Overview information for

Hydrogen cyanide

HYDROGEN CYANIDE REFERENCES					
Author Name	Title	Journal	Volume	Page number(s)	Year
Li X, Luo Y, Jiang X, Zhang H, Zhu F, Hu S, Hou H, Hu Q, Pang Y.	Chemical Analysis and Simulated Pyrolysis of Tobacco Heating System 2.2 Compared to Conventional Cigarettes.	Nicotine Tob Res.	21(1)	111-118	2019
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I U C L I D

D a t a s e t

Existing Chemical	Substance ID: 74–90–8
CAS No.	74–90–8
EINECS Name	hydrogen cyanide
EINECS No.	200–821–6
Molecular Formula	CHN

Dataset created by: EUROPEAN COMMISSION – European Chemicals Bureau

This dossier is a compilation based on data reported by the European Chemicals Industry following 'Council Regulation (EEC) No. 793/93 on the Evaluation and Control of the Risks of Existing Substances'. All (non–confidential) information from the single datasets, submitted in the IUCLID/HEDSET format by individual companies, was integrated to create this document.

The data have not undergone any evaluation by the European Commission.

Creation date: 19–FEB–2000

Number of Pages: **113**

Chapters: **all**

Edition: **Year 2000 CD–ROM edition**

Flags: **non–confidential**

1.0.1 OECD and Company Information

Name: ACN Product Group
Street: Koestraat 1
Town: Geleen
Country: Netherlands
Phone: 31 46 73886
Telefax: 31 46 70085

Name: Atochem
Street: 4, Cours Michelet
Town: 92080 Paris la Defense
Country: France

Name: BASF AG
Street: Karl–Bosch–Str
Town: 67056 Ludwigshafen
Country: Germany

Name: BASF plc
Town: SK8 6QG Cheadle Cheshire
Country: United Kingdom

Name: BP Chemicals Ltd.
Street: 76, Buckingham Palace Road
Town: SW1 WOSU London
Country: United Kingdom

Name: Degussa AG
Street: Weissfrauenstrasse 9
Town: 60287 Frankfurt am Main
Country: Germany

Name: Degussa Antwerpen N.V.
Street: Tijsmanstunnel West
Town: 2040 Antwerpen 4
Country: Belgium

Name: EC Erdölchemie GmbH
Street: Alte Strasse 201
Town: 50769 Köln
Country: Germany
Phone: 0(49)2133557118
Telefax: 0(49)2133557149
Telex: 2133302 EC koeln

Name: ELF ATOCHEM ITALIA S.r.l.
Street: VIA DELLA CHIMICA,5
Town: 30175 PORTO MARGHERA (VE)
Country: Italy
Phone: 041-2913146
Telefax: 041-2912796

Name: Enichem S.p.A.
Street: Via Taramelli,26
Town: 20124 Milan
Country: Italy

Name: Hoechst AG
Street: Postfach 80 03 20 Brüningstrasse 50
Town: 65903 Frankfurt/Main
Country: Germany

Name: Imperial Chemical Industries PLC
Street: 9 Millbank
Town: SW1P 3JF London
Country: United Kingdom
Phone: 0044/71/834-4444
Telefax: -2042

Name: PCK AG Schwedt
Street: Passower Chaussee
Town: D-16303 Schwedt/Oder
Country: Germany
Phone: (03332)462701
Telefax: (03332)465271
Telex: 371350 pck d

Name: REPSOL QUIMICA, S.A.
Street: PASEO DE LA CASTELLANA, 280
Town: 28046 MADRID
Country: Spain
Phone: 91-3488000
Telefax: 91-3489494
Telex: 49840

Name: ÖMV - Chemie Linz GMBH
Street: St. Peterstrasse 25
Town: 4021 Linz
Country: Austria
Phone: *43/(0)732/5916-2386
Telefax: *43(0)732/5916-3738
Telex: 221324

1.0.2 Location of Production Site

-

1.0.3 Identity of Recipients

-

1.1 General Substance Information

Substance type: inorganic
Physical status: gaseous

Substance type: inorganic
Physical status: liquid

Substance type: organic
Physical status: liquid

Substance type:
Physical status: liquid

Substance type:
Physical status:

1.1.1 Spectra

-

1.2 Synonyms

Acido hidrociánico
Source: REPSOL QUIMICA, S.A. MADRID

Blausaeure
Source: Degussa Antwerpen N.V. Antwerpen 4
Degussa AG Frankfurt am Main

Blausäure
Source: Hoechst AG Frankfurt/Main
EC Erdölchemie GmbH Köln

Blausäure, Hydrocyanic acid, Cyanwasserstoff
Source: ÖMV - Chemie Linz GMBH Linz

Carbon hydride nitride (CHN)
Source: BASF AG Ludwigshafen
BASF plc Cheadle Cheshire

Cianuro de hidrógeno
Source: REPSOL QUIMICA, S.A. MADRID

Cyanwasserstoff
Source: Degussa Antwerpen N.V. Antwerpen 4
BASF AG Ludwigshafen
BASF plc Cheadle Cheshire
Hoechst AG Frankfurt/Main
Degussa AG Frankfurt am Main
EC Erdölchemie GmbH Köln

Evercyn
Source: BASF AG Ludwigshafen
BASF plc Cheadle Cheshire

Formic anammonide
Source: BASF AG Ludwigshafen
BASF plc Cheadle Cheshire

Formonitrile
Source: ACN Product Group Geleen
Degussa Antwerpen N.V. Antwerpen 4
BASF AG Ludwigshafen
BASF plc Cheadle Cheshire
Degussa AG Frankfurt am Main

formonitrile
Source: Imperial Chemical Industries PLC London

Formonitrilo
Source: REPSOL QUIMICA, S.A. MADRID

HCN
Source: ACN Product Group Geleen
Imperial Chemical Industries PLC London

Hydrocyanic acid
Source: ACN Product Group Geleen
Degussa Antwerpen N.V. Antwerpen 4
Degussa AG Frankfurt am Main

HYDROCYANIC ACID
Source: BP Chemicals Ltd. London

hydrocyanic acid
Source: Imperial Chemical Industries PLC London

Hydrocyanic acid (8CI, 9CI)
Source: BASF AG Ludwigshafen
BASF plc Cheadle Cheshire

Hydrogen cyanide
Source: BASF AG Ludwigshafen
BASF plc Cheadle Cheshire

Prussic acid
Source: Degussa Antwerpen N.V. Antwerpen 4
BASF AG Ludwigshafen
BASF plc Cheadle Cheshire
Degussa AG Frankfurt am Main

prussic acid
Source: Imperial Chemical Industries PLC London

prussic acid; hydrogen cyanide; acido cianidrico (Italian)
Source: Enichem S.p.A. Milan

Synonym a: Blausäure
Source: PCK AG Schwedt Schwedt/Oder

Synonym a: Cyanwasserstoff
Source: PCK AG Schwedt Schwedt/Oder

Synonym a: Evercyn
Source: PCK AG Schwedt Schwedt/Oder

1.3 Impurities

–

1.4 Additives

–

1.5 Quantity

Quantity 500 000 – 1 000 000 tonnes

1.6.1 Labelling

Labelling: as in Directive 67/548/EEC
Symbols: F+
T+
N
E
Specific limits: yes
R–Phrases: (12) Extremely flammable
(26) Very toxic by inhalation
(50/53) Very toxic to aquatic organisms, may cause long–term adverse effects in the aquatic environment
S–Phrases: (1/2) Keep locked up and out of reach of children
(7/9) Keep container tightly closed and in a well–ventilated place
(16) Keep away from sources of ignition – No smoking
(36/37) Wear suitable protective clothing and gloves
(38) In case of insufficient ventilation, wear suitable respiratory equipment
(45) In case of accident or if you feel unwell, seek medical advice immediately (show the label where possible)
(60) This material and/or its container must be disposed of as hazardous waste
(61) Avoid release to the environment. Refer to special instructions/Safety data sets

1.6.2 Classification

Classification: as in Directive 67/548/EEC
Class of danger: dangerous for the environment
R–Phrases: (50) Very toxic to aquatic organisms
(53) May cause long–term adverse effects in the aquatic environment

Classification: as in Directive 67/548/EEC
Class of danger: extremely flammable
R–Phrases: (12) Extremely flammable

Classification: as in Directive 67/548/EEC
Class of danger: very toxic
R–Phrases: (26) Very toxic by inhalation

1.7 Use Pattern

Type: type
Category: Non dispersive use

Type: type
Category: Use in closed system

Type: type
Category: Use resulting in inclusion into or onto matrix

Type: industrial
Category: Agricultural industry

Type: industrial
Category: Basic industry: basic chemicals

Type: industrial
Category: Chemical industry: used in synthesis

Type: industrial
Category:

Type: industrial
Category: other

Type: use
Category: Intermediates

Type: use
Category: Laboratory chemicals

Type: use
Category: Pesticides

Type: use
Category: other: organic and inorganic synthesis

1.7.1 Technology Production/Use

-

1.8 Occupational Exposure Limit Values

Type of limit: MAC (NL)
Limit value: 11 mg/m3
Short term expos.
Limit value: 5 mg/m3
Source: ACN Product Group Geleen

Type of limit: MAK (DE)
Limit value: 11 mg/m3
Short term expos.
Limit value: 22 mg/m3
Schedule: 30 minute(s)
Frequency: 4 times
Remark: H
Source: Degussa Antwerpen N.V. Antwerpen 4
Degussa AG Frankfurt am Main

(1)

Type of limit: MAK (DE)
Limit value: 10 ml/m3
Short term expos.
Limit value: 20 ml/m3
Schedule: 30 minute(s)
Frequency: 4 times
Remark: H
Source: Degussa Antwerpen N.V. Antwerpen 4
Degussa AG Frankfurt am Main

(1)

Type of limit: MAK (DE)
Limit value: 11 mg/m3
Short term expos.
Limit value: 22 mg/m3
Schedule: 30 minute(s)
Frequency: 4 times
Source: Atochem Paris la Defense

(2)

Type of limit: MAK (DE)
Limit value: 11 mg/m3
Source: ÖMV - Chemie Linz GMBH Linz

Type of limit: MAK (DE)
Limit value: 10 mg/m3
Short term expos.
Limit value: 20 mg/m3
Schedule: 30 minute(s)
Frequency: 4 times
Remark: Skin notation
Source: Imperial Chemical Industries PLC London

Type of limit: MAK (DE)
Limit value: 10 ml/m3
Short term expos.
Limit value: 20 ml/m3
Schedule: 30 minute(s)
Frequency: 4 times
Source: BASF AG Ludwigshafen
BASF plc Cheadle Cheshire

(3)

Type of limit: MAK (DE)
Limit value: 11 mg/m3
Remark: hautresorptiv
Source: BASF AG Ludwigshafen
BASF plc Cheadle Cheshire

(3)

Type of limit: MAK (DE)
Limit value: 10 ml/m3
Short term expos.
Limit value: 20 ml/m3
Schedule: 30 minute(s)
Frequency: 4 times
Source: BASF AG Ludwigshafen
BASF plc Cheadle Cheshire

(3)

Type of limit: MAK (DE)
Limit value: 11 mg/m3
Remark: hautresorptiv
Source: BASF AG Ludwigshafen
BASF plc Cheadle Cheshire

(3)

Type of limit: MAK (DE)
Limit value: 10 ml/m3
Short term expos.
Limit value: 20 ml/m3
Schedule: 30 minute(s)
Frequency: 4 times
Source: BASF AG Ludwigshafen

(3)

Type of limit: MAK (DE)
Limit value: 11 mg/m3
Remark: hautresorptiv
Source: BASF AG Ludwigshafen

(3)

Type of limit: MAK (DE)
Limit value: 10 ml/m3
Short term expos.
Limit value: 20 ml/m3
Schedule: 30 minute(s)
Frequency: 4 times
Source: BASF AG Ludwigshafen

(3)

Type of limit: MAK (DE)
Limit value: 11 mg/m3
Remark: hautresorptiv
Source: BASF AG Ludwigshafen

(3)

Type of limit: MAK (DE)
Limit value: 11 mg/m3
Short term expos.
Limit value: 22 mg/m3
Schedule: 30 minute(s)
Frequency: 4 times
Source: Hoechst AG Frankfurt/Main

(4) (5)

Type of limit: MAK (DE)
Limit value: 10 ml/m3
Short term expos.
Limit value: 20 ml/m3
Schedule: 30 minute(s)
Frequency: 4 times
Remark: Stoff der Kategorie II,1: Resorptiv wirksamer Stoff, Wirkungseintritt innerhalb von 2 h, Halbwertszeit (Zeitdauer < 2h).
Source: PCK AG Schwedt Schwedt/Oder

(6)

Type of limit: MAK (DE)
Limit value: 10 ml/m3
Remark: Spitzenbegrenzung Kategorie II,1
H = Gefahr der Hautresorption
Source: EC Erdölchemie GmbH Köln

(7)

Type of limit: MEL (UK)
Limit value:
Short term expos.
Limit value: 10 ml/m3
Remark: No 8 hour TWA allocated. MEL carries a skin annotation.
Source: BP Chemicals Ltd. London

Type of limit: MEL (UK)
Limit value: 10 mg/m3
Schedule: 10 minute(s)
Remark: Skin notation
Source: Imperial Chemical Industries PLC London

Type of limit: TLV (US)
Limit value: 11 mg/m3
Remark: Ceiling value
Source: Degussa Antwerpen N.V. Antwerpen 4

Type of limit: TLV (US)
Limit value: 11 mg/m3
Source: Atochem Paris la Defense

(2)

Type of limit: TLV (US)
Limit value: 11 mg/m3
Source: REPSOL QUIMICA, S.A. MADRID

Type of limit: TLV (US)
Limit value: 11 mg/m3
Remark: Notation:skin
Threshold Limit Value-Celling (TLV-C):The concentration that should not be exceeded during any part of the working exposure
Source: Enichem S.p.A. Milan

(8)

Type of limit: TLV (US)
Limit value: 5 mg/m3
Remark: Notation:skin
Threshold Limit Value-Celling (TLV-C):The concentration that shold not be exceeded during any part of the working exposure
Notice of Intended Changes (1993-1994).
Source: Enichem S.p.A. Milan

(8)

Type of limit: TLV (US)
Limit value: 5 mg/m3
Source: ELF ATOCHEM ITALIA S.r.l. PORTO MARGHERA (VE)

Type of limit: TLV (US)
Limit value: 5 mg/m3
Schedule: 15 minute(s)
Remark: Skin notation
Source: Imperial Chemical Industries PLC London

Type of limit: other: MAC (Denmark)
Limit value: 5 mg/m3
Schedule: 8 hour(s)
Remark: Skin notation
Source: Imperial Chemical Industries PLC London

Type of limit: other: MAC (Finland)
Limit value: 11 mg/m3
Remark: Skin notation
Source: Imperial Chemical Industries PLC London

Type of limit: other: MAC (France)
Limit value: 2 mg/m3
Short term expos.
Limit value: 10 mg/m3
Schedule: 15 minute(s)
Source: Imperial Chemical Industries PLC London

Type of limit: other: MAK (Austria)
Limit value: 10 mg/m3
Schedule: 8 hour(s)
Remark: Skin notation
Source: Imperial Chemical Industries PLC London

Type of limit: other: PEL(OSHA): Permitted Exposure Level
Limit value: 10 ml/m3
Short term expos.
Limit value: 4.7 ml/m3
Remark: OSHA: Occupational Safety Health Administration
Source: REPSOL QUIMICA, S.A. MADRID

(9)

Type of limit: other: VME
Limit value: 2 mg/m3
Short term expos.
Limit value: 10 mg/m3
Schedule: 15 minute(s)
Frequency: 4 times
Country: France
Source: Atochem Paris la Defense

(10)

1.9 Source of Exposure

Remark: The HCN process is a closed process. There is no loading and shipping of the product. Exposure only possible by leaking of the system.
Source: ACN Product Group Geleen

Remark: see data set on sodium cyanide (CAS-no. 143-33-9) and potassium cyanide (CAS-no. 151-50-8).
Source: Degussa Antwerpen N.V. Antwerpen 4

Remark: Process "Andrussov" : CH4 + NH3 with Pt as catalyst.
Events : incinerator.
Waste waters : decyanuration - Biological treatment plant.
Gas treatments : neutralisation of the excess of NH3 with sulfuric acid. Formation of amonium sulfate. This chemical is retreated to form pure sulfates and oleum (94 %).
One production site with ambient HCN detectors. If problems occur, waste gas go to air.
Source: Atochem Paris la Defense

Remark: CONTROL DE EXPOSICION : Usar equipo eléctrico antideflagrante. Se recomienda ventilación.
Se recomienda extracción local de aire.
Source: REPSOL QUIMICA, S.A. MADRID

Remark: Manufacture
==========

HCN is manufactured in major hazard registered plants. HCN is manufactured from ammonia and natural gas. In the UK, both raw materials are received by pipeline from other locations on the same manufacturing site. Any release of HCN from the manufacturing plant is destroyed either in a two stage process involving sodium hydroxide and sodium hypochlorite or by burning.

Containment of HCN
==========

Manufacture of HCN in the UK is typical of general practice. All operations handling liquid HCN or its concentrated solutions are located within enclosed ventilated cubicles.

Cubicles are steel formed, panel clad structures designed to confine any conceivable spillages or leaks. Any vapour discharge inside the cubicle is extracted by means of a fan via a stack.

Vent Headers
==========

A series of enclosed vent headers collects and directs to the Flarestack final uncondensed vents from reacter vessels, outbreathings and intermediate vessels. The Flarestack is fuelled with natural gas and is continuously lit, except for brief periods during start up of the HCN plant when there may be a flammable gas mixture in the plant. A flame failure device is fitted to the Flarestack which sounds an alarm in the Control Room on flame failure.

The Cubicle Vent Fan has sufficient capacity that even with the maximum number of doors and windows which could reasonably be envisaged to be open simultaneously, face velocities would not fall below these values recommended by safety guidelines. The Cubicle Vent Stack is continuously monitored for HCN.

The floor underneath the cubicalised plant is concreted and bunded. The floor is sloped so that spillages are directed to a small sump within the cubicle. Liquid collecting here is samples before being pumped for HCN Toxic Effluent Treatment or other disposal, depending upon the liquid's contents.

Doors into the Cubicle are normally kept shut and locked and access is controlled by a permit to enter procedure.

Handling HCN outside cubicles
==========

HCN in gas or weak liquid form is fully contained in welded pipe systems.

Maintenance
==========

A series of enclosed pipework systems is used to drain down and decontaminate process vessels. Cyanide waste is either recycled or burned in a high efficiency incinerator.

Source: Imperial Chemical Industries PLC London

(11)

Remark: see data set on sodium cyanide (CAS-No. 143-33-9) and potassium cyanide (CAS-No. 151-50-8).
Source: Degussa AG Frankfurt am Main

Remark: Der in der Feinreinigung der Acrylnitrilanlage entstehende Cyanwasserstoff wurde bis zum 31.12.1993 zu einem geringen Anteil (8-48t)isoliert, mit Stabilisator (Essigsäure 1,2%) und mit einem Warnstoff (Bromessigsäuremethylester 0,3 %) versetzt, konfektioniert und als Schädlingsbekämfungsmittel über einen Großabnehmer in den Verkehr gebracht. Diese Art der Produktion wurde zum 01.01.1994 eingestellt.
Ein Teil des Cyanwasserstoffs wird in der Thermischen Abgasreinigungsanlage verbrannt. Die Technische Abgasreinigungsanlage ist so ausgelegt, daß der Grenzwert nach TA Luft von 5 mg/m³ unterschritten wird.
Source: PCK AG Schwedt Schwedt/Oder

1.10.1 Recommendations/Precautionary Measures

-

1.10.2 Emergency Measures

-

1.11 Packaging

-

1.12 Possib. of Rendering Subst. Harmless

-

1.13 Statements Concerning Waste

-

1.14.1 Water Pollution

Classified by: KBwS (DE)
Labelled by: KBwS (DE)
Class of danger: 3 (strongly water polluting)
Remark: no legislation in Belgium
Source: Degussa Antwerpen N.V. Antwerpen 4

(12)

Classified by: KBwS (DE)
Labelled by: KBwS (DE)
Class of danger: 3 (strongly water polluting)
Source: BASF AG Ludwigshafen
BASF plc Cheadle Cheshire

Classified by: KBwS (DE)
Labelled by: KBwS (DE)
Class of danger: 3 (strongly water polluting)
Source: BASF AG Ludwigshafen
BASF plc Cheadle Cheshire

Classified by: KBwS (DE)
Labelled by: KBwS (DE)
Class of danger: 3 (strongly water polluting)
Source: BASF AG Ludwigshafen

Classified by: KBwS (DE)
Labelled by: KBwS (DE)
Class of danger: 3 (strongly water polluting)
Source: BASF AG Ludwigshafen

Classified by: KBwS (DE)
Labelled by: KBwS (DE)
Class of danger: 3 (strongly water polluting)
Source: Degussa AG Frankfurt am Main

(12)

Classified by: other: Deg
Labelled by:
Class of danger: 3 (strongly water polluting)
Source: Imperial Chemical Industries PLC London

Classified by: other: Wassergefährdungsklasse
Labelled by:
Class of danger: 3 (strongly water polluting)
Source: Hoechst AG Frankfurt/Main

(4)

1.14.2 Major Accident Hazards

Legislation: Stoerfallverordnung (DE)
Substance listed: yes
Remark: Stoerfall-Stoff-Nr. 93
Source: BASF AG Ludwigshafen
BASF plc Cheadle Cheshire

(13)

Legislation: Stoerfallverordnung (DE)
Substance listed: yes
Source: Hoechst AG Frankfurt/Main

(4) (14)

Legislation: Stoerfallverordnung (DE)
Substance listed: yes
Source: Degussa AG Frankfurt am Main

(15)

Legislation: other
Substance listed:
Remark: As a major hazard listed chemical emergency systems are in place for the manufacture, use and transportation of HCN. Emergency systems present in the UK are typical of general practice.

Emergency Systems
==========

HCN Ambulance Alarm Systems

All locations on the site where cyanides are handled are linked with the site gatehouse, Medical Centre and Fire Service Control room by a manually operated HCN Ambulance Alarm system.

The ambulance alarm system is a call for medical help in dealing with a person affected or suspected of being affected by 'cyanide' poisoning, ie. HCN gassing. salt absorption or poisoning.

Manufacturing Site Toxic Alarm System (Inclusing Toxic Refuges)

There is a system, operated over the whole of the site whereby a siren warns people on the site to take refuge in designated buildings. The system is activated on intelligence received by the site controller from local operating teams on each plant.

There are two toxic refuges; one is a dedicated building and the other is the Control Building.

Local Toxic Alarm System

Surrounding the cyanide plants is a ring of 12 HCN detectors, mounted in the open air at about 1.5m above ground level. The detectors are judiciously positioned so that, depending upon the wind direction, one or another of them is likely to detect HCN as early as possible after a relase of HCN into the atmosphere.

The response to hearing the Local Toxic alarm by people on the plant is to leave the site area and report to an assembly point, that is, either of the toxic refuges.

Fire Alarm System

There is a fire alarm system activated by a number of switches around the plant areas, switch rooms and inside the control room. On activating the system an alarm sounds in the plant area, inside the control room and in the site fire station. Written procedures will tell the operators and visitors what to do when the alarm sounds.

Expert Advice and Assistance

There is a system operating 24 hours a day 365 days a year to provide expert technical backup and attendance at the scene for any incident involving HCN.

Transporation Hazards

Small quantities of HCN are moved by rail. Formal risk assessments have been carried out and operational audits are conducted annually. HCN is moved over short distances (< 10 miles) in specially designed rail tanks at low speeds through lightly populated areas. No other trains are moving in the line at the same tome. Loading and unloading is conducted in enclosed cubicles. (see section 1.9).

Source: Imperial Chemical Industries PLC London

(11)

Legislation: other: legislation dd. 21.01.87
Substance listed: yes
Remark: annex II, part I, no. 13
Source: Degussa Antwerpen N.V. Antwerpen 4

1.14.3 Air Pollution

Classified by: TA-Luft (DE)
Labelled by: TA-Luft (DE)
Number: 3.1.6 (gaseous inorganic substances)
Class of danger: II
Source: BASF AG Ludwigshafen
BASF plc Cheadle Cheshire

Classified by: TA-Luft (DE)
Labelled by: TA-Luft (DE)
Number: 3.1.6 (gaseous inorganic substances)
Class of danger: II
Source: Degussa AG Frankfurt am Main

(16)

Classified by: other: VLAREM II (Flandern – Belgium) Art. 81, Paragraph 1, no. 3 of the list
Labelled by:
Number:
Class of danger:
Source: Degussa Antwerpen N.V. Antwerpen 4

Classified by:
Labelled by:
Number: 3.1.6 (gaseous inorganic substances)
Class of danger: II
Source: Hoechst AG Frankfurt/Main

(4)

1.15 Additional Remarks

Remark: Captive use inside ACN PG with a small storage capacity.
Source: ACN Product Group Geleen

Remark: Distribution:
Media : air-biota-sediment-soil-water
Method: calculation according to Mackay, level I (1981)
Result: Hydrogen cyanide (%) in different compartments:

Air	10.27 - 10.29 %
Water	89.57 - 89.68 %
Soil	0.08 - 0.02 %
Sediment	0.08 - 0.01 %
Suspended matter, aquatic	0.00 %
Biota	0.00 %

Source: Degussa Antwerpen N.V. Antwerpen 4

(17)

Remark: ELIMINACION : Retírense todas las fuentes de ignición. Ventilar el área. Detener los derrames de líquido con arena, tierra, poliuretano u hormigón espumado. Absorber el vertido espolvoreando cenizas o cemento en polvo. Si el derrame es sobre agua, neutralizar con CaO, caliza (CaCO2) o bicarbonato sódico (NaHCO3). Aplíquese agua pulverizada a los vapores de ácido cianhídrico y posteriormente recójanse en contenedores cerrados (el producto es corrosivo).

MANIPULACION : Usese protección adecuada (aparato respiratorio autónomo, máscara de gas, indumentaria y guantes de neopreno, botas y guantes con revestimiento de PVC, protector facial). Consérvese alejado de fuentes de ignición, de luz y de agua. No fumar. No respirar los vapores. Comprobar todas las válvulas antes y después de retirar el ácido cianhídrico de las botellas. Nunca retener ácido cianhídrico entre dos válvulas.

MEDIDAS HIGIENICAS : No comer ni almacenar comida en el área de trabajo. Se recomienda ducharse y cambiarse de ropa después de trabajar con el ácido cianhídrico. La ropa utilizada debe de ser manipulada evitando el contacto directo personal. Utilice buenas medidas internas de orden y limpieza.

ALMACENAMIENTO : Mantener las botellas de ácido cianhídrico alejadas del calor y las llamas. Almacenarlas verticalmente sobre el suelo, bien sujetas y adecuadamente inhibidas. Vida de conservación limitada. Consérvese lejos de otros productos. Almacenarlas en cabinas estándar para líquidos inflamables.

MATERIALES DE EMBALAJE APROPIADOS : Consérvese

en envases de acero inoxidable.

TRANSPORTE :
Nº ONU : 1613
Tierra–Carretera/Ferrocarril :
Clase ADR/RID : 6.1
Nº de Item ADR/RID : 2
Nº de Identificación de Peligros : 663
Vías de Navegación Interior :
Clase ADNR : IVa
Mar :
Clase IMDG : 6.1 (I)
Nº de Pág. IMDG : 6162
Aire :
Clase IATA–DGR : 6.1
Normativa Nacional de Transporte :
Coincidente con la normativa internacional de transporte anteriormente citada.

Source: REPSOL QUIMICA, S.A. MADRID

Remark: Anlage wurde mit 31.03.1991 stillgelegt und abgebaut.
Source: ÖMV – Chemie Linz GMBH Linz

Remark: Distribution:
Media : air–biota–sediment–soil–water
Method: calculation according to Mackay, level I (1981)
Result: Hydrogen cyanide (%) in different compartments:

Air	10.27 – 10.29 %
Water	89.57 – 89.68 %
Soil	0.08 – 0.02 %
Sediment	0.08 – 0.01 %
Suspended matter, aquatic	0.00 %
Biota	0.00 %

Source: Degussa AG Frankfurt am Main

(17)

Remark: Der Transport der Blausäure innerhalb des Betriebes erfolgt über Rohrleitungssysteme. Das Inverkehrbringen der Blausäure erfolgte bis 1994 über zugelassenePackmittel nach Gefahrgutrecht.
Source: PCK AG Schwedt Schwedt/Oder

1.16 Last Literature Search

–

1.17 Reviews

–

1.18 Listings e.g. Chemical Inventories

–

2.1 Melting Point

Value: = -15 degree C
Method: other
Year: 1954
GLP: no data
Source: REPSOL QUIMICA, S.A. MADRID
(18)

Value: = -13.4 degree C
Decomposition: yes
Method: other
GLP: no data
Source: Imperial Chemical Industries PLC London
(19)

Value: = -13.3 degree C
Decomposition: yes
Method: other
GLP: no data
Source: Imperial Chemical Industries PLC London
(20)

Value: -13.3 degree C
Method: other
Source: Imperial Chemical Industries PLC London
(21) (22)

Value: = -13.3 degree C
Source: BASF AG Ludwigshafen
(23)

Value: = -13.2 degree C
Decomposition: ambiguous
Sublimation: ambiguous
Method: other
GLP: no data
Source: Imperial Chemical Industries PLC London
(24) (25)

2.2 Boiling Point

Value: = 25.6 degree C
Source: Imperial Chemical Industries PLC London
(26) (20) (19)

Value: = 25.7 degree C
Source: Imperial Chemical Industries PLC London
(27) (24)

Value: = 25.7 degree C at 1013 hPa
Decomposition: no
Source: BASF AG Ludwigshafen
(23)

Value: 40 – 100 degree C at 1013 hPa
Method: other
GLP: yes
Source: REPSOL QUIMICA, S.A. MADRID
(28)

Value: 25.7 degree C at 1013 hPa
Decomposition: no
Source: Imperial Chemical Industries PLC London
(22)

Value:
Source: Imperial Chemical Industries PLC London

2.3 Density

Type: density
Value: = .9782 g/cm3 at 0 degree C
Method: other
Year: 1961
GLP: no data
Source: REPSOL QUIMICA, S.A. MADRID
(29)

Type: density
Value: = .687 – .688 g/cm3 at 20 degree C
Method: other
GLP: no data
Source: Imperial Chemical Industries PLC London
(27) (24)

Type:
Value: = .687 g/cm3 at 20 degree C
Source: BASF AG Ludwigshafen
(23)

Type: density
Value: .687 g/cm3 at 20 degree C
Source: Imperial Chemical Industries PLC London
(22)

2.3.1 Granulometry

–

2.4 Vapour Pressure

Value: = 474.219 hPa at 18 degree C
Method: other (calculated)
Year: 1959
GLP: no data
Source: REPSOL QUIMICA, S.A. MADRID
(30)

Value: = 83 hPa at 20 degree C
Source: Imperial Chemical Industries PLC London
(27) (24)

Value: = 830 hPa at 20 degree C
Source: BASF AG Ludwigshafen
(23)

Value: = 120 hPa at 30 degree C
Source: Imperial Chemical Industries PLC London
(27) (24)

Value: = 250 hPa at 50 degree C
Source: Imperial Chemical Industries PLC London
(27) (24)

Value:
Remark: The vapour pressure of HCN above liquid HCN has been measured at a range of temperatures between -40 and +60 deg C.

Temp Deg C	Vapour Pressure HCN hPa
-40	4.2
-30	7.6
-20	13.2
-10	22.0
0	35.3
10	54.5
20	81.6
30	118.9
40	168.9
50	234.7
60	319.7

Source: Imperial Chemical Industries PLC London
(31)

2.5 Partition Coefficient

log Pow: ca. .35 - 1.07
Method: other (calculated)
Year:
Remark: no more information available
Source: Imperial Chemical Industries PLC London
(20)

log Pow:
Method:
Year:
Remark: nicht anwendbar
Source: BASF AG Ludwigshafen
(32)

2.6.1 Water Solubility

Qualitative: soluble
Source: REPSOL QUIMICA, S.A. MADRID

Qualitative: miscible
Source: Imperial Chemical Industries PLC London
(33) (19)

Qualitative: miscible
pH: < 4 at 90 vol% and 20 degree C
Source: Imperial Chemical Industries PLC London
(34)

Qualitative: miscible
pH: < 4 and 20 degree C
Remark: pH < 4 gilt fuer 90 %ige Loesung
Source: BASF AG Ludwigshafen
(34)

2.6.2 Surface Tension

-

2.7 Flash Point

Value: < -20 degree C
Type:
Method:
Year:
Source: Imperial Chemical Industries PLC London
(27) (22)

Value: = -20 degree C
Type:
Method:
Year:
Source: BASF AG Ludwigshafen
(23)

Value: -18.5 degree C
Type: closed cup
Method:
Year:
Source: Imperial Chemical Industries PLC London
(35)

Value: -17.8 degree C
Type: closed cup
Method:
Year:
Source: Imperial Chemical Industries PLC London
(21)

Value:
Type:
Method:
Year:
Remark: Punto ignición (HCN puro): -17.78 grados centígrados (copela cerrada)
Source: REPSOL QUIMICA, S.A. MADRID
(36)

2.8 Auto Flammability

Value: = 535 - 537 degree C
Source: Imperial Chemical Industries PLC London
(27) (33)

Value: = 535 degree C
Source: BASF AG Ludwigshafen
(23)

Value: = 538 degree C at 1013 hPa
Method: other
Year: 1986
GLP: no data
Source: REPSOL QUIMICA, S.A. MADRID
(37)

Value: = 538 degree C
Source: Imperial Chemical Industries PLC London
(21)

Value: 535 degree C
Source: Imperial Chemical Industries PLC London
(22)

2.9 Flammability

Result: flammable
Source: Imperial Chemical Industries PLC London
(38)

Result: non flammable
Remark: Límite de inflamabilidad superior: 41% (HCN puro)
Límite de inflamabilidad inferior: 6% (HCN puro)
Source: REPSOL QUIMICA, S.A. MADRID
(36)

Result:
Remark: flammable
Source: BASF AG Ludwigshafen
(39)

2.10 Explosive Properties

Result: explosive under influence of a flame
Remark: Lower explosive limit (LEL) 5.5% v/v
Upper explosive limit (UEL) 40% v/v.
Source: Imperial Chemical Industries PLC London
(22)

Result: other
Remark: Límite de explosión inferior: 5.6% (HCN puro)
Límite de explosión superior: 40% (HCN puro)
Source: REPSOL QUIMICA, S.A. MADRID
(40)

Result:
Remark: Lower explosive limit (LEL) 6% v/v (20 deg C)
Upper explosive limit (UEL) 41% v/v (20 deg C)
Source: Imperial Chemical Industries PLC London
(31)

Result:
Remark: Explosionsgrenzen in Luft: 5,5 – 40 Vol. %
Source: BASF AG Ludwigshafen
(23)

2.11 Oxidizing Properties

Result: no oxidizing properties
Source: Imperial Chemical Industries PLC London
(38)

Result:
Remark: no oxidizing properties
Source: BASF AG Ludwigshafen
(39)

2.12 Additional Remarks

Remark: ESTABILIDAD : Es estable a temperatura ambiente y por debajo de ésta temperatura si está estabilizado con ácido ácido sulfúrico (0.1%) o ácido fosfórico (0.05).
MATERIALES A EVITAR : Consérvese lejos de agentes oxidantes, aminas y disoluciones básicas. Reacciona violentamente con acetaldehido.
PRODUCTOS TOXICOS DE DESCOMPOSICION : Humos tóxicos de ácido cianhídrico.
POLIMERIZACION PELIGROSA : Cuando no está estabilizado o a temperatura > 40 grados C polimeriza espontáneamente acompañado de una explosión violenta. También puede polimerizar en contacto con materiales alcalinos.
MEDIOS DE EXTINCION APROPIADOS : Polvo químico seco, espuma de alcohol. Manténgase el recipiente frío rociándolo con agua fría.
Source: REPSOL QUIMICA, S.A. MADRID

Remark: Viscosity: 0,192 mPa x s at 20 degree C.
Source: Imperial Chemical Industries PLC London
(24)

Remark: Triple point: –13.32 deg C
Source: Imperial Chemical Industries PLC London
(21)

Remark: Liquid density (P) = 715.9 – 1.457 T where density is in kg/m3 and T = temp in deg C.
Source: Imperial Chemical Industries PLC London
(31)

Remark: Vapour density: 0.947 @ 31 deg C
Source: Imperial Chemical Industries PLC London
(31)

Remark: Dissociation constant = 4.37 x 10–10 mol/m3 at 20 deg C. Pka = 9.36
Source: Imperial Chemical Industries PLC London
(35)

3.1.1 Photodegradation

Type: air
Light source: Sun light
INDIRECT PHOTOLYSIS
Sensitizer: OH
Conc. of sens.: 800000 molecule/cm3
Rate constant: = .00000000000003 cm3/(molecule * sec)
Degradation: = 50 % after 334 day
Method: other (calculated)
Year: 1988 **GLP:** no data
Test substance: no data
Remark: La reacción de HCN con radicales hidroxilo generados fotoquímicamente es muy lenta. La vida media del vapor de ácido cianhídrico en la atmósfera al reaccionar con los radicales hidroxilo es aproximadamente 334 días. El ácido cianhídrico es resistente a la fotólisis directa. Su relativamente bajo porcentaje de degradación también contribuye a que pueda ser transportado extensivamente antes de ser eliminado por procesos químico o físico. Dado que el HCN es soluble en agua, parece que la deposición húmeda (lluvia) será un importante proceso de eliminación de la atmósfera. Las partículas de cianuros metálicos se eliminarán del aire por procesos de deposición húmeda y seca.
Source: REPSOL QUIMICA, S.A. MADRID

(41)

Type: air
Light source: other
Light spect.: = 193 – 248 nm
Conc. of subst.: at 21.9 degree C
DIRECT PHOTOLYSIS
Halflife t1/2: = .5 year
INDIRECT PHOTOLYSIS
Rate constant: = .00000000000003 cm3/(molecule * sec)
Method: other (measured): laser photolysis/resonance fluorescence (LPRF)
Year: **GLP:** no data
Test substance: other TS
Source: Imperial Chemical Industries PLC London
Test condition: Initial OH–concentration: 1 x 10E12 molecules/cmE3; HNO3 used as OH–precursor

(42)

3.1.2 Stability in Water

Type:
Method:
Year: **GLP:**
Test substance:
Remark: El ácido cianhídrico es muy soluble. Vertido al medioambiente se volatiliza en parte y el resto se biodegrada.
Durante la cloración de aguas potables para consumo de las ciudades, se convierte en cianato. Los pH alcalinos favorecen la oxidación por el cloro, mientras un pH ácido favorece la volatilización del HCN a la atmósfera.
Source: REPSOL QUIMICA, S.A. MADRID

(43)

Type:
Method:
Year: **GLP:**
Test substance:
Remark: At low concentrations (less that 0.1 mol/dm3) HCN is stable. Addition of traces of acid prevent decomposition. In alkali solution exothermic polymerisation occurs.
Source: Imperial Chemical Industries PLC London

(35)

Type:
Method:
Year: **GLP:**
Test substance:
Remark: Hydrogen cyanide undergoes abiotic degradation by the following routes:

HCN + 1/2 O2 –> HCNO + H20 –> CO2 + NH3
HCN + S –> HCNS –> HSCONH2 –> COS + NH3
–> 2COS + 302 –> 2CO2 + SO2
HCN + 2H2O –> NH4COOH + 1/2 02 –> NH3 CO2 + H20

Source: Imperial Chemical Industries PLC London

(44)

Type:
Method:
Year: **GLP:**
Test substance:
Remark: Volatilization is expected to be an important (if not dominant) elimination process in water for hydrogen cyanide and also for cyanide salts mainly at pH–values less than 9.2. The volatilization is affected by a number of parameters including temperature, pH, wind speed, and cyanide concentration. Therefore wide variations in the rate of volatilization are expected. Because of the lack of data on this topic, the half–life for this process can not be estimated.
Source: Imperial Chemical Industries PLC London

(45) (46)

3.1.3 Stability in Soil

Type: **Radiolabel:**
Concentration:
Cation exch. capac.
Microbial biomass:
Method:
Year: **GLP:**
Test substance:
Remark: Similarmente a lo que sucede en el agua, el destino del HCN en el suelo será igualmente dependiente del pH. El cianuro puede estar en forma de cianúro de hidrógeno, sales de metales alcalinos o complejos inmóviles metalocianurosos. En suelos con pH < 9.2, probablemente el cianuro de hidrógeno es bastante móvil. En el subsuelo y a concentraciones muy bajas probablemente llega a biodegradarse.
Adsorción en el suelo: La movilidad del cianhídrico en suelos de bajo pH, alta concentración de óxidos de hierro libre y partículas cargadas. La movilidad es más alta a pH más altos y alta concentración de carbonato de calcio libre y bajo contenido en arcillas.
Source: REPSOL QUIMICA, S.A. MADRID

(47)

Type: **Radiolabel:**
Concentration:
Cation exch. capac.
Microbial biomass:
Method:
Year: **GLP:**
Test substance:
Remark: Some parameters influence the elimination process or cyanides in soil. Increase in temperature and decrease in soil pH will enhance volatilization of cyanide. In dependence on alumina and organic matter content of the soil, the soil sorption/reaction of cyanides will increase. However, Callahan et al (1979) reported that cyanides may be presumed not adsorb significantly to suspended solids and sediments.
Source: Imperial Chemical Industries PLC London

(45) (46)

Type: **Radiolabel:**
Concentration:
Cation exch. capac.
Microbial biomass:
Method:
Year: **GLP:**
Test substance:
Remark: At soil surfaces with pH < 9.2, volatilization of hydrogen cyanide is expected to be a possible loss mechanism for cyanides. In subsurface soil, cyanide present at low concentrations would probably biodegrade. In cases where levels of cyanide are toxic to microorganisms (ie. landfills, spills) hydrogen cyanide may leach into ground water.
Source: Imperial Chemical Industries PLC London

(46)

3.2 Monitoring Data (Environment)

Type of measurement: background concentration
Medium: other: rios (US)
Remark: Un estudio realizado en ríos de US durante todo un año, reveló una concentración de hasta 30–60 ug/l en algunos casos.
Source: REPSOL QUIMICA, S.A. MADRID

(48)

Type of measurement: background concentration
Medium: other
Remark: Las fuentes mayoritarias de vertido al medioambiente son las industrias de terminado de metales e industrias químicas. La fuente más importante de vertido al aire es el humo de los coches, y al suelo son los residuos de cianhídrico depositados en vertederos.
Source: REPSOL QUIMICA, S.A. MADRID

(49)

3.3.1 Transport between Environmental Compartments

Type: adsorption
Media: water – soil
Method:
Year:
Remark: El ácido cianhídrico no se adsorbe en grandes cantidades en el suelo debido a su alta solubilidad en el agua.Si hay transporte, el suelo debe tener un pH alto, alta concentración de carbonato cálcico libre (alta carga negativa) y bajo contenido en arcilla.
Source: REPSOL QUIMICA, S.A. MADRID

(50)

Type: volatility
Media: water – soil
Method:
Year:
Remark: La volatilización del ácido cianhídrico es un proceso importante (si no el dominante). A pH <9.2 la mayoría del cianuro estará en la forma de cianuro de hidrógeno, que es volatil. La velocidad de volatilización de este último varía con parámetros tales como la temperatura, pH, velocidad del viento, concentración etc, y dado que no existen datos sobre este tema la vida media para este proceso no ha podido determinarse.
Source: REPSOL QUIMICA, S.A. MADRID

(51)

Type:
Media:
Method: other
Year:
Remark: Data from the study of acetone cyanohydrin (approx 1 mg/L) fate in open systems, eg. in Daugava River water, indicates that decompounded HCN (from the dissociation of ACH to acetone and HCN) will evaporate. The evaporation rate increases with the rise of temperature; decrease of depth; increase in wind rate, water surface area, and intensity of mixing.

9 per cent of the substance was aerated from water in 4 hours.
Source: Imperial Chemical Industries PLC London

(52) (53)

Type:
Media:
Method: other
Year:
Remark: HCN will evaporate from the surface of concentrated solution of HCN in water. The HCN content of vapours (expressed as a percentage of a saturated vapour) above HCN/water mixtures was measured in a static (closed) system. Temperature was not indicated.

% HCN in water	HCN Vapour Level (% of a saturated vapour level)
0	0
2.5	20
5	34
20	76
40	92
60	97
80	99
100	100

Source: Imperial Chemical Industries PLC London

(35)

Type:
Media:
Method: other
Year:
Remark: Hydrogen cyanide
Source: Imperial Chemical Industries PLC London

3.3.2 Distribution

Media: air – biota – sediment(s) – soil – water
Method: Calculation according Mackay, Level I
Year:
Remark: Test Condition:–

Molecular weight 27.0 g/mol
Aqueous solubility 6.880E+05 g/m3 or 2.545E+04 mol/m3
Vapour pressure 8.300E+03 pa or 8.191E–02 atm or 6.226E+01 mm hg
Henry's constant 3.2609E–01 pa m3/mol
Octanol–water part coeff (log) 0.35 or 2. part coeff
Temperature 20.0 deg C or 293.2 K

Level 1

compartment	volume m3	percent
1 air	6.0000E+09	10.29
2 water	7.0000E+06	89.68
3 soil	4.5000E+04	0.02
4 sediment	2.1000E+04	0.01
5 susp aquat mat	3.5000E+01	0.00
6 biota	7.0000E+00	0.00
		100.00

Fugacity 4.178E–06 Pa

Use of octanol–water partition coefficient 1.07 has little effect on the distribution according to Mackay, Level 1. Percent air, water, soil, sediment, susp. aquat. mat. and biota are 10.29, 89.68, 0.02, 0.01, 10, 0 resp.
Source: Imperial Chemical Industries PLC London
(54)

Media:
Method:
Year:
Source: REPSOL QUIMICA, S.A. MADRID

3.4 Mode of Degradation in Actual Use

Remark: El ácido cianhídrico puede ser producido de forma natural por microorganismos así como de la degradación de los glicósidos.
Muchos organismos fotosintéticos , entre ellos las algas verde-azuladas, pueden producir cianhídrico en sus procesos de metabolismo del nitrito.
Diversas plantas sintetizan cianoglucósidos que pueden descomponerse en HCN.
El ácido cianhídrico se utiliza como producto intermedio en la síntesis de metacrilatos, polímeros, resinas, sales cianhídricas, tintes, pesticidas y rodenticidas. También se usa en la industria metalúrgica y fotogáfica. En estos procesos se pueden liberar al medioambiente emisiones fugitivas.
Vertido al medioambiente, se volatiliza en gran medida siendo el resto biodegradado por los microorganismos de suelo y agua. En la atmósfera se degrada fundamentalmente por fotólisis indirecta, gracias a la acción de radicales hidroxilos.
Source: REPSOL QUIMICA, S.A. MADRID

(48)

Remark: Options for disposal of waste material
==========

The standard method of disposal of waste HCN is conversion into soluble cyanide salts by the action of alkali, followed by conversion of salts into the relatively non-toxic cyanates by the action of sodium hypochlorite at a pH of greater than 11. The cyanate subsequently decomposes slowly to carbon dioxide and nitrogen in the presence of the hypochlorite. The detoxified waste is subsequently de-chlorinated with sodium thiosulphate or suphur dioxide before running to drain.
Source: Imperial Chemical Industries PLC London

(55)

Remark: Sewage Treatment
==========

HCN in chemical drain waters is biodegraded in water treatment plants before discharge.

Nitrification of formed ammonia occurs at concentrations up to 60 mg/L (as CN-) above which it is inhibited. Cyanide is removed by sewage treatment processes. However, it is recommended that unacclimatised treatment plants should not received more than 10 mg/L (as CN-) to avoid inhibition of treatment.
Source: Imperial Chemical Industries PLC London

(56)

3.5 Biodegradation

Type: aerobic
Inoculum: activated sludge
Method: other
Year: **GLP:** no data
Test substance: other TS: Sodium cyanide
Remark: Respirometric test with 14C-labelled test substance; activated sludge acclimated to photographic processing effluent; initial concentration not mentioned: 25.7% 14CO2 recovery after 5 d of incubation; measurement of 14CO2 by liquid scintillation spectrometer.
Source: Imperial Chemical Industries PLC London
Test substance: Incubation in the dark at room temperature; addition of salt solution or potassium phosphate buffer (simulated industrial effluent); pH 7.3.

(57)

Type: aerobic
Inoculum: aerobic microorganisms
Result: inherently biodegradable
Method: other
Year: 1973 **GLP:** no data
Test substance: no data
Remark: Diversas bacterias y protozoos degradan los cianuros convirtiendolos a CO2 y amoniaco.
Source: REPSOL QUIMICA, S.A. MADRID

(58)

Type: aerobic
Inoculum: Bacillus sp. (Bacteria)
Concentration: .0065 mg/l related to Test substance
Degradation: 60 % after 36 hour(s)
Result: inherently biodegradable
Method: other
Year: **GLP:** no data
Test substance: other TS: Potassium cyanide
Remark: No growth of inoculum observed. No more details.
Source: Imperial Chemical Industries PLC London

(59)

Type: aerobic
Inoculum: Pseudomonas putida (Bacteria)
Concentration: 400 mg/l related to Test substance
Degradation: > 99 % after 7 day
Result: readily biodegradable
Method: other
Year: 1992 **GLP:** no data
Test substance: other TS: Sodium cyanide
Remark: Batch bioreactor–test (aerated) with alignate–immobilized cells of inoculum, isolated from contaminated industrial wastewaters and soil (inoculum accliminated to test substance); degradation of NaCN to NH3 and CO2 (colorimetric and titrimetric analysis)
Source: Imperial Chemical Industries PLC London
Test substance: 25 degree C; pH 6,7–8,5;

(60)

Type: aerobic
Inoculum: Pseudomonas sp. (Bacteria)
Result: inherently biodegradable
Method: other
Year: 1984 **GLP:** no data
Test substance: no data
Remark: Se estudió la biodegradación de los cianuros y tiocianatos de aguas residuales por Pseudomonas paucimobilis.
Source: REPSOL QUIMICA, S.A. MADRID

(61)

Type: aerobic
Inoculum: other fungi: phanerochaete chrysosporium
Concentration: 1.3 mg/l related to Test substance
Degradation: 45 % after 3 day
Method: other
Year: **GLP:** no data
Test substance: other TS: Potassium cyanide
Remark: 6% mineralisation to CO2 of 651.2 mg/l 14C–KCN (6 day old stationary culture) in a static closed bottle test at room temperature (CO2 trapped in Ba (OH)2, 14C–BaCO3 quantified by scintillation spectrometry).
Source: Imperial Chemical Industries PLC London

(62)

Type: aerobic
Inoculum: other fungi: spores of spemphylium loti
Method: other
Year: 1972 **GLP:** no data
Test substance: other TS: Potassium cyanide
Remark: Spores were able to convert HCN to formamide. No further information available other than spores were incubated in 6.5 mg/L KCN for 2 hours.
Source: Imperial Chemical Industries PLC London

(63)

Type:
Inoculum: activated sludge
Concentration: 25 mg/l
Degradation: after 24 hour(s)
Result: inherently biodegradable
Method: other
Year: 1983 **GLP:** no data
Test substance: no data
Source: REPSOL QUIMICA, S.A. MADRID
Test condition: Tratamiento de aguas residuales de HCN con digestión de lodos activos a distintas concentraciones :
Hasta 25mg/l no se onservan efectos adversos.
A 30mg/l se observa un efecto retardado inicial de 6 días.
A 50mg/l se observa una reducción de un 10% en la producción de gas.

(64)

Type:
Inoculum:
Method:
Year: **GLP:**
Test substance:
Remark: Hydrogen cyanide is degraded by activated sludge that has been acclimatised for two weeks at the following test concentration:

99.8% removal at 35 mg/L (as CN-)
98.4% removal at 50 mg/L (as CN-)
90.0% removal at 75 mg/L (as CN-)
> 60% removal at 180 mg/L (as CN-)

BOD measurements are of little value for cyanide owing to initial inhibition of unacclimatised organisms.
Source: Imperial Chemical Industries PLC London

(56)

Type:
Inoculum:
Method:
Year: **GLP:**
Test substance:
Remark: Sodium and potassium salts of cyanide will reaily dissociate with the resultant formation of molecular (undissociated) hydrocyanic acid (HCN) which will undergo biodegradation. Data on the biodegradation of cyanide salts is therefore relevant.
Source: Imperial Chemical Industries PLC London

3.6 BOD5, COD or BOD5/COD Ratio

-

3.7 Bioaccumulation

Species:
Exposure period:
Concentration:
BCF:
Elimination:
Method:
Year: **GLP:**
Test substance:
Remark: El HCN no se acumula en ninguna de las especies de mamíferos estudiados. No presenta potencial de bioacumulación.
Source: REPSOL QUIMICA, S.A. MADRID

(65)

Species:
Exposure period:
Concentration:
BCF:
Elimination:
Method:
Year: **GLP:**
Test substance:
Remark: Hydrogen cyanide is not expected to bioaccumulate significantly in aquatic organisms. This is in agreement with the calculated log Pow of 0.35 and 1.07.
Source: Imperial Chemical Industries PLC London

(45) (20)

3.8 Additional Remarks

-

AQUATIC ORGANISMS

4.1 Acute/Prolonged Toxicity to Fish

Type: flow through
Species: Jordanella floridae (Fish, fresh water)
Exposure period: 5 day
Unit: mg/l **Analytical monitoring:** yes
Method: other
Year: **GLP:** no data
Test substance: as prescribed by 1.1 - 1.4
Remark: Effect of different sublethal test concentrations on embryonic stages of test fish;
0.0075 mg/l HCN: reduction of hatching success to 37 %; egg production among embryos which successfully reached sexual maturity was reduced by 30 %;
0.0065 mg/l (exposure during embryonic and juvenile stage): 40 % reduction in egg production at sexual maturity;
0.15 mg/l: 99 % mortality of embryos beyond posthatching period within 48 h; mean hatching time doubled and mean hatching success reduced by 96.6 %.
Source: Imperial Chemical Industries PLC London
Test condition: 25 degree C; pH 7.9-8.2; 9 mg/l O2; dechlorinated water.

(66)

Type: flow through
Species: Lepomis macrochirus (Fish, fresh water)
Exposure period: 96 hour(s)
Unit: µg/l **Analytical monitoring:** no data
LC50: = 232 - 365
Method: other
Year: 1983 **GLP:** no data
Test substance: no data
Source: REPSOL QUIMICA, S.A. MADRID

(67)

Type: flow through
Species: Lepomis macrochirus (Fish, fresh water)
Exposure period: 96 hour(s)
Unit: µg/l **Analytical monitoring:** no data
LC50: 535 - 693
Method: other
Year: 1983 **GLP:** no data
Test substance: no data
Remark: Huevos.
Source: REPSOL QUIMICA, S.A. MADRID

(67)

Type: flow through
Species: Oncorhynchus mykiss (Fish, fresh water)
Exposure period: 12 day
Unit: mg/l **Analytical monitoring:** yes
Method: other: colorimetric analysis
Year: **GLP:** no data
Test substance: as prescribed by 1.1 – 1.4
Remark: At sublethal test concentration of 0.01 mg/l: dopamine–level in brain significantly higher (24.2 %) (HPLC–analysis); testes from males had higher numbers of spermatogonial cysts (90 % relative to control); mean diameters of oocyte from ovaries of the vitellogenic females were significantly reduced (20 %)
Source: Imperial Chemical Industries PLC London
Test condition: test organisms acclimated to test conditions; 11.5 degree C; pH 7.8; total hardness 125.0 mg/l (as CaCO3); dechlorinated water

(68)

Type: flow through
Species: Perca flavescens (Fish, fresh water)
Exposure period: 96 hour(s)
Unit: µg/l **Analytical monitoring:** no data
LC50: 76 – 108
Method: other
Year: 1983 **GLP:** no data
Test substance: no data
Source: REPSOL QUIMICA, S.A. MADRID

(67)

Type: flow through
Species: Pimephales promelas (Fish, fresh water)
Exposure period: 96 hour(s)
Unit: µg/l **Analytical monitoring:** no data
LC50: 82 – 137
Method: other
Year: 1983 **GLP:** no data
Test substance: no data
Remark: En estadío juvenil.
Source: REPSOL QUIMICA, S.A. MADRID

(67)

Type: flow through
Species: Pimephales promelas (Fish, fresh water)
Exposure period: 96 hour(s)
Unit: mg/l **Analytical monitoring:** yes
Method: other
Year: **GLP:** no data
Test substance: as prescribed by 1.1 - 1.4
Remark: Exposure of 6 h-old larvae in a 24 to 96 h-test at 0.06 mg/l HCN: 16.7 % in protein- and 15.4 % reduction in RNA-content only within the first 24 h of exposure; ca. 10 % reduction of larval growth rate after 72 h of exposure
no further information available
Source: Imperial Chemical Industries PLC London
Test condition: 25 degree C; pH 8.2; 6.7 mg O2/l

(69)

Type: flow through
Species: Pimephales promelas (Fish, fresh water)
Exposure period: 96 hour(s)
Unit: mg/l **Analytical monitoring:** no data
LC50: = .12
Method: other: colorimetric analysis
Year: **GLP:** no data
Test substance: as prescribed by 1.1 - 1.4
Remark: LC50 at other pH-values: 0.11 mg/l at pH 7.5
0.10 mg/l at pH 9.0
0.08 mg/l at pH 9.2
no further information available
Source: Imperial Chemical Industries PLC London
Test condition: Test organisms acclimated to test temperature for 20 weeks; 20 degree C; pH 6.8; 7.5 mg O2/l

(70)

Type: flow through
Species: Salmo gairdneri (Fish, estuary, fresh water)
Exposure period: 96 hour(s)
Unit: mg/l **Analytical monitoring:** no data
LC0: = .018
LC50: = .028
LC100: = .037
Method: other
Year: **GLP:** no data
Test substance: as prescribed by 1.1 - 1.4
Source: Imperial Chemical Industries PLC London
Test condition: Juvenile test organisms acclimated for 3 weeks to test temperature; 6 degree C; pH 7.9-8.1; total hardness 127 mg/l (as CaCO3); O2-saturation 88.8-90.1 %

(71)

Type: flow through
Species: Salmo gairdneri (Fish, estuary, fresh water)
Exposure period: 96 hour(s)
Unit: mg/l **Analytical monitoring:** no data
LC0: = .032
LC50: = .042
LC100: = .053
Method: other
Year: **GLP:** no data
Test substance: as prescribed by 1.1 - 1.4
Source: Imperial Chemical Industries PLC London
Test condition: Juvenile test organisms acclimated for 3 weeks to test temperature; 12 degree C; pH 8.1; total hardness 127 mg/l (as CaCO3); O2-saturation 95.2-98.5 %

(71)

Type: flow through
Species: Salmo gairdneri (Fish, estuary, fresh water)
Exposure period: 96 hour(s)
Unit: mg/l **Analytical monitoring:** no data
LC0: = .06
LC50: = .068
LC100: = .087
Method: other
Year: **GLP:** no data
Test substance: as prescribed by 1.1 - 1.4
Source: Imperial Chemical Industries PLC London
Test condition: Juvenile test organisms acclimated for 3 weeks to test temperature; 18 degree C; pH 7.8-7.9; total hardness 127 mg/l (as CaCO3); O2-saturation 85.7-88.3 %

(71)

Type: flow through
Species: Salmo gairdneri (Fish, estuary, fresh water)
Exposure period: 96 hour(s)
Unit: µg/l **Analytical monitoring:** no data
LC50: = 57
Method: other
Year: 1983 **GLP:** no data
Test substance: no data
Source: REPSOL QUIMICA, S.A. MADRID

(67)

Type: flow through
Species: Salmo gairdneri (Fish, estuary, fresh water)
Exposure period: 12 day
Unit: mg/l **Analytical monitoring:** yes
Method: other: colorimetric analysis
Year: **GLP:** no data
Test substance: as prescribed by 1.1 – 1.4
Remark: Test during early vitellogenesis with female fish; sublethal test concentration of 0.01 mg/l reduced vitellogenin-level in plasma; the gonado-somatic index declined
Source: Imperial Chemical Industries PLC London
Test condition: test organisms acclimated to test conditions; 12.5 degree C; pH 7.2; total hardness 122.0 mg/l; O2-saturation > 85 %; dechlorinated water

(72)

Type: flow through
Species: Salmo salar (Fish, fresh water, marine)
Exposure period: 12 day
Unit: mg/l **Analytical monitoring:** yes
Method: other: colorimetric analysis
Year: **GLP:** no data
Test substance: as prescribed by 1.1 – 1.4
Remark: Test during late vitellogenesis with female fish; at sublethal concentration of 0.005 mg/l: plasma-vitellogenin-level increased; vitellogenin-level in liver did not change; vitellogenin-levels declined in the gonad by day 12; inhibition of uptake of vitellogenin at theovarian- and liver-level (35.3 % reduced relative to control)
Source: Imperial Chemical Industries PLC London
Test condition: 7 degree C; pH 6.8; total hardness 14.9 mg/l; O2-saturation 90 %

(73)

Type: flow through
Species: Salvelinus fontinalis (Fish, estuary, fresh water)
Exposure period: 96 hour(s)
Unit: µg/l **Analytical monitoring:** no data
LC50: 53 – 143
Method: other
Year: 1983 **GLP:** no data
Test substance: no data
Remark: Estadío juvenil.
Source: REPSOL QUIMICA, S.A. MADRID

(67)

Type: other: no especificadas
Species: Lepomis humilis (Fish, fresh water)
Exposure period: 24 hour(s)
Unit: mg/l **Analytical monitoring:** no data
TLm : = .18
Method: other
Year: 1983 **GLP:** no data
Test substance: no data
Source: REPSOL QUIMICA, S.A. MADRID

(67)

Type: static
Species: Lagodon rhomboides (Fish, estuary, marine)
Exposure period: 24 hour(s)
Unit: mg/l **Analytical monitoring:** no data
LC0: = .05
Tlm : = .069
Method: other
Year: **GLP:** no data
Test substance: no data
Remark: no further information available
Tlm value related to molecular HCN
Source: Imperial Chemical Industries PLC London
Test condition: Test in sea water

(74)

Type: static
Species: Lagodon rhomboides (Fish, estuary, marine)
Exposure period:
Unit: mg/l **Analytical monitoring:** no data
LC0: = .05
LC100: = .1
Method: other
Year: **GLP:** no data
Test substance: other TS
Remark: Tests were allowed to continue until all fish died or until it was evident that the remainig fish would survive.
Source: Imperial Chemical Industries PLC London
Test condition: sea water; 13.7-20.4 degree C

(75)

Type: static
Species: Oncorhynchus mykiss (Fish, fresh water)
Exposure period: 48 hour(s)
Unit: mg/l **Analytical monitoring:** no data
Tlm : = .07
Method: other
Year: **GLP:** no data
Test substance: no data
Remark: no further information available
Tlm value related to molecular HCN
Source: Imperial Chemical Industries PLC London
Test condition: Test in fresh water

(74)

Type: other
Species: Oncorhynchus mykiss (Fish, fresh water)
Exposure period: 48 hour(s)
Unit: mg/l **Analytical monitoring:** no data
LC50: = .07
Method: other
Year: **GLP:** no data
Test substance: as prescribed by 1.1 – 1.4
Remark: no further information available
Source: Imperial Chemical Industries PLC London
Test condition: 15 degree C; pH 7.6; total hardness 320 mg/l (as CaCO3); O2-saturation 50 %

(76)

4.2 Acute Toxicity to Aquatic Invertebrates

Species: Daphnia magna (Crustacea)
Exposure period: 48 hour(s)
Unit: **Analytical monitoring:** yes
Method: other: calculated from data on other cyanide
Year: 1981 **GLP:** yes
Test substance: other TS: Acetone cyanohydrin
Remark: Acetone cyanohydrin readily dissociates to acetone and hydrocyanic acid (HCN), the half life of a 0.1% solution has been estimated as 0.13 hrs at pH 6.8.
Test method: US EPA 1975; Methods for acute toxicity tests with fish, microinvertebrates and amphibians. Ecological Research Series (EPA-660/3-75-009, p61). Temperature 21-23 deg C.

Data quoted for molar equivalent hydrocyanic acid (HCN) calculated from data given for acetone cyanohydrin (ACH).

LCO (96 hrs) 0.07 mg/L (ACH) = 0.024 mg/L (as HCN)
LC50 (24 hrs) 0.27 mg/L (ACH) = 0.086 mg/L (as HCN)
LC50 (48 hrs) 0.12 mg/L (ACH) = 0.041 mg/L (as HCN)
Source: Imperial Chemical Industries PLC London
Test substance: 98.5% acetone cyanohydrin. Certificate of analysis.

(77)

Species: Daphnia magna (Crustacea)
Exposure period:
Unit: **Analytical monitoring:** no data
Method: other: calculation from data of inorganic cyanides
Year: **GLP:** no data
Test substance: other TS: Sodium cyanide
Remark: Effect on juveniles at various test conditions; test organisms (wild stock from Como Lake, St. Paul, Minnesota) acclimated to test conditions for 7 days. PH 8-815, 5.7-5.8 O2/L.

Data quoted for molar equivalent hydrocyanic acid (HCN) calculated from data given for sodium cyanide.

LC threshold 0.09-0.35 mg/L (as NaCN) = 0.05 - 0.075 mg/L (as HCN)

LC50 0.16 mg/l (as NaCN) = 0.09 mg/L (as HCN)
Source: Imperial Chemical Industries PLC London

(74)

Species: Daphnia sp. (Crustacea)
Exposure period: 48 hour(s)
Unit: mg/l **Analytical monitoring:** no data
EC50: = 1.8
Method: other
Year: 1983 **GLP:** no data
Test substance: no data
Source: REPSOL QUIMICA, S.A. MADRID

(67)

Species: other aquatic crustacea: Gammarus pseudolimnaeus
Exposure period: 96 hour(s)
Unit: **Analytical monitoring:** no data
Method: other: calculated from data of inorganic cyanides
Year: **GLP:** no data
Test substance: other TS: Sodium cyanide
Remark: Test in a flow-through-system (collected from a small stream, Minnesota) at various test temperatures; test organisms acclimated to test temperature for 7 days. Test conditions; 15 deg C, pH 7.91, dissolved oxygen 7.0 mg/L total hardness 225 mg/L as CaCO3.

Data quoted for molar equivalent hydrocyanic acid (HCN) calculated from date given for sodium cyanide.

LC threshold 0.076 mg/L (as NaCH) = 0.042 mg/L (as HCN)
LC50 0.17 mg/L (as NaCN) = 0.094 mg/L (as HCN)

At 20 deg C, pH 8.14, 6.7 mg O2/L:

LC threshold 0.058 mg/L (as NaCN) = 0.032 mg/L (as HCN)
LC50 0.084 mg/L (as NaCN) = 0.046 mg/L (as HCN)
Source: Imperial Chemical Industries PLC London

Species: other: Asellus communis
Exposure period: 96 hour(s)
Unit: mg/l **Analytical monitoring:** no data
EC50: = 2.29
Method: other
Year: 1983 **GLP:** no data
Test substance: no data
Source: REPSOL QUIMICA, S.A. MADRID

(67)

Species: other: Gammarus pseudolimnaeous
Exposure period: 96 hour(s)
Unit: mg/l **Analytical monitoring:** no data
EC50: = .17
Method: other
Year: 1983 **GLP:** no data
Test substance: no data
Source: REPSOL QUIMICA, S.A. MADRID

(67)

Species: other: aquatic crustaces: asellus communis
Exposure period: 96 hour(s)
Unit: **Analytical monitoring:** no data
Method: other: by claculation from data of inorganic cyanide
Year: **GLP:** no data
Test substance: other TS: Sodium cyanide
Remark: Solutions of cyanides are acutely toxic to aquatic organisms. It is believed that this toxicity is predominantly attributable to dissociation of the cyanide salt with the resultant formation of molecular (undissociated) hydrocyanic acid (HCN). Hydrocyanic acid, by virtue of its small size and lack of charge, readily penetrates the external membranes of aquatic organisms. Internally the mechanism of toxicity is believed to be by formation of cyanide ion (CN–).
Test in a flow–through–system (collected from Rainy Lake, Minnesota); test organisms acclimated to test temperature for 7 days. Test conditions, 18 deg C, pH 8.13, dissolved oxygen 7.52 mg/L, total hardness 225 mg/L as CaCO3.

Data quoted as molar equivalent hydrocyanic acid (HCN) calculated from data given for sodium cyanide.

LC threshold 1.83 mg/L (as NaCN) = 1.01 mg/L (as HCN)
LC50 2.33 mg/L (as NaCH) = 1.29 (as HCN)
Source: Imperial Chemical Industries PLC London

(78)

Species:
Exposure period:
Unit: **Analytical monitoring:**
Method:
Year: **GLP:**
Test substance:
Remark: Sodium and potassium salts of cyanide will reaily dissociate with the resultant formation of molecular (undissociated) hydrocyanic acid (HCN) which will undergo biodegradation. Data on the biodegradation of cyanide salts is therefore relevant.
Source: Imperial Chemical Industries PLC London

(79)

4.3 Toxicity to Aquatic Plants e.g. Algae

Species: Ankistrodesmus falcatus (Algae)
Endpoint: biomass
Exposure period:
Unit: **Analytical monitoring:** no data
Method: other: calculated from data of inorganic cyanides
Year: 1983 **GLP:** no data
Test substance: other TS: Potassium cyanide
Remark: Test method: Static system. pH 8.0 to 10. Temperature 20 deg C.

Data quoted for molar equivalent hydrocyanic acid (HCN) calculated from data given for potassium cyanide, as CN.

EC10 0.265 mg/l (as CN-) = 0.275 mg/L (as HCN)
EC50 1.25 mg/l (as CN-) = 1.3 mg/L (as HCN)
EC90 5.91 mg/l (as CN-) = 6.13 mg/L (as HCN)
Source: Imperial Chemical Industries PLC London

(80)

Species: Microcystis aeruginosa (Algae, blue, cyanobacteria)
Endpoint: growth rate
Exposure period: 8 day
Unit: **Analytical monitoring:** no data
Method: other: calculated from data of inorganic cyanides
Year: 1978 **GLP:** no data
Test substance: other TS: Potassium cyanide
Remark: No data for HCN

Test method: Cell multiplication inhibition test. Static system run at 27 deg C. pH 7.0.

Data quoted for molar equivalent hydrocyamic acid (HCN) 0.03 mg/L calculated from data given for KCN (LC) threshold 0.07 mg/L (mol wt 65.12).
Source: Imperial Chemical Industries PLC London

(81)

Species: Scenedesmus quadricauda (Algae)
Endpoint: growth rate
Exposure period: 8 day
Unit: **Analytical monitoring:** no data
Method: other: calculated from data of inorganic cyanides
Year: 1978 **GLP:** no data
Test substance: other TS: Potassium cyanide
Remark: Test method: Cell multiplication inhibition test. Static system run at 27 deg C.

Data quoted for molar equivalent hydrocyanic acid (HCN) 0.03 mg/L calculated from data given for potassium cyanide (as CN-) LC threshold 0.03 mg/l.
Source: Imperial Chemical Industries PLC London
(82) (81) (83)

Species: Scenedesmus quadricauda (Algae)
Endpoint: other
Exposure period: 4 day
Unit: **Analytical monitoring:** no data
Method: other: calculated from data of inorganic cyanides
Year: 1973 **GLP:** no data
Test substance: other TS: Potassium cyanide
Remark: Data quoted for molar equivalent hydrocyanic acid (HCN) LC threshold 0.066 mg/l calculated from data given for potassium cyanide 0.16 mg/l (0.064 mg/l CN-). Threshold concentration in a static test at 24 deg C.
Source: Imperial Chemical Industries PLC London
(84)

Species:
Endpoint:
Exposure period:
Unit: **Analytical monitoring:**
Method:
Year: **GLP:**
Test substance:
Remark: Sodium and potassium salts of cyanide will reaily dissociate with the resultant formation of molecular (undissociated) hydrocyanic acid (HCN) which will undergo biodegradation. Data on the biodegradation of cyanide salts is therefore relevant.
Source: Imperial Chemical Industries PLC London
(79)

4.4 Toxicity to Microorganisms e.g. Bacteria

Type: aquatic
Species: Chilomonas paramaecium (Protozoa)
Exposure period: 48 hour(s)
Unit: **Analytical monitoring:** yes
Method: other: by calculation from data of inorganic cyanides
Year: **GLP:**
Test substance: other TS: Potassium cyanide dissolved in distilled water
Remark: Test conditions; 20 deg C, pH 6-9. Determination by cell counter (coulter counter).

Data quoted for molar equivalent hydrocyanic acid (HCN) LOEC 0.12 mg/L calculated from data given for potassium cyanide 0.1 mg/L, as CN-
Source: Imperial Chemical Industries PLC London

(85) (86)

Type: other
Species: other bacteria: Bacterias y protozoos.
Exposure period:
Unit: **Analytical monitoring:** no data
Method: other
Year: 1973 **GLP:** no data
Test substance: no data
Remark: Diversas bacterias y protozoos degradan los cianuros convirtiendolos a CO2 y amoniaco.
Source: REPSOL QUIMICA, S.A. MADRID

(58)

4.5 Chronic Toxicity to Aquatic Organisms

4.5.1 Chronic Toxicity to Fish

Species: Salmo gairdneri (Fish, estuary, fresh water)
Endpoint: other: efectos en la natación
Exposure period: 20 day
Unit: µg/l **Analytical monitoring:** no data
Method: other
Year: 1976 **GLP:** no data
Test substance: no data
Remark: La exposición a concentraciones de HCN entre 15-45ug/l, a diversas temperaturas, demostraron afectar la capacidad natatoria de la trucha arcoiris. En las exposiciones agudas, al eliminar el HCN del agua, las truchas recuperaban al poco tiempo la capacidad natatoria. Sin embargo, en exposiciones crónicas (15-20 días), la capacidad de recuperación no era completa.
Source: REPSOL QUIMICA, S.A. MADRID

(87)

Species: Oncorhynchus mykiss (Fish, fresh water)
Endpoint: other: effect on oocyte development in a flow-through system
Exposure period: 20 day
Unit: mg/l **Analytical monitoring:** yes
Method: other
Year: **GLP:** no data
Test substance: as prescribed by 1.1 - 1.4
Remark: at 0.01 and 0.02 mg/l HCN: abnormalities in cytoplasma among oocytes during early development; delaying of secondary yolk deposition (93 %) during early summer ovarian growth (0.02 mg/l);
at exposition of test organisms during mid-summer 60% of the oocytes failing to reach the secondary yolk deposition at both concentrations; complete reduction of number of viable eggs (control contained 27 % of viable eggs)
Source: Imperial Chemical Industries PLC London
Test condition: test organisms acclimatised to test conditions for 12 d; 10 degree C; pH 7.85; total hardness 122 mg/l (as CaCO3); dechlorinated water

(88)

Species: Oncorhynchus mykiss (Fish, fresh water)
Endpoint: other: see remarks
Exposure period: 18 day
Unit: mg/l **Analytical monitoring:** no data
Method: other
Year: **GLP:** no data
Test substance: as prescribed by 1.1 - 1.4
Remark: at 0.01 and 0.03 mg/l: number of dividing spermatogonia reduced by 13 % and 50 % resp.; increasing in the prophase stage spermatogonia; blockage of mitotic process; affecting the formation of mitotic spindle (0.01 mg/l HCN); permanent damage to the fixed number of primary spermatogonia within the testis
Source: Imperial Chemical Industries PLC London
Test condition: Test in a continuous flow-through system with juvenile male fish; test organisms acclimated to test conditions for 12 d; 12.5 degree C; pH 7.9; total hardness 127.7 mg/l (as CaCO3); dechlorinated water

(89)

Species: Lepomis macrochirus (Fish, fresh water)
Endpoint: other: see remarks
Exposure period: 57 day
Unit: mg/l **Analytical monitoring:** yes
LC50 : .03
Method: other
Year: **GLP:** no data
Test substance: other TS
Remark: at 0.03 mg/l 50 % mortality and at 0.06 mg/l 100 % mortality (18,6 % mortality of control fish)
no further information available
semistatic test with newly fertilized eggs
Source: Imperial Chemical Industries PLC London
Test condition: 25 degree C; pH 7.9-8.0; 5.8-6.4 mg O2/l

(90)

Species: Lepomis macrochirus (Fish, fresh water)
Endpoint: other: see remarks
Exposure period: 289 day
Unit: mg/l **Analytical monitoring:** yes
LC10 : .03
Method: other: colorimetric analysis
Year: **GLP:** no data
Test substance: as prescribed by 1.1 – 1.4
Remark: at 0.03 mg/l 10 % mortality; at 0.08 mg/l 60 % mortality compared to control; < 0.005 mg/l inhibited the spawning of fish to some degree
no further information available
semi–static test on long–term survival of adults
Source: Imperial Chemical Industries PLC London
Test condition: 25 degree C; pH 8.1; 6.2 mg O2/l

(90)

Species: Salmo gairdneri (Fish, estuary, fresh water)
Endpoint: weight of young fish
Exposure period: 18 day
Unit: mg/l **Analytical monitoring:** no data
Method: other
Year: 1981 **GLP:** no data
Test substance: no data
Remark: Se utilizaron diversas concentraciones (0, 0.01, 0.02, 0.03mg/l) en agua continuamente renovada a 12.5 grados C para evaluar el efecto crónico del HCN en trucha arcoiris en fase juvenil. Se observó que a concentraciones de 0.02 y 0.03 mg/l el crecimiento se redujo de un 40% a un 95% después de 18 días. A todas las concentraciones se observo una inhibición severa de la velocidad específica de crecimiento, seguida de un incremento posterior, insuficiente para compensar la inhibición inicial. A todas las concentraciones valoradas se produjo necrosis degenerativa de las células del hígado.
Source: REPSOL QUIMICA, S.A. MADRID

(91)

Species: Oncorhynchus mykiss (Fish, fresh water)
Endpoint: weight of young fish
Exposure period: 20 day
Unit: mg/l **Analytical monitoring:** yes
LLC: = .015
Method: other: colorimetric analysis
Year: **GLP:** no data
Test substance: as prescribed by 1.1 – 1.4
Remark: at 0.015, 0.03 and 0.045 mg/l HCN at 6, 12 and 18 degree C resp.: 25, 50 and 58 %/d reducing of specific growth rate (dry and wet weight) resp.;
at 0.005 mg/l at 6 degree C and at 0.03 mg/l at 12 degree C: decreasing of swimming activity and reduction of food consumption during the first 10 d of exposure
Source: Imperial Chemical Industries PLC London
Test condition: Test with juveniles in a continuous flow–through system at various temperatures; test organisms acclimatised to test temperatures

(92)

Species: Salmo salar (Fish, fresh water, marine)
Endpoint: other
Exposure period: 58 day
Unit: mg/l **Analytical monitoring:** yes
LLC: <= .005
Method: other
Year: **GLP:** no data
Test substance: as prescribed by 1.1 – 1.4
Remark: 0.08–0.1 mg/l: hatching delayed by 6–9 d;
0.1 mg/l: significantly increasing of abnormalities in larval development;
>=0.01 mg/l: conversion of yolk into body tissues was reduced;
<=0.005 mg/l: max. acceptable concentration of test substance protecting larval development of test organisms
effect of sublethal concentrations on embryogenesis of newly fertilized eggs up to the end of the sac–fry stage
Source: Imperial Chemical Industries PLC London
Test condition: continuous flow–through system; 5.4 degree C; pH 7.6; 93 % of HCN in the undissociated form

(93)

Species: Salvelinus fontinalis (Fish, estuary, fresh water)
Endpoint: other
Exposure period: 234 day
Unit: **Analytical monitoring:** yes
Method: other: calculation from data of inorganic cyanides
Year: **GLP:** no data
Test substance: other TS: Sodium cyanide
Remark: Effect on precentage survival and egg production (% viability) of two generations of 19 month-old adults (FO) in a flow-through-system 144 d prior to spawning 9-15 deg C; pH 7.94-8.01; 64-74% oxygen saturation; total hardness 236-239 mg/l as CaCO3.

Authors reported data as free HCN concentration. No significant reduction of growth and of mean survival rate at 0.075 mg/l. At 0.006 mg/l 98% viability and at 0.065 mg/l 0% viability of produced eggs (control 93.5%). 75.8% reduction in mean eggs spawned per female at 0.065 mg/l.

Growth of embryos and juveniles (F1) in a 90-day test: 26% weight reduction compared with control at 0.033 mg/l and 81% at 0.077 mg/l. 69.6% mean survival rate from hatch to 90 day old juveniles (F1) at 0.07 mg/l.
Source: Imperial Chemical Industries PLC London
(94) (95)

Species: Pimephales promelas (Fish, fresh water)
Endpoint: other
Exposure period: 283 day
Unit: **Analytical monitoring:** yes
Method: other: calculation from data of inorganic cyanides
Year: **GLP:** no data
Test substance: other TS: Sodium cyanide
Remark: Test with newly hatched larvae in a flow-through system; 24.8-25.1 degree C; pH 8.1; 5.9-6.3 mg 02/1; at 25 degree C and pH 8.1 93% of free cyanide (expressed as HCN) is in the molecular form.

Authors reported data as free HCN concentration. 82.8% mortality at 0.1 mg/L as HCN 100% survival at 0.025-0.1 mg/l offer 56-84 days egg production/demale, started at the 149th day, was significantly reduced at 0.02 mg/L 82% reduction in hatch ability of new generation (started after 227 days of experiment) at 0.044 mg/L.
Source: Imperial Chemical Industries PLC London
(96)

Species: Pimephales promelas (Fish, fresh water)
Endpoint: other
Exposure period: 312 day
Unit: **Analytical monitoring:** yes
Method: other: calculation from data of inorganic cyanides
Year: **GLP:** no data
Test substance: other TS: Sodium cyanide
Remark: Effect on precentage survival and hatchability in a flow-through-test over two generations (FO and F1); test started with newly hatched larvae:
24.8-25.1 degree C; pH 8.06-8.09; diss. oxygen 5.9-6.3 mg/l total hardness 225 mg/l as CaCO3.

Authors reported data as free HCN concentration. No significant reduction of mean survival rate of newly hatched larvae after 84 days of exposure: 98-100% survival (control 100%) of test organisms at 0.006 - 0.001 mg/l as HCN, 61.5% survival at 0.006 mg/l and 19.5 % at 0.073 mg/l (control 71.2%) 51 days after exposure of F1 generation survival was 95-100% at < 0.096 mg/l and 81% at 0.106 mg/l.
Source: Imperial Chemical Industries PLC London
(95)

Species: Lepomis macrochirus (Fish, fresh water)
Endpoint: other
Exposure period: 289 day
Unit: **Analytical monitoring:** yes
Method: other: calculation from data with inorganic cyanides
Year: **GLP:** no data
Test substance: other TS: Sodium cyanide
Remark: Effect on survival of adult fish in a flow-through-test; 24.7-25.1 deg C, pH 8.97-8.11, dissolved oxygen 6.07-6.3 mg/L, total alkalinity 236 mg/L. Colorimetric analysis - no further information. Authors reported data as free HCN concentration. 40% survival (control 100%) at 0.08 mg/L (as HCN).
Source: Imperial Chemical Industries PLC London
(95)

4.5.2 Chronic Toxicity to Aquatic Invertebrates

Species: other aquatic crustacea: Gammarus pseudolimnaeus
Endpoint: mortality
Exposure period: 83 day
Unit: **Analytical monitoring:** yes
Method: other
Year: **GLP:** no data
Test substance: other TS: Sodium cyanide
Remark: Effect on individual number of Gammarus pseudolimnaeus (collected from a small stream, Minnesota); test organisms acclimated to test temperature 18.1 deg C, pH 8.0, dissolved oxygen content 6.8–8.0 mg/L, total hardness 236 mg/L, light intensity (16 hr) 452–667 Lux;

Data quoted by authors as relative HCN content.
59.7% of controls at 0.01 mg/L
100% mortality at 0.064 mg/L
Highest concentration with survival 0.05 mg/L, highest concentration with reproduction 0.016 mg/L.
Source: Imperial Chemical Industries PLC London
(97) (95)

Species: other aquatic crustacea: Asellus communis
Endpoint: mortality
Exposure period: 112 day
Unit: **Analytical monitoring:** yes
Method: other
Year: **GLP:** no data
Test substance: other TS: Sodium cyanide
Remark: Effect on individual number of Asellus communis (cultured in laboratory); test organisms acclimated to test temperature; 18.1 degree C; pH 7.92–7.96; diss. oxygen 5.9–6.1 mg/l; total alkalinity 236 mg/l, light intensity (16h) 506–657 lux.

Data quoted by authors as relative HCN content.
79.3% of controls at 0.01 mg/l and
25.7% of controls at 0.1 mg/l
Source: Imperial Chemical Industries PLC London
(78)

Species: other aquatic crustacea: Asellus communis
Endpoint: mortality
Exposure period: 115 day
Unit: **Analytical monitoring:** yes
Method: other
Year: **GLP:** no data
Test substance: other TS: Sodium cyanide
Remark: Effect on individual number of Asellus (cultured in laboratory); test organisms acclimated to test temperature; 18.2 deg C, pH 8.0–8.1, dissolved oxygen 6.0–6.5 mg/L, total alkalinity 236 mg/L, light intensity (16 hr) 481–660 Lux;

Data quoted by authors as relative HCN content.
5.3% of controls at 0.11 mg/L
100% mortality at 0.43 mg/L
Highest concentration with survival or reproduction 0.32 mg/L.
Source: Imperial Chemical Industries PLC London
(97) (95)

Species: Gammarus sp. (Crustacea)
Endpoint: other: sensibilidad
Exposure period:
Unit: µg/l **Analytical monitoring:** no data
Method: other
Year: 1980 **GLP:** no data
Test substance: no data
Result: Excepto para los invertebrados más sensibles, como Daphnia pulex y Gammarus pseudolimnaeus, los invertebrados suelen ser más tolerantes al HCN que las especies de peces de agua dulce, que presentan valores de toxicidad aguda entre 50–200ug/l. Después de un estudio de supervivencia a largo plazo, y dos tests de ciclo de vida completo, los peces dieron valores de toxicidad crónica de 7.9, 14 y 16ug/l respectivamente. Gammarus pseudilimnaeus es comparable en sensibilidad a los peces. Los isópodos son más tolerantes.
Source: REPSOL QUIMICA, S.A. MADRID
(98)

TERRESTRIAL ORGANISMS

4.6.1 Toxicity to Soil Dwelling Organisms

Type:
Species:
Endpoint:
Exposure period:
Unit:
Method:
Year: **GLP:**
Test substance:
Source: REPSOL QUIMICA, S.A. MADRID

4.6.2 Toxicity to Terrestrial Plants

Species: other terrestrial plant: Malus domestica
Endpoint:
Expos. period:
Unit:
Method: other
Year: 1991 **GLP:** no data
Test substance:
Remark: Effect of 27 mg/l gaseous HCN on germination, length of hypocotyls and main roots; examination 9 d after a single 6 h-treatment (20-25 degree C; 12 h-photoperiod) to apple seeds (Malus domestica): 15.6 % increasing of length of hypocotyls, but no difference in length of main roots compared to control; 82.1 % reduction of germination rate relative to control
no further information available
Source: Imperial Chemical Industries PLC London
(99)

Species:
Endpoint:
Expos. period:
Unit:
Method:
Year: **GLP:**
Test substance:
Remark: Phytotoxicity of different genera of Hawaiian cut flowers and foliage after 30 min-fumigation (closed chamber; 20-25 degree C; 40-60% RH) with test substance (eg. 0.153 g NaCH for 2825 mg/m3 HCN): Heliconiaceae: 43.4% increasing of damage symmptoms at 6215 mg/m3; Proteaceae: 82.5% at 4181 mg/m3; Zingiberaceae: 57.5% at 6215 mg/m3 relative to control; no further information.
Source: Imperial Chemical Industries PLC London
(100)

Species: other terrestrial plant
Endpoint: other
Expos. period:
Unit:
Method: other
Year: 1982 **GLP:** no data
Test substance: no data
Remark: El HCN es fitotóxico, aunque no a concentraciones de vapor mortales para los insectos. Evitar el uso en árboles con residuos de pulverizaciones de cobre, o que estén siendo tratados para corregir deficiencias de cobre.
Source: REPSOL QUIMICA, S.A. MADRID

(101)

4.6.3 Toxicity to other Non–Mamm. Terrestrial Species

Species: other terrestrial mollusc
Endpoint: mortality
Expos. period: 48 hour(s)
Unit: other: mg/l
LC50: = 3.3
Method: other
Year: 1980 **GLP:** no data
Test substance: no data
Remark: Especie: Limnaea emarginata (caracol)
Source: REPSOL QUIMICA, S.A. MADRID

(102)

Species: other terrestrial mollusc
Endpoint: mortality
Expos. period: 48 hour(s)
Unit: other: mg/l
LC50: = 1.35
Method: other
Year: 1980 **GLP:** no data
Test substance: no data
Remark: Especie: Physa integra (caracol)
Source: REPSOL QUIMICA, S.A. MADRID

(102)

Species: other: Stemonema rubrum
Endpoint: mortality
Expos. period: 48 hour(s)
Unit: other: ug/l
LC50: = 500
Method: other
Year: 1980 **GLP:** no data
Test substance: no data
Remark: Especie: Hydropsyche sp.
Source: REPSOL QUIMICA, S.A. MADRID

(102)

Species: other terrestrial mollusc
Endpoint: mortality
Expos. period: 96 hour(s)
Unit: other: mg/l
LC50: = 51.9
Method: other
Year: 1980 **GLP:** no data
Test substance: no data
Remark: Especie: Limnaea sp. (embrión de caracol)
Source: REPSOL QUIMICA, S.A. MADRID

(102)

Species:
Endpoint:
Expos. period:
Unit:
Method:
Year: **GLP:**
Test substance:
Remark: Toxicity of inorganic cyanide (99.4% sodium cyanide) studied by single oral dose in gelatin capule.

Species (bird; m/f)	NaCN LD50 (mg/kg)	HCN LD50 equivalent
Black vulture	4.8	2.65
American kestrel	4.0	2.2
Japanese quail	9.4	5.2
Domestic chicken	21	11.6
Eastern screech–owl	8.6	4.7
European starling	17	9.4

Source: Imperial Chemical Industries PLC London

(103)

4.7 Biological Effects Monitoring

–

4.8 Biotransformation and Kinetics

Type: animal
Remark: El ión cianuro se conjuga con azufre para forma tiocianato. La conjugación es catalizada por la enzima rodenasa, que está ampliamente distribuida en la mayoría de los tejidos animales, sobre todo en hígado. La rodenasa es capaz de transformar solo una cantidad limitada de cianuro, que es la que se deriva del metabolismo normal. Otro donador de azufre es el 3–mercaptopiruvato. La enzima mercaptosulfotransferasa se localiza en el citosol.
Source: REPSOL QUIMICA, S.A. MADRID

(104)

Type: animal
Result: La mayor parte del cianuro de hidrógeno absorbido por el organismo se convierte mediante sulfotransferasas al ión tiocianato. Otras vias de metabolismo minoritarias son la combinación con cisteina para formar ácido 2–imino–tiazolidina–4–carboxílico, la oxidación a CO2 y formato y la conversión a cianocobalamina.
Source: REPSOL QUIMICA, S.A. MADRID

(105)

Type: animal
Remark: Cuando se absorbe, el HCN reacciona rápidamente con la enzima citocromo oxidasa de las mitocondrias, inhibiendo la respiración celular con resultados citotóxicos de hipoxia. La respiración pulmonar se vé estimulada. Se producen convulsiones hipóxicas que terminan con parada respiratoria y muerte.
El mecanismo mayoritario de eliminación del ión cianuro en el cuerpo es la conversión enzimática a tiocianato, que es relativamente menos tóxico, catalizada por la enzima mitocondrial rodenasa.
Source: REPSOL QUIMICA, S.A. MADRID

(106)

4.9 Additional Remarks

Remark: no further information available
Toxicity to invertebrates:
Test organism: granary weevil (Sitophilus granarius)
LD50 (4 h): 8.0 mg/l HCN (as fumigant)
Source: Imperial Chemical Industries PLC London

(107)

5.1 Acute Toxicity

5.1.1 Acute Oral Toxicity

Type: LD50
Species: rat
Sex:
Number of Animals:
Vehicle:
Value: 4.5 mg/kg bw
Method: other
Year: **GLP:** no data
Test substance: no data
Source: Imperial Chemical Industries PLC London
(108)

Type: LD50
Species: rat
Sex:
Number of Animals:
Vehicle:
Value: 3.62 mg/kg bw
Method: other
Year: **GLP:** no data
Test substance: no data
Remark: females, starved
Source: Imperial Chemical Industries PLC London
(109)

Type: LD50
Species: rat
Sex:
Number of Animals:
Vehicle:
Value: 4.21 mg/kg bw
Method: other
Year: **GLP:** no data
Test substance: no data
Remark: females, unstarved
Source: Imperial Chemical Industries PLC London
(109)

Type: LD50
Species: mouse
Sex:
Number of Animals:
Vehicle:
Value: = 3.7 mg/kg bw
Method: other
Year: 1961 **GLP:** no data
Test substance: no data
Source: REPSOL QUIMICA, S.A. MADRID

(110)

Type: LD50
Species: mouse
Sex:
Number of Animals:
Vehicle:
Value: 3.7 mg/kg bw
Method: other
Year: **GLP:** no data
Test substance: no data
Source: Imperial Chemical Industries PLC London

(111)

Type: LD50
Species: mouse
Sex:
Number of Animals:
Vehicle:
Value: .4 mg/kg bw
Method: other
Year: **GLP:** no data
Test substance: no data
Source: Imperial Chemical Industries PLC London

(108)

Type: LD50
Species: mouse
Sex:
Number of Animals:
Vehicle:
Value: 8.5 mg/kg bw
Method: other
Year: **GLP:** no data
Test substance: no data
Source: Imperial Chemical Industries PLC London

(112)

Type: LD50
Species: rabbit
Sex:
Number of Animals:
Vehicle:
Value: 2.49 mg/kg bw
Method: other
Year: **GLP:** no data
Test substance: no data
Remark: females, unstarved
Source: Imperial Chemical Industries PLC London
(109)

Type: LDLo
Species: rabbit
Sex:
Number of Animals:
Vehicle:
Value: = 4 mg/kg bw
Method: other
Year: 1935 **GLP:** no data
Test substance: no data
Source: REPSOL QUIMICA, S.A. MADRID
(113)

Type: LDLo
Species: dog
Sex:
Number of Animals:
Vehicle:
Value: = 4 mg/kg bw
Method: other
Year: 1935 **GLP:** no data
Test substance: no data
Source: REPSOL QUIMICA, S.A. MADRID
(113)

Type: LDLo
Species: human
Sex:
Number of Animals:
Vehicle:
Value: = .57 mg/kg bw
Method: other
Year: 1966 **GLP:** no data
Test substance: no data
Source: REPSOL QUIMICA, S.A. MADRID
(114)

Type: LDLo
Species: pig
Sex:
Number of Animals:
Vehicle:
Value: = 2 mg/kg bw
Method: other
Year: 1971 **GLP:** no data
Test substance: no data
Source: REPSOL QUIMICA, S.A. MADRID

5.1.2 Acute Inhalation Toxicity

Type: LC100
Species: rat
Sex:
Number of Animals:
Vehicle:
Exposure time: 10 minute(s)
Value: 1000 ppm
Method: other
Year: **GLP:** no data
Test substance: no data
Source: Imperial Chemical Industries PLC London

(115)

Type: LC50
Species: rat
Sex:
Number of Animals:
Vehicle:
Exposure time: 30 minute(s)
Value: = 160 ppm
Method: other
Year: 1987 **GLP:** no data
Test substance: no data
Source: REPSOL QUIMICA, S.A. MADRID

(116)

Type: LC50
Species: rat
Sex:
Number of Animals:
Vehicle:
Exposure time: 5 minute(s)
Value: .54 mg/l
Method: other
Year: **GLP:** no data
Test substance: no data
Source: Imperial Chemical Industries PLC London

(111)

Type: LC50
Species: rat
Sex:
Number of Animals:
Vehicle:
Exposure time:
Value:
Method: other
Year: **GLP:** no data
Test substance: no data
Remark:

exposure time	LC50 (mg/l)
10 sec.	3.78
1 min.	1.13
5 min.	0.49
30 min.	0.15-0.17
60 min.	0.16

females
Source: Imperial Chemical Industries PLC London
(109)

Type: LC50
Species: rat
Sex:
Number of Animals:
Vehicle:
Exposure time: 5 minute(s)
Value: .55 mg/l
Method: other
Year: **GLP:** no data
Test substance: no data
Source: Imperial Chemical Industries PLC London
(117)

Type: LC50
Species: rat
Sex:
Number of Animals:
Vehicle:
Exposure time: 30 minute(s)
Value: .12 mg/l
Method: other
Year: **GLP:** no data
Test substance: no data
Remark: HCN inhalation produced deaths during the exposure period and the postexposure time; most of the postexposure deaths occurred between 24 h
Source: Imperial Chemical Industries PLC London
(118)

Type: other
Species: rat
Sex:
Number of Animals:
Vehicle:
Exposure time:
Value:
Method: other
Year: **GLP:** no data
Test substance: no data
Remark: CT: concentration-time product (ppm x min.) necessary to kill animals (calculated from the concentration-time curve); lethal CT: 4700 ppm = 5.3 mg/l.
Source: Imperial Chemical Industries PLC London
(119)

Type: other
Species: rat
Sex:
Number of Animals:
Vehicle:
Exposure time:
Value:
Method: other
Year: **GLP:** no data
Test substance: no data
Remark:

concentration (ppm)	exposure	symptoms of toxicity
1000	10 min	lethal
500	10 min	tolerable
142	30 min	LC50
118	12 h	LCL0
110	90 min	lethal

Source: Imperial Chemical Industries PLC London
(120) (121) (122) (115)

Type: LC50
Species: mouse
Sex:
Number of Animals:
Vehicle:
Exposure time: 5 minute(s)
Value: = 323 ppm
Method: other
Year: 1977 **GLP:** no data
Test substance: no data
Source: REPSOL QUIMICA, S.A. MADRID
(123)

Type: LC50
Species: mouse
Sex:
Number of Animals:
Vehicle:
Exposure time: 30 minute(s)
Value: .18 mg/l
Method: other
Year: **GLP:** no data
Test substance: no data
Remark: males
Source: Imperial Chemical Industries PLC London (124)

Type: other: RD50
Species: mouse
Sex:
Number of Animals:
Vehicle:
Exposure time: 30 minute(s)
Value: .07 mg/l
Method: other
Year: **GLP:** no data
Test substance: no data
Remark: RD50: concentration required to reduce respiratory rate by 50 %
Source: Imperial Chemical Industries PLC London (124)

Type: other: see remarks
Species: mouse
Sex:
Number of Animals:
Vehicle:
Exposure time:
Value:
Method: other
Year: **GLP:** no data
Test substance: no data
Remark:

concentration (ppm)	exposure time	symptoms of toxicity
1300	1-2 min	lethal
110	45 min	lethal
45	2.5 h	lethal
40	7 h	tolerable

Source: Imperial Chemical Industries PLC London (125) (120) (121)

Type: LC50
Species: rabbit
Sex:
Number of Animals:
Vehicle:
Exposure time:
Value:
Method: other
Year: **GLP:** no data
Test substance: no data
Remark:

exposure time	LC50 (mg/l)
45 sec.	2.43
5 min.	0.41
35 min.	0.21

typical signs of toxicity after inhalation of HCN include rapid breathing, weak and ataxic movements, convulsions, loss of voluntary movement, coma, decrease in respiratory rate and depth, irregularities of breathing, and death; symptoms varied in their time of onset and severity, depending on the athmospheric concentration of HCN.
females
Source: Imperial Chemical Industries PLC London
(109)

Type: other: see remarks
Species: rabbit
Sex:
Number of Animals:
Vehicle:
Exposure time:
Value:
Method: other
Year: **GLP:** no data
Test substance: no data
Remark:

concentration (ppm)	exposure	symptoms of toxicity
150	33 min	lethal
135	no data	dyspnea
125	105 min	lethal
120	no data	no toxicity

Source: Degussa AG - ZN Wolfgang Hanau 1
Imperial Chemical Industries PLC London
(126) (125) (120) (121)

Type: LC50
Species: cat
Sex:
Number of Animals:
Vehicle:
Exposure time: 1 minute(s)
Value: = 771 ppm
Method: other
Year: **GLP:** no data
Test substance: no data
Source: REPSOL QUIMICA, S.A. MADRID (127)

Type: other: see remarks
Species: cat
Sex:
Number of Animals:
Vehicle:
Exposure time:
Value:
Method: other
Year: **GLP:** no data
Test substance: no data
Remark:

concentration (ppm)	exposure	symptoms of toxicity
315	no data	respiratory arrest after 2 min, death within 5-10 min
180	10 min	spasms within 5-15 min, respiratory arrest after 30 min
125	6-7 min	marked toxicity
110	30 min	respiratory arrest
95	60 min	marked toxicity, but survived
56	60 min	tolerable, but signs of toxicity
54	110 min	spasms
48	140	lethal
27-36	4-6 h	tolerable

Source: Imperial Chemical Industries PLC London (120) (128) (129)

Type: other
Species: dog
Sex:
Number of Animals:
Vehicle:
Exposure time:
Value: .17 - .7 mg/l
Method: other
Year: **GLP:** no data
Test substance: no data
Remark: 6 adult dogs were exposed to HCN at 0.17-0.7 mg/l for 1.75-10 min.; 3 dogs died 16-20 h after exposure, and the

survivors were sacrificed 24–28 h after exposure; the brains were examined microscopically, primarily in the regions of gray matter necrosis was diagnosed; the aereas most affected were the cerebral cortex, caudate nucleus and putamen, substantia nigra, globus pallidus, pulvinar of the thalamus, and the cerebellar cortex

Source: Imperial Chemical Industries PLC London (130)

Type: other: see remarks
Species: dog
Sex:
Number of Animals:
Vehicle:
Exposure time:
Value:
Method: other
Year: **GLP:** no data
Test substance: no data
Remark:

concentration (ppm)	exposure	symptoms of toxicity
115	30 min	respiratory arrest
90	no data	tolerable for h
35–65	no data	vomiting, spasms, recovery
30	no data	tolerable

Source: Degussa AG – ZN Wolfgang Hanau 1
Imperial Chemical Industries PLC London (120) (121)

Type: other: see remarks
Species: guinea pig
Sex:
Number of Animals:
Vehicle:
Exposure time:
Value:
Method: other
Year: **GLP:** no data
Test substance: no data
Remark:

concentration (ppm)	exposure time	symptoms of toxicity
725	14 min	tolerable
315	no data	lethal
200	90 min	tolerable
45	no data	increase in respiratory rate
7.5	2 h	tolerable

Source: Imperial Chemical Industries PLC London (120) (121) (131) (132)

Type: LCLo
Species: human
Sex:
Number of Animals:
Vehicle:
Exposure time: 1 hour(s)
Value: = 113 ppm
Method: other
Year: 1942 **GLP:** no data
Test substance: no data
Source: REPSOL QUIMICA, S.A. MADRID
(133)

Type: LCLo
Species: human
Sex:
Number of Animals:
Vehicle:
Exposure time: 2 minute(s)
Value: = 363 ppm
Method: other
Year: 1982 **GLP:** no data
Test substance: no data
Source: REPSOL QUIMICA, S.A. MADRID
(134)

Type: LCLo
Species: human
Sex:
Number of Animals:
Vehicle:
Exposure time: 10 minute(s)
Value: = 181 ppm
Method: other
Year: 1970 **GLP:** no data
Test substance: no data
Source: REPSOL QUIMICA, S.A. MADRID
(135)

Type: other
Species: monkey
Sex:
Number of Animals:
Vehicle:
Exposure time: 12 minute(s)
Value: 125 ppm
Method: other
Year: **GLP:** no data
Test substance: no data
Remark: marked toxicity (no further information available)
Source: Imperial Chemical Industries PLC London
(120)

Type: other
Species: monkey
Sex:
Number of Animals:
Vehicle:
Exposure time: 30 minute(s)
Value: .1 - .2 mg/l
Method: other
Year: **GLP:**
Test substance:
Remark: 7 cynomologus monkeys (Macaca fascilaris) were exposed to HCN gas derived from pyrolysis of polyacrylonitrile; at concentrations of HCN from about 0.1 to 0.2 mg/l the following symptoms of toxicity were observed: hyperventilation, rapid induction of a state of semiconsciousness accompanied by severe disruptive changes in respiration, EEG, and ECG
Source: Imperial Chemical Industries PLC London

(136)

5.1.3 Acute Dermal Toxicity

Type: LD50
Species: rabbit
Sex:
Number of Animals:
Vehicle:
Value:
Method: other
Year: **GLP:** no data
Test substance: no data
Remark: females; application as solution
LD 50 (intact skin): 6.89 mg/kg
LD 50 (abraded skin): 2.34 mg/kg
times to onset of signs of toxicity varied between 5 min. and 1 h; times to death ranged from 15 min. to around 6 h
Source: Imperial Chemical Industries PLC London

(109)

Type:
Species:
Sex:
Number of Animals:
Vehicle:
Value:
Method:
Year: **GLP:**
Test substance:
Remark: Los cianuros se absorben por la piel y superficies mucosas siendo muy peligrosa la inhalación, ya que son absorbidos a través de las mucosas de los bronquios y por los alveolos. Los vapores no son muy irritantes, pero son extremadamente venenosos. El líquido o sólido no es muy irritante, pero es

muy venenoso si es absorbido por la piel, ojos o pulmones.
Source: REPSOL QUIMICA, S.A. MADRID
(137) (138)

5.1.4 Acute Toxicity, other Routes

Type: LD50
Species: rat
Sex:
Number of Animals:
Vehicle:
Route of admin.: i.p.
Value: 2.23 mg/kg bw
Method:
Year: **GLP:** no data
Test substance: no data
Remark: females
Source: Imperial Chemical Industries PLC London
(109)

Type: LD50
Species: mouse
Sex:
Number of Animals:
Vehicle:
Route of admin.: i.p.
Value: = 2.99 mg/kg bw
Method:
Year: 1964 **GLP:** no data
Test substance: no data
Source: REPSOL QUIMICA, S.A. MADRID
(139)

Type: LD50
Species: mouse
Sex:
Number of Animals:
Vehicle:
Route of admin.: i.p.
Value: 2.8 mg/kg bw
Method:
Year: **GLP:** no data
Test substance: no data
Remark: females
Source: Imperial Chemical Industries PLC London
(109)

Type: LD50
Species: rabbit
Sex:
Number of Animals:
Vehicle:
Route of admin.: i.p.
Value:
Method:
Year: **GLP:** no data
Test substance: no data
Remark: females: 1.95 mg/kg
males: 1.72 mg/kg
Source: Imperial Chemical Industries PLC London
(109)

Type: LD50
Species: guinea pig
Sex:
Number of Animals:
Vehicle:
Route of admin.: i.p.
Value: 2.64 mg/kg bw
Method:
Year: **GLP:** no data
Test substance: no data
Remark: females
Source: Imperial Chemical Industries PLC London
(109)

Type: LD50
Species: mouse
Sex:
Number of Animals:
Vehicle:
Route of admin.: s.c.
Value: 4 mg/kg bw
Method:
Year: **GLP:** no data
Test substance: no data
Source: Imperial Chemical Industries PLC London
(108)

Type: LD50
Species: rabbit
Sex:
Number of Animals:
Vehicle:
Route of admin.: s.c.
Value: = 2.5 mg/kg bw
Method:
Year: 1964 **GLP:** no data
Test substance: no data
Source: REPSOL QUIMICA, S.A. MADRID

(140)

Type: LD100
Species: rat
Sex:
Number of Animals:
Vehicle:
Route of admin.: s.c.
Value: 3.5 mg/kg bw
Method:
Year: **GLP:** no data
Test substance: no data
Source: Imperial Chemical Industries PLC London

(108)

Type: LD100
Species: cat
Sex:
Number of Animals:
Vehicle:
Route of admin.: s.c.
Value: 1.1 mg/kg bw
Method: other
Year: **GLP:** no data
Test substance: no data
Source: Imperial Chemical Industries PLC London

(141)

Type: LDLo
Species: human
Sex:
Number of Animals:
Vehicle:
Route of admin.: s.c.
Value: = 1 mg/kg bw
Method:
Year: 1967 **GLP:** no data
Test substance: no data
Source: REPSOL QUIMICA, S.A. MADRID

(142)

Type: LD50
Species: rabbit
Sex:
Number of Animals:
Vehicle:
Route of admin.: i.m.
Value:
Method:
Year: **GLP:** no data
Test substance: no data
Remark: females: 0.95 mg/kg
males: 1.5 mg/kg
Source: Imperial Chemical Industries PLC London

(143)

Type: LD50
Species: rabbit
Sex:
Number of Animals:
Vehicle:
Route of admin.: i.m.
Value:
Method:
Year: **GLP:** no data
Test substance: no data
Remark: females: 0.50 mg/kg
males: 0.52 mg/kg
symptoms of toxicity appeared rapidly (2-7 min.) and included rapid breathing, vocalization, weakness of movements, uncoordinated head movements, ataxia, tremors, retrocollic spasms, convulsions, and respiratory arrest; post mortem features: alveolar and subpleural hemorrhages, congestion of the tracheal mucosa
Source: Imperial Chemical Industries PLC London

(109)

Type: LD50
Species: rat
Sex:
Number of Animals:
Vehicle:
Route of admin.: i.v.
Value: = .81 mg/kg bw
Method:
Year: **GLP:** no data
Test substance: no data
Source: REPSOL QUIMICA, S.A. MADRID

(144)

Type: LD50
Species: rabbit
Sex:
Number of Animals:
Vehicle:
Route of admin.: i.v.
Value: .59 mg/kg bw
Method:
Year: **GLP:** no data
Test substance: no data
Remark: females
symptoms of toxicity appear rapidly, typically within 10-30 sec., and include panting breathing, ataxia, convulsions, and coma; death occurrs within 2-12 min.
Source: Imperial Chemical Industries PLC London
(109)

Type: LD50
Species: cat
Sex:
Number of Animals:
Vehicle:
Route of admin.: i.v.
Value: = .81 mg/kg bw
Method:
Year: **GLP:** no data
Test substance: no data
Source: REPSOL QUIMICA, S.A. MADRID
(145)

Type: LD100
Species: rat
Sex:
Number of Animals:
Vehicle:
Route of admin.: i.v.
Value: 1.8 mg/kg bw
Method:
Year: **GLP:** no data
Test substance: no data
Source: Imperial Chemical Industries PLC London
(108)

Type: LD50
Species: rabbit
Sex:
Number of Animals:
Vehicle:
Route of admin.: other
Value: 1.04 mg/kg bw
Method:
Year: **GLP:** no data
Test substance: no data
Remark: Sytemic toxicity by ocular route:

Symptoms of toxicity appeared rapidly (30-60 sec.) and included rapid breathing, weak and ataxic movements, convulsions, tonic spasms, irregular and shallow breathing, coma, and cessation of breathing; cyanide irritation induced a conjunctival hyperaemia, which facilitated the absorption of the material, that passed into the systemic circulation without fist-pass hepatic detoxification
transocular toxicity; females
Source: Imperial Chemical Industries PLC London

(146)

5.2 Corrosiveness and Irritation

5.2.1 Skin Irritation

Species:
Concentration:

Exposure:
Exposure Time:
Number of Animals:
PDII:
Result:
EC classificat.:
Method:
Year: **GLP:**
Test substance:
Remark: El HCN en su forma tanto de vapor como de líquido se absorbe por la piel. La absorción se incrementa si la piel está deterioreda, cortada o húmeda.
El ácido cianhídrico líquido puede producir irritación en la piel.
Source: REPSOL QUIMICA, S.A. MADRID

(147) (148)

5.2.2 Eye Irritation

Species: rabbit
Concentration:
Dose:
Exposure Time:
Comment:
Number of Animals:
Result: irritating
EC classificat.: irritating
Method:
Year: 1983 **GLP:** no data
Test substance: no data
Remark: El ácido cianhídrico líquido puede ocasionar irritación ocular .
LD50 (ocu–rabbit): 1.04 mg/Kg
Source: REPSOL QUIMICA, S.A. MADRID
(149) (150)

Species: rabbit
Concentration:
Dose:
Exposure Time:
Comment:
Number of Animals:
Result: irritating
EC classificat.:
Method: other
Year: **GLP:** no data
Test substance: no data
Remark: local effects: initial moderate conjunctival hyperaemia with mild chemosis; in surviving animals, the conjunctival effects became more marked and, by 24 h, diffuse corneal opacification developed; these effects subside slowly, but mild conjunctivitis and keratitis were still present at 7 days post–instillation.
Source: Imperial Chemical Industries PLC London
(109)

5.3 Sensitization

–

5.4 Repeated Dose Toxicity

Species: rat **Sex:** male
Strain: Long-Evans
Route of admin.: inhalation
Exposure period: 12.5 min.
Frequency of treatment: 5 periods at 4-day intervals
Post. obs. period: the rats were killed within 2 weeks after the last exposure
Doses: 0.22 mg/l
Control Group: yes, concurrent no treatment
Method: other
Year: **GLP:** no data
Test substance: no data
Result: mild cardiotoxicity as measured by the magnitude of release of cardiac-specific creatine phosphokinase activity and by the number of ectopic heart beats induced by norphinephrine injection.
Source: Imperial Chemical Industries PLC London

(151)

Species: rat **Sex:** male/female
Strain: other: Carworth farm
Route of admin.: oral feed
Exposure period: 104 weeks
Frequency of treatment: continously in diet
Post. obs. period:
Doses: males: 3.2, 7.8 mg/kg/day; females: 4.3, 10.8 mg/kg/day
Control Group: yes, concurrent no treatment
Method: other
Year: **GLP:** no data
Test substance: no data
Remark: the diets had been fumigated with HCN, the average measured HCN concentrations were 76 mg/kg food (low dose) and 190 mg/kg food (high dose)
Result: no differences in growth curves, food consumption, hematological values, and survival were observed in the treated groups in comparison to controls; no treatment related pathological changes were found.
Source: Imperial Chemical Industries PLC London

(152)

Species: rabbit **Sex:** no data
Strain: other: Danish
Route of admin.: inhalation
Exposure period: 28 days
Frequency of treatment: continously
Post. obs. period:
Doses: 0.00055 mg/l (0.5 ppm)
Control Group: yes, concurrent no treatment
Method: other
Year: **GLP:** no data
Test substance: no data
Remark: no other parameters (see results) were examined in this study
Result: electron microscopic examination of the myocardium did not reveal a significant difference between exposed and control rabbits.
Source: Imperial Chemical Industries PLC London

(153)

Species: dog **Sex:** no data
Strain: no data
Route of admin.: inhalation
Exposure period: 30 min.
Frequency of treatment: 7–19 periods at intervals of 2–8 days
Post. obs. period:
Doses: 0.05 mg/l
Control Group: no data specified
Method: other
Year: **GLP:** no data
Test substance: no data
Remark: the author concluded that the lesions resulted of anoxia caused by the inhibition of cytochrome oxidase.
Result: symptoms of toxicity: dyspnea, nausea, exaggerated intestinal peristalsis, diarrhea followed by tremors, loss of equilibrium, convulsions, death (within 1–2 months); microscopic examination of the brain revealed: vasodilation and hemorrhages that were pronounced in the central gray nuclei, brain stem, bulb, and medulla cervicalis; cytologic changes were also diagnosed in the Purkinje cells of the cerebellum and in the bulbar gray nuclei.
Source: Imperial Chemical Industries PLC London

(154)

5.5 Genetic Toxicity 'in Vitro'

Type: Ames test
System of testing: Salmonella typhimurium DW 379
Concentration:
Metabolic activation: with and without
Result: negative
Method: other
Year: 1989 **GLP:** no data
Test substance: no data
Source: Imperial Chemical Industries PLC London
(155)

Type: Ames test
System of testing: Salmonella typhimurium TA 98, 100
Concentration:
Metabolic activation: with and without
Result: positive
Method: other
Year: 1989 **GLP:** no data
Test substance: no data
Remark: HCN was marginally positive only in TA 100 without metabolic activation
Source: Imperial Chemical Industries PLC London
(156)

Type: Ames test
System of testing: Salmonella typhimurium, TA100, TA1535, TA97 & TA98
Concentration:
Metabolic activation: with and without
Result: negative
Method: other: Test Method: Ames B N (1975)
Mutation Research 11 347-364
Year: 1988 **GLP:** no data
Test substance: other TS: Acetone cyanohydrin
Remark: Acetone cyanohydrin readily dissociates to acetone and hydrocyanic acid (HCN), the half life of a 0.1% solution has been estimated as 0.13 hrs at pH 6.8.

Minimum concentration of test substance at which toxicity to bacteria was observed in the presence or absence of S9 mix was not indicated.
Source: Imperial Chemical Industries PLC London
(157)

Type: Ames test
System of testing: S. typhimurium TA97, TA98, TA100, TA1535
Concentration: 0.3 – 333 ug/plate
Metabolic activation: with and without
Result: negative
Method: other: according to Zeiger E et al., Environ. Mol. Mutagen. 19 (Suppl. 21), 2-141 (1992)
Year: 1992 **GLP:** no data
Test substance: other TS: Sodium cyanide
Remark: Aroclor-induced rat and hamster S9-mix was used at concentrations of 10 and 30%.
Source: Imperial Chemical Industries PLC London

(158)

Type: Ames test
System of testing: Salmonella typhimurium, TA98, TA100, TA1535, TA1537, TA1538 & TA98
Concentration: 0, 6.1, 18.3, 55, 165 & 495 microgrammes/plate
Metabolic activation: with and without
Result: negative
Method: other: similar to OECD. Plate incorporation assay using the method of Ames, McCann and Yamasaki (1981).
Sensitivity of tester strains confirmed with positive control chemicals 2-aminoanthracene and aminoacridine.
Year: 1983 **GLP:** yes
Test substance: other TS: Acetone cyanohydrin
Remark: Acetone cyanohydrin readily dissociates to acetone and hydrocyanic acid (HCN), the half life of a 0.1% solution has been estimated as 0.13 hrs at pH 6.8.
Concentration of test substance at which toxicity to bacteria was observed: with metabolic activation: 495 microgrammes/plate (all strains) without metabolic activation: 165 (TA1537 and TA1538) and 495 plate (all strains).
Source: Imperial Chemical Industries PLC London
Test substance: 98.5% acetone cyanohydrin. Certificate of analysis.

(159)

Type: Cytogenetic assay
System of testing: Chinese hamster cells
Concentration:
Metabolic activation: with and without
Result: negative
Method: other
Year: 1989 **GLP:** no data
Test substance: no data
Source: Imperial Chemical Industries PLC London

(160)

Type: Mammalian cell gene mutation assay
System of testing: Chinese hamster cells CHO-K1-BH4
Concentration: 100 – 950 microgrammes/plate
Metabolic activation: with and without
Result: negative
Method: other: Mammalian Cell Forward Gene Mutation Assay using the method of O'Neill et al, 1977 and Snee and Irr, 1981
Year: 1983 **GLP:** yes
Test substance: other TS: Acetone cyanohydrin
Remark: Acetone cyanohydrin readily dissociates to acetone and hydrocyanic acid (HCN), the half life of a 0.1% solution has been estimated as 0.13 hrs at pH 6.8.
Tested to levels of at least 10% survival and with plating efficiency in control cultures of at least 50%. Sensitivity of cell line concurrently established with ethylmethane sulphonate (200 microgrammes/ml) and dimethyl nitrosamine (100 microgrammes/ml)

Minimum concentration of test substance at which toxicity to bacteria was observed (with and without a 2% S-9 preparation):

100 microgrammes/ml (100% survival), 500 microgrammes/ml (70% survival), 700 microgrammes/ml (50% survival) 850 microgrammes/ml (20% survival) and 950 microgrammes/ml (10% survival).
Source: Imperial Chemical Industries PLC London
Test substance: 98.5% acetone cyanhydrin. Certificate of analysis.
(159) (161) (162)

Type:
System of testing:
Concentration:
Metabolic activation:
Result:
Method:
Year: **GLP:**
Test substance:
Remark: Mutagénico potencial. Se aprecian roturas cromosómicas en vicia faba.
Source: REPSOL QUIMICA, S.A. MADRID
(163)

5.6 Genetic Toxicity 'in Vivo'

Type:
Species: rat **Sex:**
Strain: Sprague–Dawley
Route of admin.: gavage
Exposure period:
Doses: 0, 1.5 & 15 mg/kg
Result:
Method: other: US EPA Health Effects guidelines, EPA Report 560/5–83–001.
Year: 1983 **GLP:** yes
Test substance: other TS: Acetone cyanohydrin
Remark: Acetone cyanohydrin readily dissociates to acetone and hydrocyanic acid (HCN), the half life of a 0.1% solution has been estimated as 0.13 hrs at pH 6.8.
Method:
Six animals per sex group at 6, 12, 24 and 48 hours after dosing. Body weights recorded before dosing and at 24 and 48hr time points. Bone marrow cells were processed according to the modified techniques described by Evans (Cytological methods for detecting chemicals mutagens, 4, Ed A, Hollaender, Plemun Press, N.Y., 1–30, 1976) and Killian et al (Handbook of mutagen testing, Elsevier/North Holland, Amsterdam, 234–260, 1977).

Animals were observed for general appearance, behaviour, toxic and pharmacological effects twice daily or prior to sacrifice.

Tested approximately to the established LD50 of acetone cyanohydrin in the rat. Although no gross signs of toxicity were apparent 17mg/kg had been established from a previous study to approximate the oral LD50. Acetone cyanohydrin demonstrates a steep dose response curve for acute toxicity with little or no signs of toxicity at sub–lethal doses. Non clastogenic. No statistically significant increase in the frequency of chromasomal aberrations compared with controls at any dose level.
Source: Imperial Chemical Industries PLC London
Test substance: 98.5% acetone cyanohydrin. Certificate of analysis.

(164)

5.7 Carcinogenicity

Species: **Sex:**
Strain:
Route of admin.:
Exposure period:
Frequency of treatment:
Post. obs. period:
Doses:
Result:
Control Group:
Method:
Year: **GLP:**
Test substance:
Remark: No se han realizados estudios de carcinogenicidad.
Source: REPSOL QUIMICA, S.A. MADRID

5.8 Toxicity to Reproduction

Type: Fertility
Species: rat **Sex:** male
Strain: Sprague-Dawley
Route of admin.: inhalation
Exposure Period: 6 hrs/day
Frequency of treatment: 5 days/week
Premating Exposure Period
male: 48 days
female: 0 days
Duration of test: 69 days
Doses: 10, 28.5 & 57.2 ppm
Control Group: yes, historical
NOAEL Parental: 57.2 ppm
Method: other: similar to OECD
Year: 1982 **GLP:** yes
Test substance: other TS: Acetone cyanohydrin
Remark: Acetone cyanohydrin readily dissociates to acetone and hydrocyanic acid (HCN), the half life of a 0.1% solution has been estimated as 0.13 hrs at pH 6.8.
Male Sprague Dawley rats were exposed by the inhalation route and mated with untreated females to assess male fertility. Exposure of males was continued through the day of the last mating opportunity (58 exposure days). Animals were exposed in 10 M3 Rochester type chambers. Males were weighed and given a thorough physical examination once per week and assessed for clinical signs of toxicity before and after exposure. Males were sacrificed at the end of the study, about three weeks after the last exposure. The tissues and organs of the thoracic, addominal and scrotal cavities were examined for gross lesions and testes, epididymides, prostrate glands and seminal vessicles preserved.

Mated females were necropsied on gd13 and external surfaces,

tissues and organs of the thoracic and abdominal cavities examined. Pregnancy status was determined as was the number of total nidations, number of resporptions, live implantations and corpora lutea. No adverse toxic effects were observed in male rats exposed by the inhalation route to acetone cyanohydrin at exposure concentrations up to 60 ppm using a 6 hour/day, 5 day/week schedule for 58 days.

In particular, no effects were observed on body weight, clinical signs or lesions detectable at necropsy. Red nasal discharge and encrustations consistent with slight irritancy observed in the 90 day inhalation study also in the rat. No treatment relates male fertility effects were observed in any exposure level groups. Acetone cyanohydrin did not exhibit reproductive toxicity in male rats exposed by inhalation to up to 60 ppm.

Source: Imperial Chemical Industries PLC London
Test substance: 98.5% acetone cyanohydrin. Certificate of analysis.

(165)

Type: Fertility
Species: rat **Sex:** female
Strain: Sprague-Dawley
Route of admin.: inhalation
Exposure Period: 6 hrs/day
Frequency of treatment: 5 day/week
Premating Exposure Period
male: 0 days
female: 21 days
Duration of test: 36 days
Doses: 10.7, 30.4 & 58.6 ppm
Control Group: yes, historical
NOAEL Parental: 58.6 ppm
Method: other
Year: 1982 **GLP:** yes
Test substance: other TS: Acetone cyanohydrin
Remark: Acetone cyanohydrin readily dissociates to acetone and hydrocyanic acid (HCN), the half life of a 0.1% solution has been estimated as 0.13 hrs at pH 6.8.
Method:
Female Sprague Dawley rats were exposed by the inhalation route and mated with untreated males to assess female fertility. Exposure of females was continued until the day of mating. Animals were exposed in 10 M3 Rochester type chambers. Females were weighed and given a thorough physical examination once per week and clinical signs recorded before and after exposure. Females were sacrificed at mid gestation (gd13-15). The tissues and organs of the thoracic and abdominal cavities were examined for gross lesions, pregnancy status was determined and, for pregnant females, nidation sites classified and counted, and corpora lutea counted. No signs of systemic toxic effects were observed in females at exposure levels up to 58.6 ppm as judged by body weights or lesions detectable at necropsy. Although there was an apparent dose response in the numbers of animals exhibiting red nasal discharge or encrustations

in the third week of exposure, no other treatment related effects were observed.

Red nasal discharge and encrustations are consistent with slight irritancy observed in the 90 day inhalation study also in the rat.

No female fertility effects were observed at any exposure level. Acetone cyanohydrin does not produce female fertility effects when administered by inhalation to female Sprague Dawley rats at exposures up to 60 ppm.

Source: Imperial Chemical Industries PLC London
Test substance: 98.5% acetone cyanohydrin. Certificate of analysis.

(166)

Type:
Species: **Sex:**
Strain:
Route of admin.:
Exposure Period:
Frequency of treatment:
Duration of test:
Doses:
Control Group:
Method:
Year: **GLP:**
Test substance:
Remark: No se conocen efectos tóxicos en la reproducción en mamíferos.
Source: REPSOL QUIMICA, S.A. MADRID

5.9 Developmental Toxicity/Teratogenicity

Species: rat **Sex:** female
Strain: other: Charles river
Route of admin.: gavage
Exposure period:
Frequency of treatment: daily (gd 6 through 15)
Duration of test: 9 days
Doses: 1, 3 & 10 mg/kg/day
Control Group: yes, concurrent vehicle
NOAEL Maternalt.: 1 mg/kg bw
NOAEL Teratogen.: 10 mg/kg bw
Method: other
Year: 1982 **GLP:** yes
Test substance: other TS: Acetone cyanohydrin
Remark: Acetone cyanohydrin readily dissociates to acetone and hydrocyanic acid (HCN), the half life of a 0.1% solution has been estimated as 0.13 hrs at pH 6.8.
Method:
Timed-pregnant 5 rats were dosed at a constant volume of 5ml/kg. Group sizes consisted of 25 animals and 25 litters were examined per group (no premature deaths). Clinical observations were performed daily and body weights recorded

on gd 0, 6, 10, 12, 16 and 20. At scheduled necropsy on gd 20, dams were sacrified and the implatation sites evaluated (number and location of viable and non-viable fetuses, early and late resorptions and number if total implantations and corpora lutea), abdominal and thoraciec cavities were examined for grossly evident morphological changes. Fetuses were removed, weighed, sexed, tagged and examined for soft tissue malformations using the method if Wilson (Teratology-Principles and techniques Univ Chicago Press Chicago, I 262-277 1965). Remaining fetuses were eviscerated, fixed and stained for subsequent skeletal examination by a method similar to that described by Dawson (Stain technol 1 123-124, 1926).

Survival of the dams was 100% for the control and all treatment groups. The antemortem and necropsy observations for treated groups was comparable to those for control groups. Signs of maternal toxicity was evident by slight reduction in body weight gain, during the overall treatment and gestation periods (days 6 to 15 and 0 to 20 respectively), in the 3 and 10 mg/kg/day group. Statistically significant differences in corpora lutea/dam and total implantation/dam ratios occurred between the 10 mg/kg/day and control groups. However, because these were pretreatment parameters they were not considered compound related. The viable fetus/dam, post implantation losses/dam, mean fetal body weight and fetal sex distribution in the 10 mg/kg/day group and all cesarean section observation parameters for the 1 and 3 mg/kg/day dosage groups were comparable with controls. The incidence of fetal malformations and developmental variations was comparable between test and control groups. Acetone cyanohydrin did not elicit a teratogenic response when administered by the oral route to Charles River rats at 10 mg/kg/day.

Non teratogenic to the rat even up to maternally toxic doses.

Source: Imperial Chemical Industries PLC London

Test substance: Acetone cyanohydrin 98.5%. Certificate of analysis.

(167) (168) (169)

Species: Syrian hamster **Sex:** female
Strain: other: LKV
Route of admin.: infusion
Exposure period: day 6 to day 9 of gestation
Frequency of treatment: continuously
Duration of test: animals killed on day 11 of gestation
Doses: 0.126, 0.127, 0.1275, 0.1295 mmol/kg/h
Control Group: yes, concurrent vehicle
Method: other
Year: **GLP:** no data
Test substance: other TS: Sodium cyanide
Remark: 5-7 hamsters/group were tested via infusion from minipumps implanted subcutaneously at the back of the neck 0.126, 0.127, 0.1275, 0.1295 mmol/kg/h = 6.18, 6.23, 6.25, 6.35 mg/kg/h.
Infusion by minipumps implanted subcutanously to the back of the neck is a non-physiological route of exposure and is not recognised as being relevant for the assessment of teratogenic hazard of industrial chemicals. Many, if not all of the effects observed could have equally been due to systemic cyanide poisoning, including anoxia, as a result of the high doses employed.

The steep dose response curve for acute cyanide posioning together with the reported signs of toxicity would suggest that the dams were severely compromised.
Result: Mild maternal toxicity was observed in about half of the hamsters in the lower dose groups, in the highest dose group signs of toxicity inclusing weight loss, dyspnea, ataxia, incordination, and hypothermia were observed in all dams; all applied doses produced high incidences of malformations and resorptions in the offspring; the most common anomalies seen were neural tube defects, including nonclosure, exencephaly and encephalocoele; other defects as hydropericardium and crooked tail and small limbs were observed less frequently.
Source: Imperial Chemical Industries PLC London

(170)

Species: other: Lepomis sp. **Sex:** male/female
Strain:
Route of admin.: other: disuelto en agua
Exposure period: 289 días
Frequency of treatment:
Duration of test:
Doses: 5.2 ug/l
Control Group: yes
Method: other
Year: 1980 **GLP:** no data
Test substance: no data
Remark: El ensayo de reproducción se realizó con peces Lepomis sp. adultos. Durante los 289 días los peces no se reprodujeron, en los grupos de control se produjeron 13 frezas. No existió relación dosis-repuesta.
Source: REPSOL QUIMICA, S.A. MADRID

(171)

Species: other: trucha arcoiris **Sex:** male/female
Strain:
Route of admin.: other: disuelto en agua
Exposure period: 7 días
Frequency of treatment:
Duration of test:
Doses: 0, 0.01, 0.02, 0.03 mg/l
Control Group: no data specified
Method: other
Year: 1984 **GLP:** no data
Test substance: no data
Remark: Ensayo con peces (trucha arcoiris) en hembras maduras. Se apreció una reducción en los niveles plasmáticos de calcio y de fosfoproteína fosforilada, calculandose los índices hepatosomáticos, como indicadores de la producción de yema en el huevo. Se observó un descenso en los niveles de cálcio y en los índices hepatosomáticos en hembras y machos. Los resultados no son concluyentes en cuanto a como se vé afectada la formación de la yema durante la vitelogénesis temprana y la reproducción de las hembras, por este desdenso observado.
Source: REPSOL QUIMICA, S.A. MADRID

(172)

Species: **Sex:**
Strain:
Route of admin.:
Exposure period:
Frequency of treatment:
Duration of test:
Doses:
Control Group:
Method:
Year: **GLP:**
Test substance:
Remark: Sodium and potassium salts of cyanide will readily dissociate with the resultant formation of molecular (undissociated) hydrocyanic acid (HCN). Solutions of cyanides are acutely toxic to all organisms. It is believed that this toxicity is predominantly attributed to dissociation of the cyanide salt with resultant formation of molecular (undissociated) HCN. Hydrocyanic acid by virtue of its small size and lack of charge readily penetrates cell membranes. Internally the mechanism of toxicity is believed to be by formation of cyanide (CN-).
Source: Imperial Chemical Industries PLC London

(79)

5.10 Other Relevant Information

Type: Distribution
Remark: 8 mg of cyanide radical/kg bw (8.3 mg HCN/kg bw) was injected into the musculature of the hind limbs of adult albino rabbits. 30 min. after death concentrations of cyanide in blood, serum, and various tissues were measured (ug CN/100 g wet tissue or ug CN/100 ml blood or serum):

skeletal muscle	35
kidney	75
liver	149
spinal cord	49
brain	145
whole blood	685
serum	275

Source: Imperial Chemical Industries PLC London

(143)

Type: Toxicokinetics
Remark: Absorption, distribution, metabolism, excretion:
HCN is rapidly absorbed into the body following inhalation, across the gastrointestinal mucosa after oral intake, and through the skin and the eyes after direct contact; the amount of cyanide available for absorption is a function of the amount to which the organism is exposed, determined by the exposure concentration, exposure time, and the frequency of exposures.
Once absorbed the cyanide is rapidly distributed by the blood throughout the body; the plasma concentration of cyanide is the major quantitative determinant of the onset and severity of toxicity; the routes of exposure clearly

influence the differential distribution of absorbed dose; inhalation provides the most rapid route of entry, sometimes resulting in symptoms of toxicity after seconds; cyanide has not been shown to accumulate in the blood or in the tissues following chronic exposure.
The major pathway for detoxification is by the enzymic transsulphuration of HCN to thiocyanate, which is excreted in the urine; there are two enzyme systems responsible for this metabolic process: thiosulphate-cyanide sulphtranspherase (rhodanese) and beta-mercaptopyruvate-cyanide sulphtranspherase; other minor pathways are: spontaneous reaction with cystine to produce 2-aminothiazoline-4-carboxylic acid, which tautomerizes to 2-amino-4-thiazolidine-carboxylic acid and is excreted with the urine and combination with hydroxycobalamin (vitamin B12) to form cyanocobalamin, which is excreted in the urine and bile; some cyanide enters the metabolism of 1-carbon compounds, and CO2 is eliminated in expired air; small amounts of absorbed cyanide are excreted unchanged in the breath, saliva, sweat and urine.

Source: Imperial Chemical Industries PLC London
(173) (109) (174) (175) (176) (177) (178)

Type: other: Mechanism of toxicity

Remark: HCN dissociates in vivo, releasing cyanide ion, that disrupts enzyme systems by complexing with heavy metal ions contained in metalloenzymes; oxidative enzymes and coenzymes in which ferric ions are present are particularly sensitive; the acute toxicity of HCN is reported to result from cytotoxic anoxia through the inhibition of cytochrome oxidase, the terminal mitochondrial respiratory enzyme; cyanide is believed to penetrate a protein crevice of cytochrome oxidase and bind initially to the protein; subsequently it binds to the trivalent iron of the enzyme forming a relatively stable complex; as result of this complex forming respiration is inhibited because oxygen utilization is impaired; the reduction in oxidative phosphorilation leads to lactate acidosis; however in severe, massive cyanide poisoning the dose usually greatly exceeds the minimal concentration necessary to inhibit cytochrome oxidase; under these conditions it is more reasonable that the toxicodynamic effect of cyanide involves more than one biochemical lesion; in addition to the binding to cytochrome oxidase, as the main target enzyme, cyanide is a potent inhibitor of a large number of enzyme systems: succinic dehydrogenase, xanthine dehydrogenase, xanthine oxidase, D-amino acid oxidase, superoxide dismutase, carbonic anhydrase, 2-keto-4-hydroxyglutarate aldolase, acetoacetate decarboxylase, lipoxygenase, nitrite reductase, ribulose diphosphate carboxylase, glutamate decarboxylase; beside the combination with metal ions, mechanisms of enzyme inhibition include formation of cyanohydrins with carbonyl compounds required for enzyme activity, slow irreversible inhibition due to scission of essential disulphide links, elimination of sulphur as thiocyanate and cyanide addition to Schiff base aldimine with formation of an aminonitrile; cyainde also binds to methemoglobin and hydroxycobalamin; in

addition there are other biochemical processes affected by cyanide, i.e. alteration of carbohydrate metabolism, resulting in an increased breakdown of glycogen and a shunting of glucose to the pentose phosphate pathway by decreasing the rate of glycolysis and inhibiting the tricarboxylic cycle; furthermore cyanide affects calcium transport and lipid peroxidation; all these reactions are believed to contribute to the toxicity of cyanide.

Source: Imperial Chemical Industries PLC London (109) (176) (177)

Type: other: Target organ toxicity

Remark: The major target side for cyanide is the brain; in acute lethal cyanide poisoning, the levels of cyanide are consistently high in the brain (parenchyma and blood of the intracerebral vessels), irrespectively of the route of exposure or species; the resulting neuronal hypoxia, decreased brain ATP-levels, and lactic acidosis induce disturbances of perception and consciousness, and loss of control functions.
Beside the brain as the primary functional target organ, also cardiovascular and respiratory effects were described in humans and animals following exposure to cyanide; clinical signs and symptoms include EKG abnormalities, increased blood levels of cardiac-specific creatinine phosphatase, and altered cardiac and respiratory rate; in most cases these effects are indirect neurogenic-mediated and can be attributed to early cyanide induced changes in the cardiac and vasomotor centers of the brain, and the reflex stimulation of cardio-inhibitory, cardio-accelerator, and vasomotor centers via carotid artery and aortic bodies; some in vivo and in vitro data show, that cyanide has also direct effects on the heart.
Beside the described organotropism also the thyroid gland can be affected by cyanide; thiocyanate, an important metabolite of cyanide, markedly inhibits the accumulation of iodine by the gland, thus decreasing its ability to maintain a concentration of iodine above that of the blood; also the iodination process can be inhibited by thiocyanate; as consequence, the organic binding of glandular iodine is interfered.

Source: Imperial Chemical Industries PLC London (109) (179) (180) (181) (177) (182) (183)

5.11 Experience with Human Exposure

Remark: Trabajadores expuestos durante años al HCN en bajas concentraciones, experimentaron un aumento de la glándula tiroidea, probablemente debido a los efectos del metabolismo del tiocianato (producto de la detoxificación del HCN).
Trabajadores expuestos durante más de 7 años a concentraciones de 4-12ppm de HCN, mostraron aumento en dolores de cabeza, debilidad, pérdidas de olfato y gusto, lacrimación, irritación de garganta, cólicos abdominales e inestabilidad nerviosa.

Source: REPSOL QUIMICA, S.A. MADRID

(184)

Remark: Toxicity:
HCN has been used in many suicides and homicides; beside that, there are many sources of exposure, that lead to accidental poisoning in humans; cyanide is present in certain household products, such as silver polish, fertilizers, and rat poison; it can be generated during industrial processes like electroplating, petroleum refining, metallurgic and photographic processing; it is also used as a fumigant to exterminate rodents and insects (i.e. in mills and warehouses); cyanide may be released from various compounds (i.e. nitrogen containing plastics like polyurethanes and natural compounds like wool and silk) by chemical reactions of pyrolysis, therefore firefighters may be exposed during a fire; natural sources of HCN were the pits and seets of different fruits including cherries, plums, apricots, peaches, and pears; cabbage, spinach and almonds can contain measurable amounts of HCN; a iatrogenic source of cyanide poisoning is the vasodilator sodium nitroprusside, that is metabolized by releasing HCN into the bloodstream.
HCN can be rapidly fatal once it overcomes the ability of the body to cope; the clinical signs and symptoms reflect the extent of cellular hypoxia and include weakness, giddiness, dizziness, headache, confusion, a drop in blood pressure, sometimes nausea and vomiting; breathing is rapid and deep at first, then becomes slow and gasping; the skin appears bright pink or red; the patient may feel an irregular heart beat and tightness of the chest; uncontrollable urination and bowel movements may occur, unconsciousness and death follow; after oral ingestion local effects like burning of the tongue, salivation, nausea, and gastrointestinal irritations are reported; an odour of bitter almonds may be in the breath and vomit.
In adults breathing cyanide in concentrations of 0.2–0.3 mg/l is immediately fatal, whereas inhaling 0.12–0.15 mg/l cause death in about 1 h.; even when cyanide is absorbed through the skin or ingested orally, symptoms of toxicity can occur within minutes; the minimum lethal dose of cyanide after oral ingestion is about 50 mg; injection of about 25 mg is probably sufficient to cause death.
In humans, chronic low level cyanide exposure i.e. through cassava (cyanogenic plant) consumption and possibly through tobacco smoke inhalation has been associated with a number of diseases such as neuropathy, tobacco amblyobia, and Leber’s hereditary optic atrophy; it has been discussed, that defects in the metabolic conversion of cyanide to thiocyanide, as well as nutritional deficiencies of proteins and vitamin B12 play a role in the developement of these described disorders;a wide range of symtoms have been reported in workers after occupational long–term exposure to low cyanide levels, often less than 0.01 mg/l;they include persistent running nose, weakness, dizziness, gigginess, headache, nausea, abdominal pain, vomiting, throat irritation, changes in taste and smell, muscle cramps, weight loss, flushing of the face, and enlargement of the

thyroid gland.
It has been suggested, that chronic poisoning is rare, because only certain people are susceptible; HCN is metabolised to thiocyanate, which is normally excreted with the urine; however for some reasons, not yet fully understood, some people are not able to eliminate thiocyanate from the body as readily as others; they may then suffer from symptoms caused by the accumulation of thiocyanate and health effects reported to be caused by long-term exposure of cyanide are similar to those symptoms; in people exposed to low levels of cyanide over a long period of time high thiocyanate concentrations were found.

Source: Imperial Chemical Industries PLC London
(185) (109) (186) (187) (188) (189) (190) (191) (192) (193) (194) (195) (196)

Remark: Hydrogen cyanide is the dissociation product of cyanide salts and the industrial intermediate acetone cyanohydrin. Hence experience with occupational exposure during the manufacture and use of cyanide salts is relevent to the assessment of the long term health effects of HCN.

There have been reports since the 19th cenury of the suspected effects of chronic cyanide exposure. The value of many of these is marred by their anecdotal nature and the lack of any knowledge of the extent of exposure. Two studies E1 Ghawabi et al. 1975 and Blanc and Hogan et al, 1985 are most recent examples. As the available literature is suggestive of some adverse effects from occupational exposure to cyanide, but there is little to indicate the threshold to development of these sysmptoms ICI conducted a cross-sectional study of the health of its cyanide salt workers.

Source: Imperial Chemical Industries PLC London

Remark: Electroplating workers

El Ghawabi et al, reported a study in which the effects of chronic cyanide exposure in 36 weeks from the electroplating sections of three Egyption factories was compared with a control group.

Increased percentages of haemoglobin and lymphocyte count were present in all exposed workers, in addition to punctate basophilia in 28 workers. The latter is not typical of reports of cyanide exposure. Cyanomethaemoglobin was also found to be characteristic. Apart from other complaints, two men with psychosis similar to one case reported in theraputic intoxication were found.

Twenty of the workers had thyroid enlargements to a variable degree and consistent, in two whom it resembled lymphoadenoid goitre. The thyroid gland may be metabolically be inhibited by thiocyanate, the sulphur metabolite of cyanide. The maximum exposure was reported as 12.4 ppm. The most commonly complained symptoms were headache, weakness and change in taste and smell. Such

highly subjective symptoms are typical of the syndrome which authors attribute to chronic poisoning. Electroplating workers, by the nature of the work, are subject to occupational exposure levels that may be vary widely from task to task and with time. It is likely therefore that many of these recorded symptoms were due not only to chronic exposure to relatively high levels, but also to repeated mild attacks of acut poisoning (Saia et al, 1970 Rilien Sull'intossicanzione cronica da cianum. Med. lavoro. 61 11 580-586 (Ital).

Source: Imperial Chemical Industries PLC London

(191)

Remark: Silver-reclaiming workers:
Blanc et al in 1985 reported their investigation of a silver reclaiming works where one worker had died. Thirty six former employees were studied. They had been exposed long term to excessive levels of cyanide (15 ppm estimated TWA from results taken 24hrs after plant closure). The study involved physical examination, laboratory studies, and a questionnaire to determine exposure, current and past symptoms. The questionnaire showed that during employment there was a high prevalence of dose-related symptoms indicative of acute cyanide poisoning. Some symptoms occurring seven or more months after exposure had ceased also exhibited a dose related trend. Mild abnormalities of vitamin B12, folate and thyroid function were detected suggested long term cyanide effects (Vitamin B12 will bind cyanide forming cyanocobalamin).
The authors state that symptoms were due to both chronic exposure to high levels and acute cyanide poisoning.

Source: Imperial Chemical Industries PLC London

(188)

Remark: Cyanide salt production workers:

Leeser et al in 1990 reported a cross-sectional study of the health of cyanide salt production workers. Sixty three cyanide workers were compared with one hundred control workers from a diphenyl oxide plant. All workers had full medical examinations, routine blood tests and blood samples taken for blood cyanide and carboxyhaemoglobin. In addition blood levels of vitamin B12 and thyroxin (T4) were measured. Occupational personal hygiene monitoring for cyanide exposure showed that levels were 0.01 to 3.6 mg/m3 (Total cyanide ie HCN and dust). Draeger tube measurements for the workplace were between 1 and 3 ppm HCN. Blood cyanide levels in exposed workers whilst still low were higher than in control workers. Blood cyanide levels also showed seasonal variation with levels in the autumn being higher than in the spring, probably due to somewhat higher exposures. Haemaglobin tended to be higher in exposed workers as did lymphocyte count, although neither was pathologically raised. No relationship between the haematological parameters and exposure and the absence of a dose-response indicated cyanide exposure was not causal. Vitamin B12 and thyroxin levels showed no difference between

exposed and control groups. The result of clinical histories and examinations also showed no inter-group differences. Cyanide workers exposed chronically to levels of cyanide up to 1-3 ppm were generally as healthy as their non-cyanide producing colleagues.

An Occupational No Observable Effect Level of between 1 and 3 ppm is indicated.

Source: Imperial Chemical Industries PLC London

(197)

Remark: Case report of apnoe and skin burns experienced by one employee after exposure to HCN, sulphuric acid and olefine. Memory impairment and lack of drive was present six months later.

Source: Imperial Chemical Industries PLC London

(38)

Remark: Worker experience at BASF:
From 1969 to 1992 a total of 4 cases were hospitalised for further treatment after exposure to HCN. They experienced dyspnoe, dizziness and nausea.

Source: Imperial Chemical Industries PLC London

(198)

Remark: Case report of apnoe and skin corrosion in worker after accidental exposure to a mixture of hydrogen cyanide, sulfiric acid, and olefine. After six still a lack of drive and memory was observed.

Source: BASF AG Ludwigshafen

Reliability: (2) valid with restrictions
acceptable study, meets basic scientific principles

(199)

Remark: From 1969 to 1992 a total of 4 cases with dyspnoe, dizziness, and nausea after accidental exposure to hydrogen cyanide were observed, which were sent to the clinic for further treatment.

Source: BASF AG Ludwigshafen

Reliability: (2) valid with restrictions
basic data given, acceptable ristrictions

(200)

Remark: Report on one case of nausea, vomiting, and dizziness after accidental inhalativ exposure to hydrogen cyanide, which was sent for further treatment to the clinic.

Source: BASF AG Ludwigshafen

Reliability: (2) valid with restrictions
basic data given, acceptable restrictions

(201)

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7.1 Risk Assessment

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Social Europe

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

SCOEL/SUM/115

June 2010

European Commission

Table of Contents

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

8 hour TWA	: 1 mg/m³ (expressed as cyanide)
STEL (15 min)	: 5 mg/m³
Additional classification	: Sk (Skin notation)

Substance Identification and Properties

Chemical name	Hydrogen cyanide (HCN)	Potassium cyanide (KCN)	Sodium cyanide (NaCN)
IUPAC name	Hdyrocyanic 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/m³ = 0.890 ppm 1 ppm = 1.124 mg/m³		

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/m³; people sensitive to odour). Many people cannot perceive the odour at all (Holland and Kozlowski, 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^3 (mean 0.45 mg/m^3). In the breathing zone of the general workroom atmosphere in the same factory, the concentration ranged from 0.1 to 0.2 mg/m^3 (mean 0.15 mg/m^3) (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^3 (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^3. In a work area of other plating facilities it ranged from 1.7-4.3 mg/m^3 (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^{-4} 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 actvities 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 □-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*)

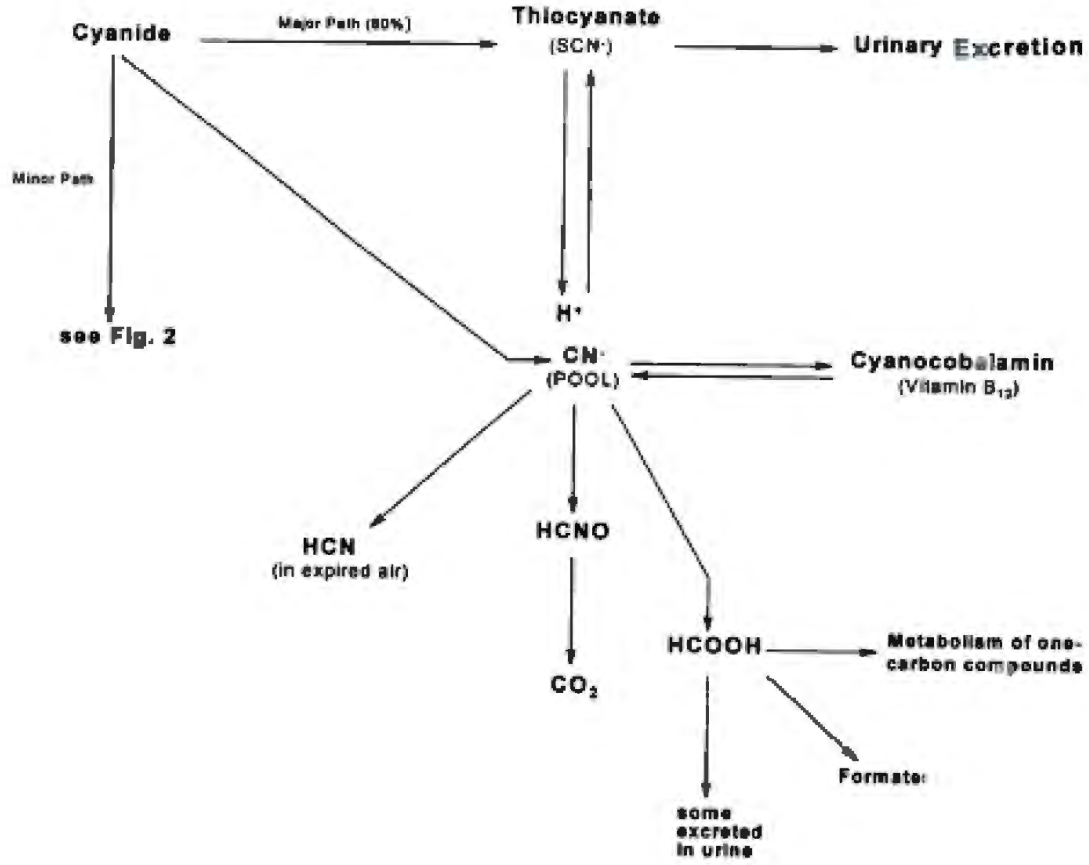

Fig 1: Basic processes involved in the metabolism of cyanide in mammals (Health Council of Netherlands, 2002)

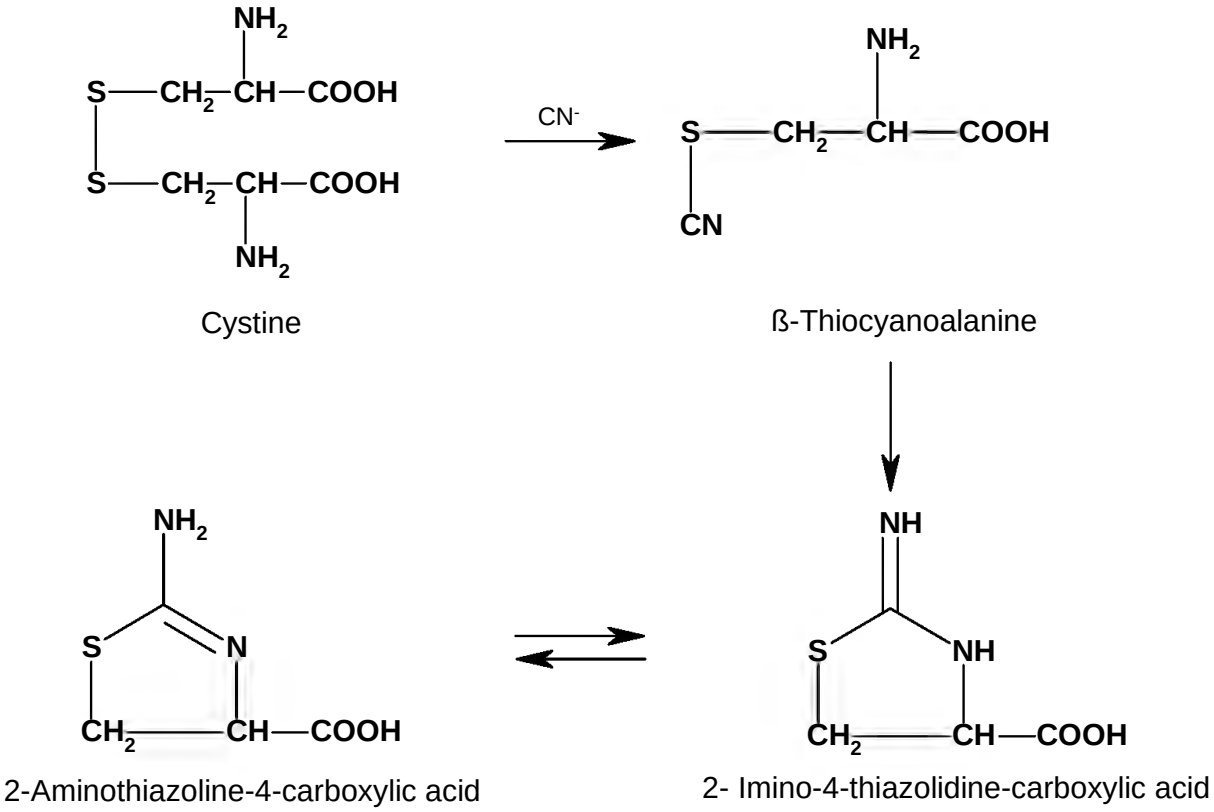

Fig 2: Minor path for the removal of cyanide from the body (Scheme based on Health Council of Netherlands, 2002)

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 x 10^{-4} cm/h) (Greim, 2001). The dermal LD_{50} for HCN in humans has been reported to be 100 mg/kg of body weight (no further details; US-EPA 1992). Low LD_{50} 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^3 is immediately fatal, whereas a concentration of 150 mg/m^3 is fatal after about 30 minutes and 10-20 mg/m^3 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^3 (270 ppm)
Fatal after 10 min	200 mg/m^3 (181 ppm)
Fatal after 30 min	150 mg/m^3 (135 ppm)
Fatal after 0.5 – 1 h or later (or dangerous to life)	120-150 mg/m^3 (110-135 ppm)
Tolerated for 20 min – 1 h (without immediate or late effects)	50-60 mg/m^3 (45-54 ppm)
Slight symptoms after several hours	20-40 mg/m^3 (18-36 ppm)

2.2.2. Animal data

HCN is a very toxic compound by inhalation. Inhalation studies provided an approximate LC_{50} of 166 mg/m^3/30 min. in the mouse, 151-173 mg/m^3/30 min. in the rat and 208 mg/m^3/35 min. for rabbits (Ballantyne, 1987; ATSDR, 1997).
The oral LD_{50} 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^3 (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/m3 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/m3 - 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/m3 CN- (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/m3). 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/m3 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 anomalities 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/m3 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/m3 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 ≥ 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 ≥ 0.3 mg/kg bw. At concentrations ≥ 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 ≥ 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/m3 leads to only slight effects, exposure to concentrations larger than 120 mg HCN/m3 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-/m3 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-/m3. 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/m3 (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/m3 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/m3 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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Hydrogen Cyanide

Toxicological Overview

Key Points

Kinetics and metabolism

- hydrogen cyanide is rapidly absorbed and distributed following inhalation, oral or dermal exposure
- the cyanide ion blocks oxidative respiration; this causes failure of oxygen usage, leading to hypoxia and metabolic acidosis
- metabolism of hydrogen cyanide occurs primarily through conversion to thiocyanate, which is readily excreted in the urine

Health effects of acute exposure

- hydrogen cyanide may be fatal following exposure by all routes
- onset of signs and symptoms following exposure is rapid
- features of toxicity include non-specific CNS symptoms, muscular and neurological effects, tachyponea and tachycardia
- severe features include seizures, a rapid loss of consciousness, cardiorespiratory depression and collapse, pulmonary oedema and death
- lactic acidosis is a key feature and correlates with the severity of intoxication
- on survival of severe intoxication, profound neurological impairment may develop

Health effects of chronic exposure

- long-term exposure to low levels may lead to non-specific neurological symptoms, effects on the thyroid, and optic neuropathy
- hydrogen cyanide has no mutagenic properties and is not considered to be a carcinogen

PHE publications gateway number: 2014790
Published: February 2016

Summary of Health Effects

Hydrogen cyanide is highly toxic, with rapid onset of symptoms noted following acute exposure. Symptoms may occur within seconds following inhalation and minutes following ingestion or dermal contact.

The cyanide ion blocks oxidative respiration, causing tissue hypoxia; tissues with high metabolic demand such as the central nervous system (CNS) are therefore key targets for toxicity. Early features of systemic toxicity include non-specific CNS symptoms, muscular and neurological effects, tachyponea and tachycardia. Late effects or those following larger exposures may include seizures, a rapid loss of consciousness, cardiorespiratory depression and collapse, pulmonary oedema and death. Lactate acidosis may also be noted.

After a single, brief exposure to a low concentration of hydrogen cyanide from which an individual recovers quickly, no long-term health effects are anticipated. However, survivors of larger exposures may suffer long-term CNS damage; observed sequelae include intellectual deterioration, confusion, personality changes, memory deficits and Parkinsonism. Chronic exposure to hydrogen cyanide has been linked to a range of non-specific neurological effects, thyroid effects, optic neuropathy and effects on the skin and the gastrointestinal (GI) system.

Hydrogen cyanide has no structural alerts for DNA reactivity. Hydrogen cyanide has not been classified as a human carcinogen and there is no evidence to suggest that it has mutagenic potential.

There is limited data on reproductive and developmental toxicity for hydrogen cyanide.

Kinetics and Metabolism

The cyanide ion (CN^-) is the toxic moiety in hydrogen cyanide. This is also true of simple cyanide salts such as potassium and sodium cyanide; therefore their toxicology is similar to that of hydrogen cyanide [1]. For more information on these compounds please refer to the incident management and general information compendium entries for sodium and potassium cyanide.

Owing to its small size and moderate lipid solubility, hydrogen cyanide is readily absorbed following inhalation, ingestion and dermal contact [2, 3]. Data on absorption by inhalation in humans is limited; results from a volunteer study measuring pulmonary retention of a 3-minute dose of 0.5–20 mg/m^3 in 10 individuals led to an estimated absorption of 58–77% [4]. Ingested simple cyanide salts (ie sodium and potassium cyanide) are rapidly and completely converted into hydrogen cyanide in the stomach; the free cyanide ion is bound to the hydrogen ion in the acidic environment [1]. Liquid hydrogen cyanide is rapidly absorbed through the skin [5]. Absorption of hydrogen cyanide across abraded skin may be enhanced [6].

The distribution of hydrogen cyanide following absorption is rapid and widespread [4]. Following ingestion, cyanide is found in the stomach, with lesser amounts found in the spleen, blood, liver, brain and kidney; it is found in the lung, blood, brain and kidneys following inhalation [3, 4]. The majority of hydrogen cyanide in blood is sequestered in erythrocytes and a small proportion is transported in the plasma to target organs [4, 7]. Cyanide is unlikely to accumulate in human tissues after chronic oral exposure [2, 7].

Metabolism of hydrogen cyanide primarily involves its conversion to soluble and less acutely toxic thiocyanate (SCN^-) by the enzyme rhodanese, with about 80% of hydrogen cyanide metabolised by this route [1, 4, 7]. This requires sulphane-sulphur as a co-factor, ie one sulphur atom bonded to another sulphur atom such as in a thiosulphate salt (eg sodium thiosulphate). This conversion is irreversible; the thiocyanate ion may then be readily excreted in the urine. The process is typically rapid, with the supply of sulphur-containing donor molecules being rate limiting [4]. Rhodanese is widely distributed in the mitochondria of all tissues, with the highest concentrations found typically in the liver, kidney, brain and muscle [4, 7]. Hydrogen cyanide may also be metabolised by lesser pathways, including the complexing of cyanide with cobalt in hydroxocobalamin to form cyanocobalamin (vitamin B_{12}) and metabolism by other sulphur transferases [7, 8]. The rate of spontaneous detoxification of cyanide in humans has been estimated to be about 1 µg/kg per minute, which is far slower than that in rodents [7].

The majority of absorbed cyanide is excreted in the urine as thiocyanate. Small amounts may also be excreted unchanged in the lungs, saliva, sweat or urine or converted to carbon dioxide in expired air [1, 4]. A plasma half-life of 20 minutes to 1 hour has been estimated for cyanides in humans [2].

Sources and Route of Human Exposure

Hydrogen cyanide is an important industrial reagent; it is used in the production of nylon, acrylates and acetonitrile [5]. It is also used as a fumigant and pesticide, in metal cleaning, gardening, ore extraction, electroplating, dying, printing and photography [5].

A number of edible plants contain low concentrations of hydrogen cyanide in the form of cyanogenic glycocides [7, 9]. Notable examples are the kernels of wild (bitter) almonds, apricots and black cherries, bamboo shoots, lima beans and cassava [7]. Cyanogenic glycocides within plants may liberate hydrogen cyanide when the plant is damaged (eg ground or chewed) or enzymatically hydrolysed within the body [7].

Industrial use is the origin of most cyanide in the environment, although some will be present by natural processes such as biomass combustion [4]. Hydrogen cyanide may be released from a range of combustion process, particularly those that involve nitrogen-containing materials such as polyurethane and PVC. The half-life of hydrogen cyanide in the atmosphere is 1–3 years [10]. Hydrogen cyanide does not generally enter soils [10]. It has a tendency to volatilise from water, where it has a half-life of hours to a few days [11].

People may be exposed to hydrogen cyanide released as a combustion product during house fires [9]. Hydrogen cyanide intoxication is a contributing factor to morbidity and mortality arising from smoke inhalation, together with other toxicants such as carbon monoxide [12, 13].

For the general population (excluding those exposed to high levels of cyanogenic glycosides in food), cigarette smoke is considered to be the greatest source of exposure to hydrogen cyanide [7]. Mainstream smoke from one filter cigarette contains about 100 µg of hydrogen cyanide, while the amount from non-filter cigarettes may be five times that amount [1]. Human exposure may also occur in industrial settings or from accidents during storage or transportation. Ambient levels of cyanide in the atmosphere and in drinking water are low and are considered not to be sources of significant exposure in the UK.

A workplace exposure limit (WEL) for hydrogen cyanide has been set in the UK, to protect workers from its harmful effects. The short-term WEL (15-minute reference period) for hydrogen cyanide is 11 mg/m^3 [14].

Health Effects of Acute/Single Exposure

Human data

Mechanism

Hydrogen cyanide has a high affinity for the ferric moiety of cytochrome c oxidase in mitochondria, forming a stable but reversible complex [5]. Binding of cyanide to cytochrome a-a_3 complex blocks the last stage in the electron transfer chain and thus blocks ATP production [5]. This results in cellular hypoxia and a shift of aerobic to anaerobic respiration, leading to cellular ATP depletion, lactic acidosis, and cell and tissue death [2, 8, 15]. Anaerobic respiration increases to compensate, with a concomitant increase in plasma lactate levels [5, 12, 16]. Tissue damage (histiotoxic hypoxia) throughout the body results from the reduced cellular utilisation of oxygen, the most sensitive tissues being those with high oxygen demand or low detoxifying capacity [2]. The central nervous system (CNS) is particularly vulnerable to the effects on hydrogen cyanide intoxication, owing to its high oxygen demand and limited capacity for anaerobic oxidation [7]. Cyanide may also inhibit other metalloenzymes [3].

General toxicity

Hydrogen cyanide is highly toxic by all routes [5]. Its acute toxicity is characterised by a steep dose-response curve, with lethality occurring by any route [4].

Features of poisoning include anxiety, excitement, nausea, faintness, headache, dizziness, weakness, confusion, lethargy, vomiting, constricting sensation in the chest, incontinence, ataxia, convulsions, tachypnea and tachycardia [4, 7]. Later features of severe poisoning may include seizures, deep coma, fixed unreactive pupils, pulmonary oedema, cardiovascular collapse, respiratory depression and arrest, and death [4, 9]. Haemodynamic status may become unstable; the affected individual may develop ventricular arrhythmias, bradicardia, heart block and cardiac arrest [17]. Cyanosis may be a late sign and does not always occur [5].

Following lower level acute exposures, individuals may display symptoms of hypoxia, including flushing, light-headedness, dizziness and headache [4].

Inhalation

Exposure to a massive concentration of hydrogen cyanide gas may render an individual unconscious within seconds and may lead to coma and death within minutes [18, 19]. Some estimates of lethal concentrations are reported in Table 1.

Table 1: Time to death following hydrogen cyanide inhalation in humans

Dose		
mg/m^3	ppm	Time to death
120–150	110–135	30 min – 1 h or later
200	180	10 min
300	270	Immediate

Reference

World Health Organization (WHO). Hydrogen Cyanide and Cyanides: Human Health Aspects. Concise International Chemical Assessment Document; 61, 2004. World Health Organization: Geneva.

Only mild effects may occur after exposure to 20–40 mg/m^3 for several hours [7, 20]; 50–60 mg/m^3 may be tolerated for 20 minutes to 1 hour without immediate or late effects [7]. Features following inhalation exposure are typical of those following other routes (see the general toxicology section above).

Hydrogen cyanide is reported to have a characteristic odour of almonds or bitter almonds [5]. However, not all individuals can detect this, so odour is not to be considered to be a reliable indicator of exposure [5].

Ingestion

Ingestion of hydrogen cyanide, or compounds that may liberate hydrogen cyanide within the body, may rapidly lead to an onset of systemic toxicity (see the general toxicity section) [6].

Features noted after deliberate ingestion of cyanide compounds may include nausea, retching and collapse [21]. Patients may be unresponsive to painful stimuli and have restless, non-purposeful movements with intermediate decorticate posturing of upper and lower extremities, together with severe anion gap metabolic acidosis [21, 22].

The acute lethal oral dose for hydrogen cyanide has been reported at between 50 and 90 mg; for potassium or sodium cyanide it has been reported at 200 mg (equivalent to 81 and 110 mg of hydrogen cyanide, respectively) [23].

Dermal/ocular exposure

Dermal exposure to hydrogen cyanide may cause dermatitis and rash [3]. Reportedly, death has occurred following dermal contact with hydrogen cyanide; a worker (wearing a gas mask) died following a 5-minute exposure to liquid hydrogen cyanide on the hand [3].

Ocular exposure to hydrogen cyanide may result in pain, swelling, blepharospasm, lacrimation, conjunctivitis, palpebral oedema and photophobia [5].

Delayed effects following acute exposure

After a single, brief exposure to a low concentration of hydrogen cyanide from which an individual recovers quickly, no long-term health effects are anticipated. However, there are rare reports of long-term sequelae in individuals who have survived a substantial exposure [5]. Survivors of larger exposures may suffer long-term CNS damage; observed sequelae include intellectual deterioration, confusion and Parkinsonism [5]. Magnetic resonance imaging investigations have revealed effects in the basal ganglia, including multiple areas of low signal intensity in the globus pallidus and posterior putamen [24–26]. These findings in CNS structures with a high metabolic demand such as the basal ganglia, cerebral cortex and sensorimotor cortex have been attributed to both direct toxicity of cyanide and a consequence of cerebral hypoxia secondary to the cyanide intoxication [27–29].

A slow recovery from severe dystonia syndromes arising from cyanide intoxication has been noted in some cases and has involved treatment with Parkinsonism therapies such as levodopa [24, 27, 28, 30].

The onset of toxicity from dermal exposure may be delayed for several hours [5].

Animal and in-vitro data

Inhalation

In a study of five cynomologus monkeys, incapacitation (defined in the study as semi-consciousness and loss of muscle tone) occurred within 8–19 minutes of exposure to 100–156 ppm (110–172 mg/m^3) of hydrogen cyanide [31]. Early in the exposure period, marked hyperventilation developed and was associated with an increase in EEG delta wave activity. Respiration then slowed and a pattern of slow deep breaths occurred, with a pause at the end of expiration between each successive breath. Heart rate decreased over the exposure period. Exposure was terminated before the full 30-minute period in three out of five animals as a precautionary measure due to the severity of the signs noted. A rapid recovery to a conscious and fairly active state was noted in the first 10 minutes of a recovery period. Consciousness was regained in 3–7 minutes with the heart rate normal within 5 minutes of the start of the recovery period [31]. One animal was noted to have signs of convulsions after exposure for 28 minutes to 123 ppm (136 mg/m^3) of hydrogen cyanide.

Maximal non-lethal concentrations in a number of species have been reported in an early study as approximately 100 mg/m^3 (dogs and rats), 140 mg/m^3 (mice), 180 mg/m^3 (rabbits, monkeys and cats) and 400 mg/m^3 (guinea pigs) [1].

The concentration of hydrogen cyanide inhaled markedly affects the acute toxicity and is illustrated below in the rat (Table 2). The total dose of hydrogen cyanide leading to death is disproportionately larger at low concentrations than at high concentrations; consequently the time to death is disproportionately longer [1]. This effect has been attributed to the proportionally greater detoxification of cyanide at the lower delivery levels [32].

Table 2: Acute inhalation toxicity of hydrogen cyanide in rats

Exposure duration	Medium lethal toxicity	
	as LC_{50} (mg/m^3)	as total dose (mg/m^3 min)
10 s	3,778	631
1 min	1,471	1,471
5 min	493	2,463
30 min	173	5,070
60 min	158	9,441

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World Health Organization (WHO). Hydrogen Cyanide and Cyanides: Human Health Aspects. Concise International Chemical Assessment Document; 61, 2004. World Health Organization: Geneva.

Ballantyne B. The influence of exposure route and species on the acute lethal toxicity and tissue concentrations of cyanide. In: Developments in the Science and Practice of Toxicology (AW Hayes et al, Eds), 1983, pp 583–6. Elsevier Science Publishers: New York NY.

Ingestion

Oral LD_{50} values in the range 3–4 mg/kg have been reported in the rat (using hydrogen, potassium or sodium cyanide) and slightly lower values in the rabbit (2–3 mg/kg). Signs of toxicity occur within minutes of dosing [1].

Dermal/ocular exposure

Dermal LD_{50} values in the range 7–10 mg/kg have been reported following application of cyanides in aqueous solutions to rabbit skin. Toxicity is markedly greater following application to abraded skin [1].

Health Effects of Chronic/Repeated Exposure

Human data

General toxicity

Chronic exposure to cyanide may result in a range of neurological effects (similar to those described in the section on delayed effects following acute exposure above) and effects on the thyroid [3].

Thyroid effects following chronic exposure to cyanide have been reported in a number of studies on workers; effects include enlargement (goitre), functional changes and altered thyroid hormone levels [4]. Thiocyanate is generated in the detoxification of cyanide (see the kinetics and metabolism section above) and is known to disrupt iodine uptake by the thyroid; the observed effects on the thyroid may then be a result of increased thiocyanate and not due to direct hydrogen cyanide toxicity [3, 7].

Optic neuropathy has been observed in some cases of chronic cyanide toxicity, including atrophy, amblyopia and colour deficits [5]. Respiratory tract irritation, breathlessness, hoarse voice, chronic rhinitis and deafness have also been reported [5]. Some gastrointestinal and skin effects have been observed, which are likely to be due to cyanide's irritant effects [3]. There is some debate as to whether the effects observed on repeat exposure to cyanide are truly due to repeat dose toxicity or the result of acute intoxication [3].

Inhalation

Data on chronic inhalation exposure to hydrogen cyanide is limited. In one study, workers exposed chronically (duration not specified) to 15 ppm hydrogen cyanide reported a range of effects, including fatigue, dizziness, headache, disturbed sleep, tinnitus and paraesthesia of the extremities [2]. Similar findings have been reported in another study which also included delayed memory and/or visual impairment in 31.5% of workers. The concentrations of hydrogen cyanide were not, however, specified [2]. Neurological features have been reported to persist on cessation of chronic exposure [2].

Ingestion

Limited data was identified for chronic exposure to hydrogen cyanide by ingestion in humans. It is be expected that repeated small exposures to cyanide over time would result in less toxicity than a single acute exposure of the same dose, owing to first-pass metabolism by the liver [7].

Genotoxicity

There is no in-vivo human data on which to assess the genotoxicity of hydrogen cyanide. However, hydrogen cyanide has no structural alerts for DNA damage and, taking into account the in-vitro data, it can be concluded that hydrogen cyanide does not have significant mutagenic potential.

Carcinogenicity

There is insufficient evidence to classify hydrogen cyanide as a carcinogen in humans and it has not been classified by the International Agency for Research on Cancer. Hydrogen cyanide is considered not to be a carcinogen.

Reproductive and developmental toxicity

There are no epidemiological studies on hydrogen cyanide poisoning during pregnancy, only case reports on outcomes in poisonings by cyanogenic compounds [9]. The data is insufficient to assess the risk to the fetus following maternal exposure [9]. Limited data suggests that cyanide can cross the placenta [4].

Animal and in-vitro data

Inhalation

Dogs were repeatedly exposed to 50 mg/m^3 hydrogen cyanide (enough to give signs of acute toxicity) for 12.5 minute periods, with a break in exposure that was sufficient for nine of twelve dogs to recover from acute effects (the remaining three died) [3]. Subsequent histology suggested that repeated toxic exposures had led to severe brain damage [3].

Histology on rabbits exposed to 0.5 mg/m^3 hydrogen cyanide continuously for up to 4 weeks showed no effects on the heart, lung and adjacent arteries [3].

Ingestion

There is limited data on the chronic ingestion of hydrogen cyanide in experimental animals. In a 2-year feeding study, rats were provided with food fumigated with hydrogen cyanide, with customised jars used to limit loss through volatilisation. Intakes in treated animals were 4.3 and 10.8 mg/kg bw/day. No treatment-related effects on survival or growth rate, signs of toxicity, haematological or histopathological changes in examined organs were noted; a no observed adverse effect level of 10.8 mg/kg bw/day was established [1].

Genotoxicity

There are limited studies on which to assess the genotoxicity of hydrogen cyanide. When tested on *S. typhimurium* strains TA1535, TA1538, TA98, TA100, TA97, TA102, hydrogen cyanide only gave a positive result in one case, TA100, without metabolic activation [3, 33, 34]. The weight of evidence suggests that cyanide is not genotoxic [1].

Carcinogenicity

In a dietary study, rats were fed every 2 days for 2 years on feed which had been exposed to hydrogen cyanide gas (the highest dose being around 3.5 mg/kg bw/day). No effects (including cancer endpoints) were seen; however, the study size was small and the endpoints tested were restricted; therefore it is not possible to draw any definitive conclusions regarding carcinogenicity [3].

Reproductive and developmental toxicity

Insufficient data is available on the reproductive or developmental toxicity of hydrogen cyanide [35].

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This document from the PHE Centre for Radiation, Chemical and Environmental Hazards reflects understanding and evaluation of the current scientific evidence as presented and referenced here.

First published: February 2016

For queries relating to this document, please contact: generaltox@phe.gov.uk