationer av kalium eller natrium bindes til anionet cyanid fås henholdsvis KCN og NaCN (eksempel som vist i figur (c), [https://commons.wikimedia.org/wiki/File:Sodium\\_cyanide-2D.svg](https://commons.wikimedia.org/wiki/File:Sodium_cyanide-2D.svg)).

## 2. Fysikalske og kjemiske data

Hydrogencyanid er en meget giftig fargeløs væske eller en fargeløs gass med en karakteristisk lukt av bitre mandler. Dette er et svært giftig stoff som kan drepe raskt, selv i svært lave konsentrasjoner. Den dødelige dosen skal være 50-70 mg.

Ved standard betingelser er både natriumcyanid og kaliumcyanid hvite krystallinske stoffer med tilsvarende lukt som for hydrogencyanid, bare svakere. Det vises til tabell 2 for fysikalske og kjemiske data for hydrogencyanid, kaliumcyanid og natriumcyanid.

**Tabell 2.** Fysikalske og kjemiske data for stoffene hydrogencyanid, kaliumcyanid og natriumcyanid.

Molekylformel	H <sub>2</sub> CN	KCN	NaCN
Molekylvekt (g/mol)	27,03	65,12	49,01
Fysisk tilstand (20 °C, 101,3 kPa)	Fargeløs væske el. fargeløs gass	Fargeløst/hvitt krystallinsk stoff	Fargeløst/hvitt krystallinsk stoff
Smeltepunkt (°C)	-13,24	634,5 <sup>4</sup>	560
Kokepunkt (°C)	25,70	-	-
Løselig i vann	Løselig i alle forhold	Svært løselig i vann.	Svært løselig i vann.
Løselighet i andre løsemidler		Løselig i ammoniakk og formamid; delvis løselig i etanol og dimetylformamid.	Løselig i ammoniakk. Delvis løselig i formamid, etanol, metanol, furfural, dimetylformamid og eter.
Damptrykk ved 20 °C (hPa)	830 <sup>1</sup>	-	-
Damp tetthet (air = 1) (g/cm <sup>3</sup> )	0,69 <sup>2</sup>	-	1,60 <sup>4</sup>
Fordelingskoeffisient n-oktanol/vann (log K <sub>ow</sub> )	-0,25 <sup>3</sup>	-	-
Omregningsfaktor (20 °C, 101 kPa)	1 ppm = 1,123 mg/m <sup>3</sup> 1 mg/m <sup>3</sup> = 0.891 ppm	1 ppm = 1,123 mg/m <sup>3</sup> 1 mg/m <sup>3</sup> = 0.891 ppm	1 ppm = 1,123 mg/m <sup>3</sup> 1 mg/m <sup>3</sup> = 0.891 ppm

<sup>1</sup> <https://echa.europa.eu/registration-dossier/-/registered-dossier/14996/4/7>

<sup>2</sup> Handbook of Chemistry

<sup>3</sup> <https://echa.europa.eu/registration-dossier/-/registered-dossier/14996/4/8>

<sup>4</sup> <https://echa.europa.eu/registration-dossier/-/registered-dossier/13737/4/>

## 2.1 Forekomst og bruk

Hydrogencyanid blir produsert ved en direkte reaksjon av alkaner med ammoniakk, og indirekte som et biprodukt ved produksjon av akrylnitril. Mudder og Botz rapporterte i 2000<sup>1</sup> at 1,4 millioner tonn hydrogencyanid ble produsert årlig hvorav 13% omdannes til natriumcyanid for bruk i gruvedrift.

Den viktigste bruken av hydrogencyanid er utgassing av skip, bygninger, frukthager og ulike matvarer, i produksjon av for eksempel EDTA og i metallprosesser. Hydrogencyanid har også mange bruksområder som kjemisk mellomprodukt.

Natriumcyanid og kaliumcyanid blir brukt til utvinning av gull og sølv fra malm, varmebehandling av metaller, og galvanisering. Videre tjener de som utgangsstoff i kjemiske synteser.

## 3. Grenseverdier

### 3.1 Nåværende grenseverdier

Nåværende grenseverdi (8 timer) i Norge for hydrogencyanid er:  
5 ppm, 5 mg/m<sup>3</sup> med anmerkningene H (hudopptak) og takverdi (T).

Norge har ingen grenseverdier for kaliumcyanid og natriumcyanid, men for cyanider (beregnet CN<sup>-</sup>):  
5 mg/m<sup>3</sup> med anmerkning H (hudopptak).

### 3.2 Grenseverdier fra EU

Den europeiske vitenskapskomiteen, SCOEL foreslår grenseverdi, korttidsverdi og anmerkning for cyanidene (hydrogencyanid, kaliumcyanid og natriumcyanid) uttrykt som cyanid, CN<sup>-</sup> i sitt kriteriedokument av juni 2010<sup>2</sup>:

IOELV (Indicative Occupational Exposure Limit Value) (8 timer): 0,9 ppm, 1 mg/m<sup>3</sup>

STEL (Short Term Exposure Limit) (15 minutter): 5 mg/m<sup>3</sup>

Anmerkning: sk (skin notation)

### 3.3 Grenseverdier fra andre land og organisasjoner

Grenseverdier fra andre land og organisasjoner for stoffene hydrogencyanid, kaliumcyanid og natriumcyanid er gitt i avsnittene 3.3.1-3.3.3 nedenfor. De oppgitte grenseverdiene for kaliumcyanid og natriumcyanid er gjeldende verdier for cyanider beregnet som CN<sup>-</sup>.

#### 3.3.1 Grenseverdier for hydrogencyanid

Nåværende grenseverdier for hydrogencyanid fra andre land og organisasjoner er gitt i tabell 3 nedenfor.

**Tabell 3.** Grenseverdier for hydrogencyanid fra andre land og organisasjoner. Land og organisasjoner som ikke har grenseverdi for stoffet er markert med -.

Land/organisasjon	Grenseverdi (8 timer)	Korttidsverdi (15 min)	Anmerkning Kommentar
Sverige <sup>1</sup>	1,8 ppm; 2 mg/m <sup>3</sup>	3,6 ppm; 4 mg/m <sup>3</sup>	H (hudopptak) V (veiledende korttidsverdi)
Danmark <sup>2</sup>	5 ppm; 5 mg/m <sup>3</sup>	-	H (hudopptak)
Finland <sup>3</sup>	1 mg/m <sup>3</sup>	5 mg/m <sup>3</sup>	Hud (hudopptak)
Storbritannia <sup>4</sup>	-	10 ppm; 11 mg/m <sup>3</sup>	Sk (hudopptak)
Nederland <sup>5</sup>	1 mg/m <sup>3</sup>	10 mg/m <sup>3</sup>	H (hudopptak)
ACGIH, USA <sup>6</sup>	-	4,7 ppm	Hudopptak C, takverdier EPA-II (karsinogenkategori)
NIOSH, USA <sup>6</sup>	-	4,7 ppm	Hudopptak EPA-II (karsinogenkategori) Også salter av cyanid
Tyskland, MAK <sup>6</sup>	1,9 ppm; 2,1 mg/m <sup>3</sup>	-	Hudopptak C, takverdi EPA-II (karsinogenkategori) II (2): overskridelsesfaktor II: systemisk effekt,
Tyskland, Myndighetene <sup>7</sup>	-	-	-

<sup>1</sup> Arbetsmiljöverkets Hygieniska gränsvärden AFS 2015:7,

<https://www.av.se/globalassets/filer/publikationer/foreskrifter/hygieniska-gransvarden-afs-2015-7.pdf>.

<sup>2</sup> At-vejledning, stoffer og materialer - C.0.1, 2007, <https://arbejdstilsynet.dk/da/regler/at-vejledninger/g/c-0-1-graensevaerdi-for-stoffer-og-mat>.

<sup>3</sup> Social og hälsovårdsministeriet, HTP-värden, Koncentrationer som befunnits skadliga, 2016,

Helsingfors, [http://julkaisut.valtioneuvosto.fi/bitstream/handle/10024/79110/STM\\_9\\_2016\\_HTP-varden\\_2016\\_Ruotsi\\_22122016\\_NETTI.pdf](http://julkaisut.valtioneuvosto.fi/bitstream/handle/10024/79110/STM_9_2016_HTP-varden_2016_Ruotsi_22122016_NETTI.pdf).

<sup>4</sup> EH40 andre utgave, 2013, <http://www.hse.gov.uk/pubns/priced/eh40.pdf>.

<sup>5</sup> [http://www.ser.nl/en/oel\\_database.aspx](http://www.ser.nl/en/oel_database.aspx); <http://www.ser.nl/en/grenswaarden/hydrogen%20cyanide.aspx>

<sup>6</sup> Guide to occupational exposure values compiled by ACGIH, 2017.

<sup>7</sup> Baua, TRGS 900, oppdatert 2016, [https://www.baua.de/DE/Angebote/Rechtstexte-und-Technische-Regeln/Regelwerk/TRGS/pdf/TRGS-900.pdf;jsessionid=439FFF321DF2323E60F868CD08E9CD3A.s1t2?\\_blob=publicationFile&v=2](https://www.baua.de/DE/Angebote/Rechtstexte-und-Technische-Regeln/Regelwerk/TRGS/pdf/TRGS-900.pdf;jsessionid=439FFF321DF2323E60F868CD08E9CD3A.s1t2?_blob=publicationFile&v=2)

### 3.3.2 Grenseverdier for kaliumcyanid

Nåværende grenseverdier for kaliumcyanid (cyanider som CN) fra andre land og organisasjoner er gitt i tabell 4 nedenfor.



**Tabell 4.** Grenseverdier for kaliumcyanid fra andre land og organisasjoner. Land og organisasjoner som ikke har grenseverdi for stoffet er markert med -.

Land/organisasjon	Grenseverdi (8 timer)	Korttidsverdi (15 min)	Anmerkning Kommentar
Sverige <sup>1</sup>	2 mg/m <sup>3</sup>	4 mg/m <sup>3</sup>	H (hudopptak)
Danmark <sup>2</sup>	-	5 mg/m <sup>3</sup>	H (hudopptak)
Finland <sup>3</sup>	5 mg/m <sup>3</sup>	10 mg/m <sup>3</sup>	-
Storbritannia <sup>4</sup>	-	5 mg/m <sup>3</sup>	Sk (hudopptak)
Nederland <sup>5</sup>	2,4 mg/m <sup>3</sup>	24 mg/m <sup>3</sup>	H (hudopptak) C (takverdi)
ACGIH, USA <sup>6</sup>	-	5 mg/m <sup>3</sup>	Hudopptak C, takverdier EPA-II (karsinogenkategori)
NIOSH, USA <sup>6</sup>	-	5 mg/m <sup>3</sup>	Hudopptak EPA-II (karsinogenkategori)
Tyskland, MAK <sup>6</sup>	2,1 mg/m <sup>3</sup>	-	Hudopptak C, takverdi EPA-II (karsinogenkategori) II (2): overskridelsesfaktor II systemisk effekt,
Tyskland, Myndighetene <sup>7</sup>	-	-	-

<sup>1</sup> Arbetsmiljöverkets Hygieniska gränsvärden AFS 2015:7,

<https://www.av.se/globalassets/filer/publikationer/foreskrifter/hygieniska-gransvarder-afs-2015-7.pdf>.

<sup>2</sup> At-vejledning, stoffer og materialer - C.0.1, 2007, <https://arbejdstilsynet.dk/da/regler/at-vejledninger/g/c-0-1-graensevaerdi-for-stoffer-og-mat>.

<sup>3</sup> Social og hälsovårdsministeriet, HTP-värden, Koncentrationer som befunnits skadliga, 2016,

Helsingfors, [http://julkaisut.valtioneuvosto.fi/bitstream/handle/10024/79110/STM\\_9\\_2016\\_HTP-varden\\_2016\\_Ruotsi\\_22122016\\_NETTI.pdf](http://julkaisut.valtioneuvosto.fi/bitstream/handle/10024/79110/STM_9_2016_HTP-varden_2016_Ruotsi_22122016_NETTI.pdf).

<sup>4</sup> EH40 andre utgave, 2013, <http://www.hse.gov.uk/pubns/priced/eh40.pdf>.

<sup>5</sup> [http://www.ser.nl/en/oel\\_database.aspx](http://www.ser.nl/en/oel_database.aspx); <http://www.ser.nl/en/grenswaarden/hydrogen%20cyanide.aspx>

<sup>6</sup> Guide to occupational exposure values compiled by ACGIH, 2017.

<sup>7</sup> Baa, TRGS 900, oppdatert 2016, [https://www.baua.de/DE/Angebote/Rechtstexte-und-Technische-Regeln/Regelwerk/TRGS/pdf/TRGS-900.pdf;jsessionid=439FFF321DF2323E60F868CD08E9CD3A.s1t2?\\_blob=publicationFile&v=2](https://www.baua.de/DE/Angebote/Rechtstexte-und-Technische-Regeln/Regelwerk/TRGS/pdf/TRGS-900.pdf;jsessionid=439FFF321DF2323E60F868CD08E9CD3A.s1t2?_blob=publicationFile&v=2)

### 3.3.3 Grenseverdier for natriumcyanid

Nåværende grenseverdier for natriumcyanid (cyanider som CN) fra andre land og organisasjoner er gitt i tabell 5 nedenfor.



**Tabell 5.** Grenseverdier for natriumcyanid fra andre land og organisasjoner. Land og organisasjoner som ikke har grenseverdi for stoffet er markert med -.

Land/organisasjon	Grenseverdi (8 timer)	Korttidsverdi (15 min)	Anmerkning Kommentar
Sverige <sup>1</sup>	2 mg/m <sup>3</sup>	4 mg/m <sup>3</sup>	H (hudopptak)
Danmark <sup>2</sup>		5 mg/m <sup>3</sup>	H (hudopptak)
Finland <sup>3</sup>	-	-	-
Storbritannia <sup>4</sup>	5 mg/m <sup>3</sup>		Sk (hudopptak)
Nederland <sup>5</sup>	1,8 mg/m <sup>3</sup>	18 mg/m <sup>3</sup>	H (hudopptak) C (takverdi)
ACGIH, USA <sup>6</sup>	-	5 mg/m <sup>3</sup>	Hudopptak C, takverdier EPA-II (karsinogenkategori)
NIOSH, USA <sup>6</sup>	-	5 mg/m <sup>3</sup>	Hudopptak EPA-II (karsinogenkategori)
Tyskland, MAK <sup>6</sup>	3,8 mg/m <sup>3</sup>	-	Hudopptak C, takverdi EPA-II (karsinogenkategori) II(1): overskridelsesfaktor I: irriterende effekter og respiratorisk allergen
Tyskland, Myndighetene <sup>7</sup>	-	-	-

<sup>1</sup> Arbetsmiljöverkets Hygieniska gränsvärden AFS 2015:7,

<https://www.av.se/globalassets/filer/publikationer/foreskrifter/hygieniska-gransvarder-afs-2015-7.pdf>.

<sup>2</sup> At-vejledning, stoffer og materialer - C.0.1, 2007, <https://arbejdstilsynet.dk/da/regler/at-vejledninger/g/c-0-1-graensevaerdi-for-stoffer-og-mat>.

<sup>3</sup> Social og hälsovårdsministeriet, HTP-värden, Koncentrationer som befunnits skadliga, 2016,

Helsingfors, [http://julkaisut.valtioneuvosto.fi/bitstream/handle/10024/79110/STM\\_9\\_2016\\_HTP-varden\\_2016\\_Ruotsi\\_22122016\\_NETTI.pdf](http://julkaisut.valtioneuvosto.fi/bitstream/handle/10024/79110/STM_9_2016_HTP-varden_2016_Ruotsi_22122016_NETTI.pdf).

<sup>4</sup> EH40 andre utgave, 2013, <http://www.hse.gov.uk/pubns/priced/eh40.pdf>.

<sup>5</sup> [http://www.ser.nl/en/oel\\_database.aspx](http://www.ser.nl/en/oel_database.aspx); <http://www.ser.nl/en/grenswaarden/hydrogen%20cyanide.aspx>

<sup>6</sup> Guide to occupational exposure values compiled by ACGIH, 2017.

<sup>7</sup> Baua, TRGS 900, oppdatert 2016, [https://www.baua.de/DE/Angebote/Rechtstexte-und-Technische-Regeln/Regelwerk/TRGS/pdf/TRGS-900.pdf;jsessionid=439FFF321DF2323E60F868CD08E9CD3A.s1t2?\\_blob=publicationFile&v=2](https://www.baua.de/DE/Angebote/Rechtstexte-und-Technische-Regeln/Regelwerk/TRGS/pdf/TRGS-900.pdf;jsessionid=439FFF321DF2323E60F868CD08E9CD3A.s1t2?_blob=publicationFile&v=2)

### 3.4. Stoffenes klassifisering

Stoffene hydrogencyanid, kaliumcyanid og natriumcyanid er klassifisert og merket i henhold til CLP Annex VI (Forordning EC No 1272/2008). Stoffenes klassifisering er gitt i avsnittene 3.4.1-3.4.3 nedenfor.

### 3.4.1 Klassifisering av hydrogencyanid

Hydrogencyanid er klassifisert og merket med koder i henhold til fareklasse, kategori og faresetninger som gitt i tabellene 6 nedenfor.

**Tabell 6.** Fareklasser, farekategori med forkortelse, merkekoder og faresetninger for hydrogencyanid.

<b>Fareklasse Farekategori Forkortelse</b>	<b>Merkekode</b>	<b>Faresetning</b>
Brannfarlige væsker Kategori Flam. Liq. 1	H 224	Ekstremt brannfarlig væske og damp
Akutt giftighet Kategori 1 og 2 Acute Tox. 1 og 2	H330	Dødelig ved innånding
Farlig for vannmiljøet Akutt kategori 1 Aquatic Acute 1	H 400	Meget giftig for liv i vann
Farlig for vannmiljøet Kronisk kategori 1 Aquatic Chronic 1	H 410	Meget giftig, med langtidsvirkning, for liv i vann

CLP ((Forordning (EC) Nr. 1272/2008), <http://www.miljodirektoratet.no/Documents/publikasjoner/M259/M259.pdf>, <https://echa.europa.eu/information-on-chemicals/cl-inventory-database>

### 3.4.2 Klassifisering av kaliumcyanid og natriumcyanid

Kaliumcyanid og natriumcyanid er klassifisert som salter til hydrogencyanid og merket med koder i henhold til fareklasse og kategori som gitt i tabellene 7 nedenfor.

**Tabell 7.** Fareklasser, farekategori med forkortelse, merkekoder og faresetninger for kaliumcyanid og natriumcyanid.

Fareklasse Farekategori Forkortelse	Merkekode	Faresetning
Akutt giftighet Kategori 1 og 2 Acute Tox. 1 og 2	H 300	Dødelig ved svelging
Akutt giftighet Kategori 1 og 2 Acute Tox. 1 og 2	H 310	Dødelig ved hudkontakt
Akutt giftighet Kategori 1 og 2 Acute Tox. 1 og 2	H330	Dødelig ved innånding
Farlig for vannmiljøet Akutt kategori 1 Aquatic Acute 1	H 400	Meget giftig for liv i vann
Farlig for vannmiljøet Kronisk kategori 1 Aquatic Chronic 1	H 410	Meget giftig, med langtidsvirkning, for liv i vann

CLP ((Forordning (EC) Nr. 1272/2008), <http://www.miljodirektoratet.no/Documents/publikasjoner/M259/M259.pdf>, <https://echa.europa.eu/information-on-chemicals/cl-inventory-database>

### 3.5. Biologisk overvåking

For å vurdere grad av eksponering for forurensning i luften på arbeidsplassen kan man anvende konsentrasjonen av forurensningen i arbeidstakerens urin, blod eller utåndingsluft, eller annen respons på eksponeringen i kroppen. EU har satt verdier for dette kalt biologisk grenseverdi (BLV).

SCOEL fremmer ikke et forslag til biologisk grenseverdi for stoffene hydrogencyanid, kaliumcyanid eller natriumcyanid.

## 4. Toksikologiske data og helseeffekter

### 4.1. Anbefaling fra SCOEL

EUs vitenskapskomite (SCOEL) har utarbeidet kriteriedokumentasjon for cyanider (hydrogencyanid, kaliumcyanid og natriumcyanid) datert juni 2010<sup>2</sup> hvor de anbefaler en 8-timers grenseverdi og en korttidsverdi (15 minutter) for stoffene hydrogencyanid, kaliumcyanid og natriumcyanid (beregnet som cyanid CN<sup>-</sup>) er henholdsvis 1 mg/m<sup>3</sup> og 5 mg/m<sup>3</sup>, se vedlegg 1.

Epidemiologiske studier av arbeidstakere i galvaniseringsindustri utført av El Ghawabi (1975)<sup>3</sup> viser en LOAEL (Lowest Observed Adverse Effect Level) på 4,7 mg CN<sup>-</sup>/m<sup>3</sup>. På grunn av effektene i

befolkningen utsatt for denne konsentrasjonen og fravær av et dose-respons-forhold i studien, anbefales en faktor 5 for ekstrapolering fra LOAEL til NOAEL (No Observed Adverse Effect Level). Basert på disse epidemiologiske studiene anbefaler SCOEL en 8-timers grenseverdi lik  $1 \text{ mg/m}^3$  ( $0,9 \text{ ppm}$ ) for hydrogencyanid. I lys av sammenlignbarheten hydrogencyanid, natriumcyanid og kaliumcyanid i form av cyanidionet bør de ikke få verdier uavhengig av hverandre. Med dette som bakgrunn anbefaler SCOEL en 8-timers grenseverdi lik  $1 \text{ mg/m}^3$  for  $\text{CN}^-$  fra en kombinasjon av de tre forbindelsene. Men siden de akutte toksiske virkningene hos mennesker er alvorlige, for eksempel død, samt ganske bratte dose-respons-relasjoner, bør topp eksponeringer unngås. Basert på det bratte dose-respons-forholdet og alvorlighetsgraden av akutte effekter hos mennesker anbefaler SCOEL en korttidsverdi på  $5 \text{ mg/m}^3$  for  $\text{CN}^-$  fra hvilken som helst kombinasjon av de tre forbindelsene. Hydrogencyanid som cyanid anioner i vandige løsninger har svært høy permeabilitet til hud, og derfor anbefaler SCOEL en hudenmerkning for alle de tre stoffene.

## 4.2. Kommentarer fra TEAN

SCOEL-dokumentet er datert juni 2010 og er basert på kriteriedokumenter utarbeidet av DECOS (2002)<sup>4</sup> og MAK (2001)<sup>5</sup>. Det er søkt i PubMed på relevante referanser etter 2002 samt innhentet kriteriedokument på cyanider fra WHO (2004)<sup>6</sup> og ECETOC (2007)<sup>7</sup>. Det er ikke funnet data som tilsier at de vurderinger som er gjort i SCOEL-dokumentet bør endres.

Cyanider er meget giftige og har en bratt dose-respons kurve. Grenseverdi knyttet til korttidseksponering er derfor viktig. Den viktigste mekanismen for toksisitet er at cyanid hemmer cellenes produksjon av energisubstratet ATP. Dette skjer meget raskt uavhengig av eksponeringsvei. Det er en betydelig kapasitet for nedbrytning av cyanider i kroppen, hovedsakelig til thiocyanat som skilles ut i urinen. De primære målorganene for cyanidforgiftning er hjerte, lunge og hjerne. Det finnes mange kasusstudier av akutt toksisitet på mennesker. Effekter som hodepine, pustebesvær, svimmelhet, kvalme, døsighet er vanlig ved lavere akutte eksponeringer. Høyere eksponeringer kan gi koma, kramper, respirasjonsstans og hjertestans. Cyanider virker irriterende på hud, øyne og luftveier. Direkte kontakt med øyne kan gi alvorlige skader.

Kritisk effekt ved kronisk eksponering er forstørret thyroidea-kjertel og antagelig endring av kjertelens funksjon. Det er kjent at metabolitten thiocyanat kan påvirke opptak av jod i thyroidea og at dette igjen resulterer i en forstørret kjertel. Det er ikke funnet studier som dokumenterer skadelige effekter av kronisk eksponering for cyanider knyttet til hormon forstyrrende mekanismer. Slike effekter er påvist for andre stoffer som påvirker jod-opptak i thyroidea kjertel. Ellers er det kjent at langtidseksponering kan gi en rekke symptomer relatert til sentralnervesystemet.

Cyanider regnes ikke som gentoksiske, og kreftfremkallende egenskaper er ikke dokumentert. De kan påvirke reproduksjon, men slike effekter er bare påvist ved så høye doser at de også gir toksiske effekter hos moren. Derfor defineres ikke stoffet som reprotoksiske.

Cyanider kan i betydelig grad tas opp gjennom huden og bør ha anmerking for dette.

Koeksponering for andre stoffer kan gi forsterket giftighet: Eksponering for karbonmonoksid (CO) kan forekomme sammen med cyanider og disse kan forsterke virkningen av hverandre.<sup>8</sup> (Kilde til CO kan være tobakksrøyking eller branngasser.)

## 5. Bruk og eksponering

### 5.1. Opplysning fra Produktregisteret

Data fra Produktregisteret er innhentet oktober 2016, og inneholder opplysninger om mengde og bruk av stoffene kaliumcyanid og natriumcyanid i deklareringspliktige produkter, men på grunn av sikkerhetsbestemmelsene i Produktregisteret er disse opplysningene unntatt offentlighet og kan derfor ikke rapporteres her. Det finnes ikke produktregisterdata for hydrogencyanid.

### 5.2. Eksponering og måledokumentasjon

I STAMIs eksponeringsdatabase EXPO er det ikke registrert eksponeringsmålinger for stoffene kaliumcyanid og natriumcyanid, men for hydrogencyanid.

#### 5.2.1 EXPO- data for hydrogencyanid

Rapporterte målinger av hydrogencyanid er hentet fra EXPO databasen.

Det ble utført stasjonære eksponeringsmålinger av hydrogencyanid i 1985 under produksjon av elektrisk utstyr ved syrevask av utstyret. Resultatene viser totalt 27 prøver hvor prøveresultater er notert med målerverdier < 2 ppm, og ingen individuelle målerverdier er rapportert i EXPO-dataene. Målerverdiene er under nåværende grenseverdi for hydrogencyanid i Norge.

#### 5.2.2 Prøvetakings- og analysemetode av hydrogencyanid

I tabell 8 er anbefalte metoder for prøvetaking og analyser av hydrogencyanid presentert. Det finnes ingen spesifikke prøvetakingsmetoder for kaliumcyanid og natriumcyanid.

**Tabell 8.** Anbefalte metoder for prøvetaking og analyse av hydrogencyanid.

Prøvetakingsmetode	Analysemetode	Referanse
Adsorbentør (Soda lime)	UV/VIS absorption	NIOSH <sup>1</sup> 6010
Adsorbentør (Silika gel) + glass fiber filter	Ion Chromatography /DC amperometry	NIOSH <sup>1</sup> 6017
Cyanides, aerosol and gas: Filter (0.8 µm PVC) + Bubbler (15 mL 0.1N KOH)	Ion specific electrode	NIOSH <sup>1</sup> 7904
Filter (mixed cellulose ester) and midget impiger (10 mL 0.1N NaOH)	Ion specific electrode	OSHA <sup>2</sup> ID 120
SKC ULTRA II Passive samplers, soda lime	Ion chromatography with Electrothermal and conductivity detector	OSHA <sup>2</sup> 1015

<sup>1</sup> NIOSH metoder, NIOSH Manual og Analytical Methods (NMAM): <https://www.cdc.gov/niosh/docs/2003-154/>

<sup>2</sup> OSHA metoder, OSHA Sampling and Analytical Methods: [www.osha.gov/dts/sltc/methods/toc.html](http://www.osha.gov/dts/sltc/methods/toc.html)

## 6. Vurdering

Eksposering for cyanider forekommer hovedsakelig ved innånding, men også ved hudabsorpsjon.

Eksposeringsstudier av kaliumcyanid og natriumcyanid er begrenset, men den aktive komponenten cyanid anionet er den samme i kaliumcyanid og natriumcyanid som i hydrogencyanid, og man kan dermed gjøre bruk av studier utført på hydrogencyanid når de helseskadelige effektene av kaliumcyanid og natriumcyanid skal vurderes. Den epidemiologiske studien av hydrogencyanideksponerte arbeidstakere i galvaniseringsindustri (Jf. Avsnitt 4.1 Anbefaling fra SCOEL) viste betydelig økning i hodepine, svakhet og endringer i smak og lukt som en følge av eksponering for hydrogencyanid i konsentrasjoner 4,7-13,9 mg/m<sup>3</sup>. Studien viste også økt forekomst av thyroidutvidelse av arbeidere som trolig skyldes tiocyanater (metabolitten) i interaksjon med jod.

På grunn av effektene i gruppen av arbeidstakere som ble eksponert for hydrogencyanid i konsentrasjoner 4,7-13,9 mg/m<sup>3</sup>, og fravær av et dose-respons-forhold i studien, anbefales en faktor 5 for ekstrapolering fra LOAEL til NOAEL, og som derfor gir en grenseverdi på 1 mg/m<sup>3</sup>.

Cyanider brytes ned i kroppen, hovedsakelig til thiocyanat som skilles ut i urinen. De primære målorganene for cyanidforgiftning er hjerte, lunge og hjerne. Det finnes mange kassstudier av akutt toksisitet på mennesker. Effekter som hodepine, pustebesvær, svimmelhet, kvalme, døsighet er vanlig ved lavere akutte eksponeringer. Høyere eksponeringer kan gi koma, kramper, respirasjonsstans og hjertestans. Cyanider virker irriterende på hud, øyne og luftveier. Direkte kontakt med øyne kan gi alvorlige skader.

Likevel, thiocyanatstudier har vist at eksponering for kaliumcyanid og natriumcyanid kan forårsake thyroidutvidelse og en rekke nevrotoksiske symptomer som hodepine, tretthet, og innåndingsproblemer og kan i verste tilfeller være dødelig. Dose-respons kurven for kaliumcyanid er bratt og toppeksposering bør unngås.

Kritisk effekt ved kronisk eksponering for natriumcyanid er forstørret thyroidea-kjertel og antagelig endring av kjertelens funksjon. Det er kjent at metabolitten thiocyanat kan påvirke opptak av jod i thyroidea og at dette igjen resulterer i en forstørret kjertel. Ellers er det kjent at langtidseksponering kan gi en rekke symptomer relatert til sentralnervesystemet.

Dose-relaterte effekter peker klart på en årsakssammenheng tilknyttet eksponering for cyanid. Det finnes ingen data for kaliumcyanid og natriumcyanid, som indikerer at stoffene forårsaker kreft eller er gentoksiske. De kan påvirke reproduksjon, men slike effekter er bare påvist ved så høye doser at de også gir toksiske effekter hos moren. Derfor defineres ikke stoffet som reprotoksiske.

Basert på vitenskapelig dokumentasjon som presentert og vurdert i kapittel 4 anbefales en grenseverdi på 1 mg/m<sup>3</sup> for hydrogencyanid, kaliumcyanid og natriumcyanid. I tillegg, fordi dose-respons kurven av hydrogencyanid er så bratt og akutt effekt av stoffet er så alvorlig foreslås en korttidsverdi for 5 mg/m<sup>3</sup> for CN<sup>-</sup> fra hvilken som helst kombinasjon av de tre forbindelsene.

Cyanider kan i betydelig grad tas opp gjennom huden og en anmerkning H (kan tas opp gjennom huden) er derfor å anbefale.

I lys av sammenlignbarheten hydrogencyanid, natriumcyanid og kaliumcyanid i form av cyanidionet bør de ikke få forskriftsfestede verdier uavhengige av hverandre.

En forskriftsfestet grenseverdi på 1 mg/m<sup>3</sup> for hydrogencyanid, kaliumcyanid og natriumcyanid antas ikke å føre til merkostnader for industrien da eksisterende eksponeringsdata bekrefter dette. I tillegg, de fleste prosesser med cyanider foregår i lukkede systemer som vil føre til redusert eksponering. Likevel, personlig verneutstyr kan være nødvendig å bruke i slike tilfeller, men vil ikke medføre store kostnader for industrien. Produktregisterdata over deklareringspliktige produkter viser at det er små mengder og lite bruk av hydrogencyanid, kaliumcyanid og natriumcyanid.

## 7. Konklusjon med forslag til ny grenseverdi

På bakgrunn av den foreliggende dokumentasjon og en avveining mellom de toksikologiske dataene og eksponeringsdata (dvs. tekniske og økonomiske hensyn), foreslås en reduksjon i dagens grenseverdi for hydrogencyanid til 1 mg/m<sup>3</sup>, og at anmerkningen for hudopptak (H) beholdes. Dagens takverdi frafaller, men korttidsverdi lik 5 mg/m<sup>3</sup> foreslås innført. Den aktive komponenten, CN<sup>-</sup> i kaliumcyanid og natriumcyanid er lik som i hydrogencyanid og derfor foreslås samme grenseverdi, korttidsverdi og anmerkninger for de tre cyanidene.

Forslag til nye grenseverdier, korttidsverdier og anmerkninger for stoffene:

### Hydrogencyanid:

**Grenseverdi (8-timers TWA):** 0,9 ppm, 1 mg/m<sup>3</sup>

**Korttidsverdi (15 min):** 4 ppm, 5 mg/m<sup>3</sup>

**Anmerkninger:** H (hudopptak), S (korttidsverdi) og E (EU har fastsatt grenseverdi for stoffet)

### Kaliumcyanid:

**Grenseverdi (8-timers TWA):** 0,9 ppm, 1 mg/m<sup>3</sup>

**Korttidsverdi (15 min):** 4 ppm, 5 mg/m<sup>3</sup>

**Anmerkninger:** H (hudopptak), S (korttidsverdi) og E (EU har fastsatt grenseverdi for stoffet)

### Natriumcyanid:

**Grenseverdi (8-timers TWA):** 0,9 ppm, 1 mg/m<sup>3</sup>

**Korttidsverdi (15 min):** 4 ppm, 5 mg/m<sup>3</sup>

**Anmerkninger:** H (hudopptak), S (korttidsverdi) og E (EU har fastsatt grenseverdi for stoffet)



## 8. Nye grenseverdier

### Hydrogencyanid:

På grunnlag av drøftinger med partene og høringsuttalelser ble ny grenseverdi og korttidsverdi for hydrogencyanid fastsatt til:

**Grenseverdi (8-timer): 0,9 ppm, 1 mg/m<sup>3</sup>**

**Korttidsverdi (15 min): 4 ppm, 5 mg/m<sup>3</sup>**

**Anmerkninger:** H (hudopptak), S (korttidsverdi) og E (EU har fastsatt grenseverdi for stoffet)

### Kaliumcyanid:

På grunnlag av drøftinger med partene og høringsuttalelser ble ny grenseverdi og korttidsverdi for kaliumcyanid fastsatt til:

**Grenseverdi (8-timer): 0,9 ppm, 1 mg/m<sup>3</sup>**

**Korttidsverdi (15 min): 4 ppm, 5 mg/m<sup>3</sup>**

**Anmerkninger:** H (hudopptak), S (korttidsverdi) og E (EU har fastsatt grenseverdi for stoffet)

### Natriumcyanid:

På grunnlag av drøftinger med partene og høringsuttalelser ble ny grenseverdi og korttidsverdi for natriumcyanid fastsatt til:

**Grenseverdi (8-timer): 0,9 ppm, 1 mg/m<sup>3</sup>**

**Korttidsverdi (15 min): 4 ppm, 5 mg/m<sup>3</sup>**

**Anmerkninger:** H (hudopptak), S (korttidsverdi) og E (EU har fastsatt grenseverdi for stoffet)

## 9. Referanser

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**Recommendation from the Scientific  
Committee on Occupational Exposure Limits  
for Cyanide (HCN, KCN, NaCN)**

SCOEL/SUM/115

June 2010



European Commission



## Table of Contents

1. Occurrence and Use .....	4
2. Health Effects .....	4
2.1. Toxicokinetics.....	4
Biotransformation .....	5
2.2. Acute toxicity .....	7
2.2.1. Human data .....	7
2.2.2. Animal data .....	8
2.3. Irritation.....	9
2.3.1. Human data .....	9
2.3.2. Animal data .....	9
2.4. Sensitisation.....	9
2.5. Repeated dose toxicity .....	9
2.5.1. Human data .....	9
2.5.2. Animal data .....	10
2.6. Mutagenicity .....	11
2.7. Carcinogenicity .....	11
2.8. Reproductive effects .....	11
Recommendations .....	12



## Recommendation from Scientific Committee on Occupational Exposure Limits for Cyanide (HCN, KCN, NaCN)

8 hour TWA	: 1 mg/m <sup>3</sup> (expressed as cyanide)
STEL (15 min)	: 5 mg/m <sup>3</sup>
Additional classification	: Sk (Skin notation)

### Substance Identification and Properties

Chemical name	Hydrogen cyanide (HCN)	Potassium cyanide (KCN)	Sodium cyanide (NaCN)
IUPAC name	Hdrocyanic acid	Potassium cyanide	Sodium cyanide
Synonyms	Cyclone prussic acid, formonitrile	Hydrocyanic acid potassium salt, cyanide of potassium	Hydrocyanic acid sodium salt, cyanide of sodium
EINECS No.	200-821-6	205-792-3	205-599-4
EEC No	006-006-00-X	006-007-00-5	006-007-00-5
EC Classification	F+: R12 T+: R26 N: R50-53	T+: R26/27/28 R32 N: R50-53	T+: R26/27/28 R32 N: R50-53
Cas Registry No.	74-90-8	151-50-8	143-33-9
MWt	27.03 g/mol	65.11 g/mol	49.02 g/mol
Conversion factor (20°C)	1 mg/m <sup>3</sup> = 0.890 ppm 1 ppm = 1.124 mg/m <sup>3</sup>		

This document is based on the Report of the Dutch Expert Committee on Occupational Standards, a committee of the Health Council of the Netherlands (2002) and the MAK report: Hydrogen cyanide, potassium cyanide and sodium cyanide (Greim, 2001).

HCN is a colourless liquid or a colourless gas with the characteristic odour of bitter almonds. Gas and liquid are miscible with water and soluble in ethanol and ether. At atmospheric pressure the boiling and melting points of HCN are 25.70°C and -13.24°C, respectively. The odour threshold is 1-5 ppm (1-6 mg/m<sup>3</sup>; people sensitive to odour). Many people cannot perceive the odour at all (Holland and Kozłowski, 1986)

At ambient conditions, NaCN and KCN are white crystalline solids, with a slight HCN odour. The melting points are about 560°C and about 620-635°C at ambient atmospheric pressure for NaCN and KCN, respectively. KCN salt is readily soluble in water, ammonia and formamide, and slightly soluble in ethanol, dimethylformamide. NaCN is readily soluble in water, ammonia and slightly soluble in formamide, ethanol, dimethylformamide, methanol, furfural and ether.



## 1. Occurrence and Use

Cyanogenic glycosides occur naturally in a variety of plant species, such as cassava, bitter almonds and the pits of stone fruits (Health Council of Netherlands, 2002).

The main uses of hydrogen cyanide are the fumigation of ships, buildings, orchards, and various foods, in electroplating; for the production of chelating agents such as EDTA, and in metal treatment processes. It also has many uses as a chemical intermediate.

NaCN and KCN are used in the extraction and recovery of gold and silver from ores, the heat treatment of metals, and electroplating. Furthermore, they serve as precursors in chemical syntheses.

Mudder and Botz (2000) reported that 1.4 million tonnes of HCN are produced annually whereby 13% is converted in NaCN for use in mining. HCN is produced by direct reaction of alkanes with ammonia, and indirectly as a by-product of the manufacture of acrylonitrile.

Workers in various occupations may be exposed to cyanides. Exposure occurs primarily through inhalation and, less frequently, by skin absorption (ATSDR, 1997). Concentrations of hydrogen cyanide and cyanide aerosols in an electroplating and casehardening factory ranged from 0.2 to 0.8 mg/m<sup>3</sup> (mean 0.45 mg/m<sup>3</sup>). In the breathing zone of the general workroom atmosphere in the same factory, the concentration ranged from 0.1 to 0.2 mg/m<sup>3</sup> (mean 0.15 mg/m<sup>3</sup>) (Chandra et al., 1980). Cyanide concentrations in air in the electroplating sections of three factories ranged from 9.2-13.9, 4.7-9.9 and 6.6-10.8 mg/m<sup>3</sup> (El Ghawabi et al., 1975). Concentrations of hydrogen cyanide in air in a plating facility of a U.S. airline company ranged from 0.001-0.004 mg/m<sup>3</sup>. In a work area of other plating facilities it ranged from 1.7-4.3 mg/m<sup>3</sup> (ATSDR, 1997).

## 2. Health Effects

### 2.1. Toxicokinetics

HCN is readily and largely absorbed by humans after respiratory, dermal and oral exposure (Landahl et al., 1950, ATSDR, 1997). It is assumed, that the cyanide salts NaCN and KCN are readily and completely absorbed by humans after respiratory exposure, in case the aerodynamic diameter of droplets of their solutions or particles of the salts in dry form falls within the inhalable range. Dermal absorption of NaCN and KCN depends on the condition of the skin and the presence of moist. Salts in dissolved form or exposure of the moistened skin to dry powders of the salts, will result in substantial absorption characterised by a permeability constant of 3.5X10<sup>-4</sup> cm/h (Health Council of Netherlands, 2002; Ballantyne and Mars, 1987).

Gattler and Baine (1938) treated three dogs with KCN by gavage and determined the amount of cyanide present in the stomach and intestines after the dogs had died (within 10 to 15 min). From total doses of 100 and 50 mg, 83.4 and 38 mg was recovered in stomach and intestines, respectively, from which the authors concluded that 16.6% and 24% of the administered dose had been absorbed before the dogs died. A similar value (45.5%) was found by Crawley and Goddard (1977) for a period of 24 h based on urinary excretion, while the percentage was 94.7%, when the urine was collected over a period of 8-14 days. Leuschner et al (1991) gave rats drinking water with cyanide for 13 weeks. Daily doses were calculated to amount to about 0, 40, 80 and 140-160 mg/kg bw. About 11% of the daily dose was excreted via the urine as thiocyanate.

After oral exposure to lethal levels of HCN, NaCN or KCN to humans and animals, cyanide is found in many tissues and in blood. In humans the main amount of cyanide concentration is found in the stomach content, followed by spleen, blood, liver, brain and kidney (Ansell et al., 1970). Relatively high concentrations are encountered in liver, lungs, kidneys, brain and blood of rats after oral and respiratory exposure (Yamamoto et al., 1982). Cyanide concentrations in the liver are much higher after oral exposure than after



dermal exposure; this may be attributed to the primary transport of cyanide to the liver via the portal vein after oral exposure (Ballantyne, 1983a).

A clear species dependence of distribution has been observed (rabbit, pig, rat, monkey and sheep). Very high relative liver concentrations were observed in sheep and very low ones in rats (Ballantyne, 1983a). No information is available about the distribution at low, clearly sub-lethal exposure levels.

#### **Biotransformation**

Cyanide is metabolized in mammals by one major route and several minor routes. The major route of metabolism for HCN and cyanides is detoxification in the liver by the mitochondrial enzyme rhodanese (E.C. 2.2.11), which catalyzes the transfer of the sulphane-sulphur of thiosulphate to the cyanide ion to form thiocyanate (Ansell and Lewis, 1970). About 80% of cyanide is detoxified by this route. The activity of rhodanese in serum of 31 healthy humans ranges from 11.4 to 36.1 U/L in males and from <7.6 to 47.5 U/L in females with an overall mean of 20.9 U/L. Rhodanese activity has been detected in virtually all tissues of mammals. In particular high activities are present in liver and kidneys (Drawbaugh and Marss, 1987). The capacity of the body to detoxify cyanide by transsulphurization is not limited by rhodanese activity (Wood, 1975). In 1948, Himwich and Saunders calculated the amount of rhodanese in dog liver and muscles to be sufficient for the detoxification of 243 and 117 mg/min, respectively. Furthermore, it has been shown that the detoxification is limited by the availability of sulphane-sulphur instead of rhodanese activity (Isom and Johnson, 1987; Bhatt and Linnell, 1987). In humans (after i.v. injection), about 0.017 mg of cyanide per kg/bw and minute (1.0 mg/kg bw/hour) can be detoxified without therapeutic measures (EPA, 1992). Dekant et al., (2001) and Schulz et al., (1982) give a figure of 0.1 mg/kg bw/hour as detoxification capacity in man.

The following minor biotransformation pathways have been identified for cyanide:

- Spontaneous reaction with cystine to cysteine and  $\alpha$ -thiocyanalanine, which compound tautomerizes to 2-imino-4-thiazolidine-carboxylic acid and 2-aminothiazoline-4-carboxylic acid
- Spontaneous reaction with hydroxocobalamine to form cyanocobalamine
- Spontaneous reaction with methaemoglobin to form cyano-methaemoglobin
- Entry into the 1-C metabolic pool

Oxidation via cyanate to carbon dioxide (only demonstrated *in vitro*)

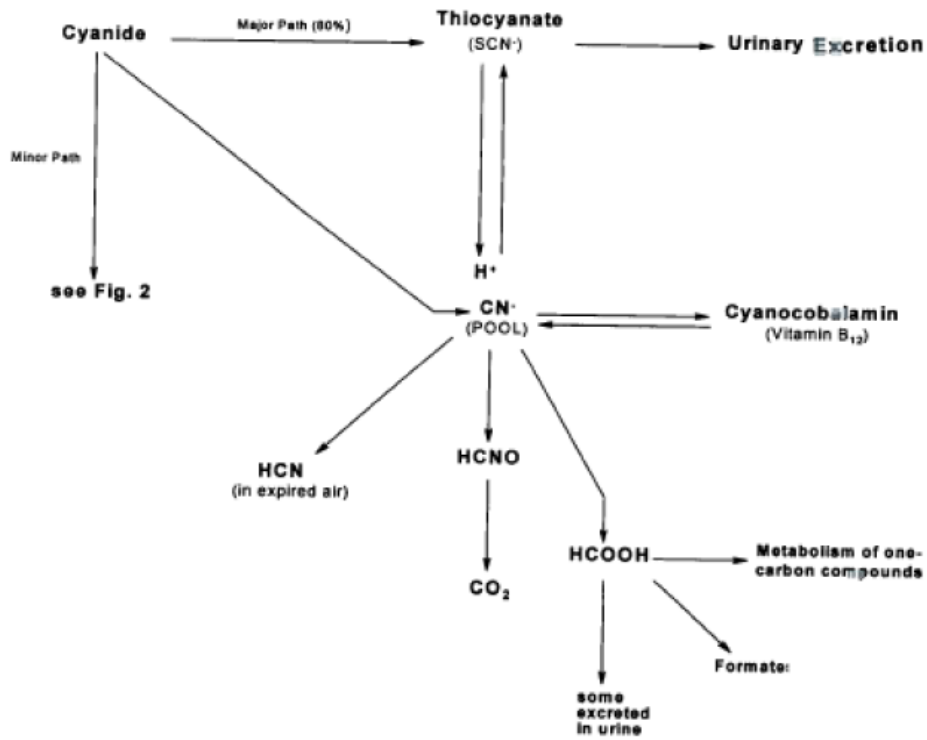


Fig 1: Basic processes involved in the metabolism of cyanide in mammals (Health Council of Netherlands, 2002)



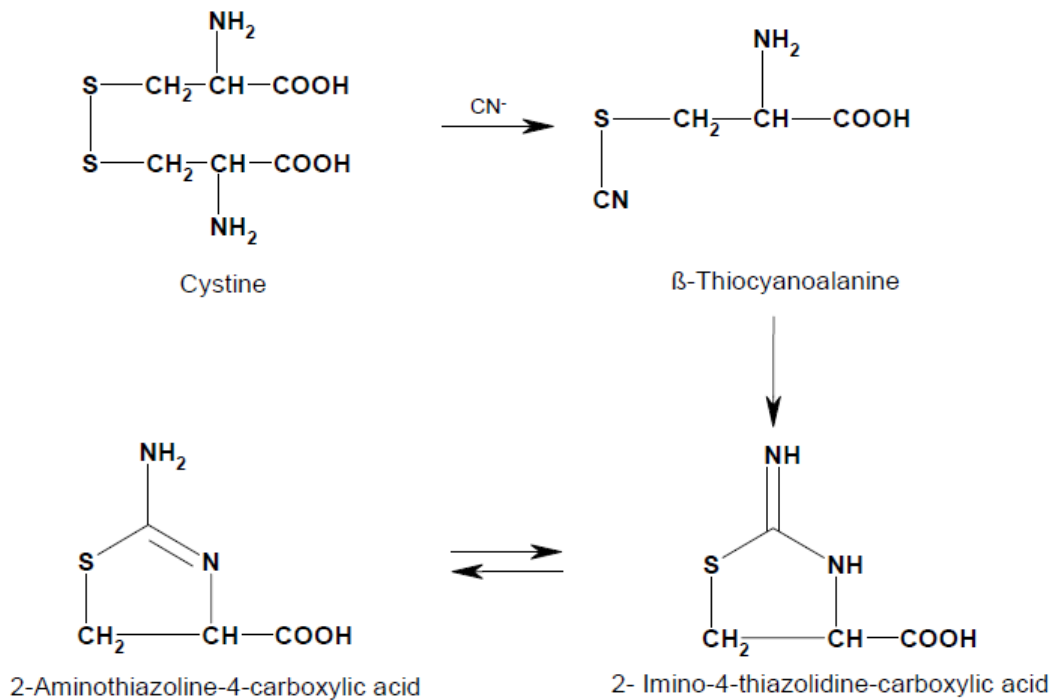


Fig 2: Minor path for the removal of cyanide from the body (Scheme based on Health Council of Netherlands, 2002)

Urinary excretion of thiocyanate is the most important elimination route in humans and in experimental animals, but it takes several days for a single, relatively high dose of cyanide to be eliminated from the body. After exposure by inhalation, a few percent of cyanide is excreted via exhalation, within the first hours upon exposure. The exhaled material consists largely (85-90%) of carbon dioxide.

The active principle in the three compounds is the cyanide ion. It reacts with the trivalent iron in the enzyme cytochrome C oxidase to give a relatively stable complex. This inhibits the enzyme and blocks the last step in oxidative phosphorylation. The result is a mitochondrial deficiency of ATP and death of cells. Particularly sensitive tissues are the CNS and the heart. Cyanide may form reversible complexes with metal ions and thus inhibit many other metalloenzymes (Greim, 2001).

## 2.2. Acute toxicity

### 2.2.1. Human data

The primary route of entry at the workplace is by inhalation, and for HCN, absorption through the skin (US-NIOSH, 1997). Observed symptoms of cyanide poisoning are: anxiety and excitement, rapid breathing, faintness, weakness, headache (pulsating), constricting sensations in the chest, facial flushing, dyspnoea, nausea, vomiting, diarrhoea, dizziness, drowsiness, confusion, convulsions, incontinence of urine and faeces, coma, respiratory irregularities. Complications of acute cyanide poisoning are rhabdomyolysis, diffuse cerebral oedema, central nervous system degenerative changes, and pulmonary oedema.



Death occurred within 5 minutes after accidental exposure of a worker's hand to aqueous HCN solution while working with a gas mask (Ballantyne 1987). *In vitro* studies of human skin showed a high dermal permeability constant ( $3.5 \times 10^{-4}$  cm/h) (Greim, 2001). The dermal LD<sub>50</sub> for HCN in humans has been reported to be 100 mg/kg of body weight (no further details; US-EPA 1992). Low LD<sub>50</sub> values after dermal exposure indicate good dermal absorption of the cyanides.

It is difficult to estimate the oral lethal doses from human case studies. A total dose of 50-100 mg HCN and 150-250 mg KCN and 0.7-3.5 mg HCN/kg bw led to deaths (Ballantyne, 1987).

The dose-response relation after inhalative exposure to HCN is quite steep, as table 2 shows. A concentration of 300 mg/m<sup>3</sup> is immediately fatal, whereas a concentration of 150 mg/m<sup>3</sup> is fatal after about 30 minutes and 10-20 mg/m<sup>3</sup> causes slight symptoms after several hours.

Table 2: Dose-response after HCN inhalation in humans (Health Council of Netherlands, 2002)

Effect	Dose
Immediately fatal	300 mg/m <sup>3</sup> (270 ppm)
Fatal after 10 min	200 mg/m <sup>3</sup> (181 ppm)
Fatal after 30 min	150 mg/m <sup>3</sup> (135 ppm)
Fatal after 0.5 – 1 h or later (or dangerous to life)	120-150 mg/m <sup>3</sup> (110-135 ppm)
Tolerated for 20 min – 1 h (without immediate or late effects)	50-60 mg/m <sup>3</sup> (45-54 ppm)
Slight symptoms after several hours	20-40 mg/m <sup>3</sup> (18-36 ppm)

### 2.2.2. Animal data

HCN is a very toxic compound by inhalation. Inhalation studies provided an approximate LC<sub>50</sub> of 166 mg/m<sup>3</sup>/30 min. in the mouse, 151-173 mg/m<sup>3</sup>/30 min. in the rat and 208 mg/m<sup>3</sup>/35 min. for rabbits (Ballantyne, 1987; ATSDR, 1997).

The oral LD<sub>50</sub> of HCN in the rat is 3.62-4.21 mg/kg bw, of KCN 7.48-10.00 mg/kg bw and of NaCN 5.00-5.72 mg/kg bw. The values for mice (8.50 mg/kg bw KCN) and rabbits (2.49 mg/kg bw HCN; 5.11 mg/kg bw, NaCN and 5.82 mg/kg bw, KCN) are in the same range. The lethality of HCN for rabbits after dermal exposure (2.34 mg/kg bw) seems to be slightly larger than that of NaCN (11.28 mg/kg bw) and KCN (14.29 mg/kg bw), especially in case of abraded skin. For the intact skin these figures are: HCN 6.90 mg/kg bw; NaCN 14.63 mg/kg bw and KCN 22.33 mg/kg bw (Ballantyne, 1994).

Acute cyanide exposure leads to acidosis, reduced carbon dioxide concentrations, increase in the oxygen concentration, increasing catabolism via the pentose phosphate pathway, reduction in catabolism via the Embden-Meyerhof pathway and the citrate cycle, and an increase in glucose and inorganic phosphates in the blood (Greim, 2001). Clinical effects were: dyspnea, irregular, shallow and gasping breathing, ataxia, tremors, retrocolic spasms, tonic spasms, loss of consciousness, convulsions and asphyxiation.



## 2.3. Irritation

### 2.3.1. Human data

Contact of the skin with HCN or solutions of the salts may result in dermatitis and rash according to the Environmental Protection Agency (US-EPA, 1992). Nasal irritation and septal ulceration were observed in electroplating workers exposed to cyanide concentrations higher than 5 mg/m<sup>3</sup> (ACGIH, 1996).

### 2.3.2. Animal data

No irritation studies were performed with the cyanides. Clear signs of eye irritation have been observed when animals were exposed via the eye to study the acute toxicity of HCN, NaCN or KCN (Ballantyne, 1983b, Ballantyne, 1988). In mice exposed to 22-112 mg/m<sup>3</sup> of HCN evidence for respiratory irritation was found by analyzing the breath rate and pattern (Matijak-Schaper et al., 1982).

## 2.4. Sensitisation

No data on sensitisation of HCN, KCN or NaCN are available.

## 2.5. Repeated dose toxicity

### 2.5.1. Human data

Observations of cases at the workplace indicate that cyanide exposure (no details of the concentrations available) leads to thyroid enlargement (goitre) and a wide range of neurotoxicity symptoms (visual disturbances, convulsions, pareses) which disappeared on ceasing to work with cyanide. There are controversial discussions in the literature about whether these really are the consequences of repeated exposure or whether the symptoms relate to acute intoxications. A few cases of goitre have been reported. There are also reports of gastrointestinal symptoms and skin changes which can probably be attributed to the irritant effect of cyanides (Ballantyne and Mars 1987; Hardy et al. 1950; Sandberg 1967).

Only two epidemiological studies are available with sufficient details on exposure and adequate medical questionnaire. In one epidemiological investigation (36 male workers from the electroplating sections of three factories – mean breathing zone cyanide concentrations ranged from 7.3 – 11.6 mg/m<sup>3</sup> - and 20 male control workers, 22 of the workers had been employed for more than 5 years in the factories), enlarged thyroids were found in 20 exposed subjects pointing to goitrogenicity. Further findings were highly elevated thiocyanate levels in the urine (5 mg compared to 0.11 mg in the controls) higher haemoglobin levels and lymphocyte counts, and punctate basophilia. All investigated persons were non-smokers, and there was no evidence of consumption of foods known to contribute to an elevated thiocyanate concentration in the urine. The frequency of headaches, weakness and changes in senses of taste and smell was significantly increased after chronic exposure to breathing zone concentrations ranging from 4.7 to 13.9 mg/m<sup>3</sup> CN<sup>-</sup> (El Ghawabi et al., 1975). Although no distinction was made in the study between acute and past symptoms, it can be concluded that the subjects from the exposed group show a clearly enhanced incidence of various symptoms associated with cyanide exposure compared to controls. Although the study does not allow for a definitive attribution of these symptoms to actual cyanide exposure, a causal relationship between exposure and symptoms is deemed highly probable.

The high incidence of thyroid enlargement in the exposed group points to goitrogenicity by thiocyanate formed from cyanide. That the exposure does indeed lead to thiocyanate exposure is clearly shown by the linear correlation between cyanide exposure and urinary thiocyanate excretion. Thiocyanate is known to interfere with iodine uptake by the thyroid



gland and, as a result, may lead to enlargement of the thyroid (Cliff et al., 1986 and Knudsen et al., 2000, 2002)

As no information is provided about dermal and oral exposure, the study does not permit direct conclusions as to the quantitative relation between respiratory exposure and effects. If the dermal and oral exposure is assumed negligible compared to respiratory exposure, it seems justifiable to assume that the effects observed are associated with exposures to 4.2-12.4 ppm (4.7-13.9 mg/m<sup>3</sup>). However, in view of the rapid and efficient dermal penetration of HCN and its simple salts, this form of exposure may not be neglected.

The second study was carried out in a silver-reclaiming facility. Seven months after closure of this silver-reclaiming factory (exposure levels were at least > 17 mg/m<sup>3</sup> CN-) 36 workers have been interviewed and examined physically. A high prevalence of several residual symptoms was found (e.g. rash, bitter or almond taste and headache). Mean serum vitamin-B12 and serum folate levels were significantly decreased, serum triiodothyronine and thyroid-stimulating hormone levels were slightly increased but no palpable thyroid anomalies were found (Blanc et al., 1985). Although the authors claim that the symptoms observed are related to chronic cyanide poisoning, it cannot be ruled out that the symptoms are related to acute intoxications rather than repeated exposure.

### 2.5.2. Animal data

#### *Inhalation*

Three inhalation studies were located, one with dogs and two with rabbits. The dog study was mainly concerned with histological effects in the brain after short exposures (12.5 min) to a concentration, which gave rise to overt signs of acute toxicity (50 mg/m<sup>3</sup> HCN) (Valade, 1952). The periods between the exposures were long enough to allow a recovery from these acute effects for 9 of the 12 dogs; 3 of them died during the study. Severe histological damage was observed in the brain. This study shows that repeated respiratory exposure to acutely toxic dose levels may lead to severe brain damage. The studies with rabbits were carried out at a 100-fold lower dose level (0.5 mg/m<sup>3</sup> HCN) with an exposure, continuously, for up to 4 weeks. These studies were aimed at the observation of possible histological effects in heart, lung and adjacent arteries. No effects were found (Hugod, 1979, US-EPA, 1992).

#### *Oral*

The repeated dose oral toxicity studies (up to 13 weeks) revealed effects on the thyroid (Jackson, 1988, Philbrick et al., 1979), central nervous system and behaviour (Jackson, 1988, Philbrick et al., 1979), glucose metabolism (Jackson, 1988), male reproductive organs (NTP, 1993). Effects on behaviour of pigs (decrease in dominance behaviour, fighting and aggression) were already encountered at the lowest dose level applied (0.4 mg KCN/kg bw/day).

In two limited studies effects on selenium metabolism, glutathione peroxidase activity (Beilstein et al., 1984) and ATPase activity (Okolie et al., 1994) were also seen. There are no specific long-term studies, conducted according to the OECD guidelines, of the possible chronic or carcinogenic effects of HCN or other cyanides. Only one long-term (2-year) oral toxicity study with rats has been found (Howard and Hanzal, 1955). This study resulted in an oral NOAEL of more than 3.5 mg/kg bw/day for a restricted set of endpoints.

#### *Other routes*

In two studies, the experimental animals were treated parenterally (i.p. and s.c.) (Gallagher et al., 1976, Kanthasamy et al., 1994). Effects were a reduced copper content of the liver, reduced adenine nucleotide binding, reduced number of tyrosine-hydroxylase positive cells in the brain, and altered behaviour.

No repeated dose dermal studies have been found.



## 2.6. Mutagenicity

Salmonella/microsome tests have been carried out with the usual Salmonella strains (TA1535, TA1538, TA98, TA100, TA97, TA102). Positive effects were only obtained in one study, when HCN was tested with strain TA 100 in the absence of metabolic activation, while the other strains employed in this study yielded negative results. KCN was found negative in two studies, when tested with strain TA 100 and other strains. Negative results were obtained in a DNA-repair test with the Escherichia coli strains WP67, CM871 and WP2, and a rec assay with the Bacillus subtilis strain M45 (Health Council of Netherlands, 2002).

NaCN did not induce DNA-strand breaks in cultured mouse lymphoma cells without metabolic activation (Garberg et al., 1988). KCN did not induce testicular DNA synthesis in mice (Health Council of Netherlands, 2002). KCN caused DNA double strand breaks in human lung epithelial cells only at concentrations which were toxic and led to a reduction of more than 40% in survival (Vock et al., 1998).

An in vivo mutagenicity study in Chinese hamsters did not indicate mutagenic properties relative to chromosome damage (WHO, 1993).

In summary, these data suggest the absence of genotoxic properties for the three cyanides.

## 2.7. Carcinogenicity

No effects were seen in an oral study with rats which lasted for 2 years in which a rather restricted range of endpoints were investigated. The highest dose applied was about 3.5 mg HCN/kg bw/day. However, the experimental set up of this study (only 10 males and 10 females per group; feed gassed with HCN was given every 2 days) precludes a definitive conclusion about the carcinogenicity.

## 2.8. Reproductive effects

In a 13-week rat study, oral administration via the drinking water of  $\geq 0.3$  mg/kg bw NaCN led to changes in some reproductive parameters in male rats and mice. In rats the weight of the cauda epididymis was significantly reduced after NaCN doses  $\geq 0.3$  mg/kg bw. At concentrations  $\geq 25$  mg/kg bw NaCN, there were significant reductions in the weights of the whole epididymis and of the testes and in the number of spermatids in the testes. The sperm count in the epididymis, however, was not decreased. In mice the weights of the epididymis and the cauda epididymis were reduced at 45.9 mg/kg bw (NTP, 1994). The authors regard the observed reductions as not biologically relevant for the rodent species, but pointed out that humans are relatively more sensitive for such changes in reproductive parameters.

In female rats at  $\geq 8.2$  mg/kg bw there were merely slight shifts in the stages of the cycle, i.e. prooestrus was longer and oestrus was shorter.

Pregnant golden hamsters exposed s.c. to NaCN (using osmotic minipumps) at doses ranging from 6.17-6.35 mg/kg bw/h (total dose amounted to 30-40 times the s.c. LD50) developed severe embryotoxic and teratogenic effects such as neural-tube effects (exencephaly, encephalocele, nondisclosure), microphthalmia, hydro-pericardium, crooked tail, reduced crown-rump length, increased % of resorptions. Mild maternal toxicity was observed (weight loss of up to 16%, hypothermia, salivation, ataxia and dyspnea) (Doherty et al., 1982).

None of the female rats given 5 or 10 g KCN/kg bw/day for 13 weeks became pregnant in contrast to 9/10 control animals (Olusi et al., 1979).

Female rats were treated with about 125 mg KCN/kg bw/day in their cassave diet during mating, pregnancy, lactation. Cyanide showed no effects on reproduction parameters. Treatment of the pups for 28 days after weaning demonstrated a significant reduction in growth and feed consumption (Tewe and Maner, 1981a).

In another study, Tewe and Maner (1981b) fed pregnant pigs (one day after breeding till parturition) diets containing 30, 277 or 521 mg CN/kg feed. This treatment had no



significant effects on reproductive performance in terms of litter size at birth, litter size at weaning, birth weight of piglets, and body weight gain during gestation. The foetuses of the high-dose group showed reduced relative weights of heart and spleen, whereas a reduced relative thyroid weight was found in foetuses of the medium-dose group. Based on the available data it can be concluded that cyanide is embryotoxic and teratogenic at maternally toxic doses. At not maternally toxic doses, cyanide does not affect reproductive performance of rats and pigs, although the studies do not allow full judgement of possible teratogenic properties.

### Recommendations

Acute toxicity in humans shows a rather steep dose-response relationship: whereas exposure for several hours to 20 mg HCN/m<sup>3</sup> leads to only slight effects, exposure to concentrations larger than 120 mg HCN/m<sup>3</sup> may be fatal. Various overt respiratory, cardiovascular and neurological effects were seen at (nearly) lethal levels in animals. However, the animal data do not allow the establishment of a dose-response relationship. The cyanide detoxification capacity of humans is given as 0.1 up to 1.0 mg/kg bw/hour. Based on this lowest figure, the amount of cyanide which can be detoxified per shift is 56 mg, or 0.8 mg/kg bw/day.

There is no evidence for carcinogenicity or effects on reproduction. The sole long-term (2 year) oral toxicity study in rat did not reveal effects of HCN to up to about 3.5 mg/kg/day on a rather restricted set of endpoints. This study is considered inadequate to serve as a basis for an OEL for effects on long-term exposure.

The epidemiological study of El Ghawabi et al (1975) on chronic exposure of workers to cyanide in electroplating industries, is considered acceptable to derive an OEL for long term exposure. In this study, with breathing zone concentrations ranging from 4.7 to 13.9 mg CN-/m<sup>3</sup> CN-, the effects observed were headache, weakness, giddiness, irritation of throat, vomiting, dyspnoea, lachrymation, salivation, disturbances of accommodation and psychosis. Although no dose dependence could be established, the nature of the effects clearly points to a causal relationship with cyanide exposure. In particular the clear signs of goitrogenicity are considered as cyanide (i.e., thiocyanate) specific and taken as the most sensitive effect.

The interpretation of the study is hampered by the uncertainty about dermal and oral exposure and about the exposure levels in the past. The risk may be overestimated when dermal or oral exposure substantially contributed to the total exposure or when exposure in the past were substantially higher than measured during the study. This is, however, regarded as a reasonable worst case for determination of an OEL for long-term exposure.

The epidemiological study of El Ghawabi (1975) demonstrated a LOAEL of 4.7 mg CN-/m<sup>3</sup>. Due to the effects observed in the exposed population at this concentration and the absence of a dose-response relationship in the study, a factor 5 is recommended for the extrapolation from the LOAEL to the NAEL.

By applying this assessment factor, an OEL 8h TWA of 1 mg/m<sup>3</sup> (0.9 ppm) for HCN is recommended.

In view of the comparability of HCN, NaCN and KCN with regard to the ultimately effective agent (i.e. the cyanide ion), they should not be regulated independently.

Therefore, an OEL, 8h TWA of 1 mg/m<sup>3</sup> is established as CN- from any combination of the three compounds.

However, since the acute effects in humans are severe (i.e. death) and show a rather steep dose-response relationship, peak exposures should be avoided.

Based on the steepness of the dose-response relationship and the severity of the acute effects in humans a STEL of 5 mg/m<sup>3</sup> is recommended as CN- from any combination of the three compounds.

Based on the very high skin permeability measured for HCN and cyanide anions in aqueous solutions, a skin notation is recommended for all three compounds.

No measurement difficulties are foreseen at the recommended OEL



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