Social Europe

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

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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*)

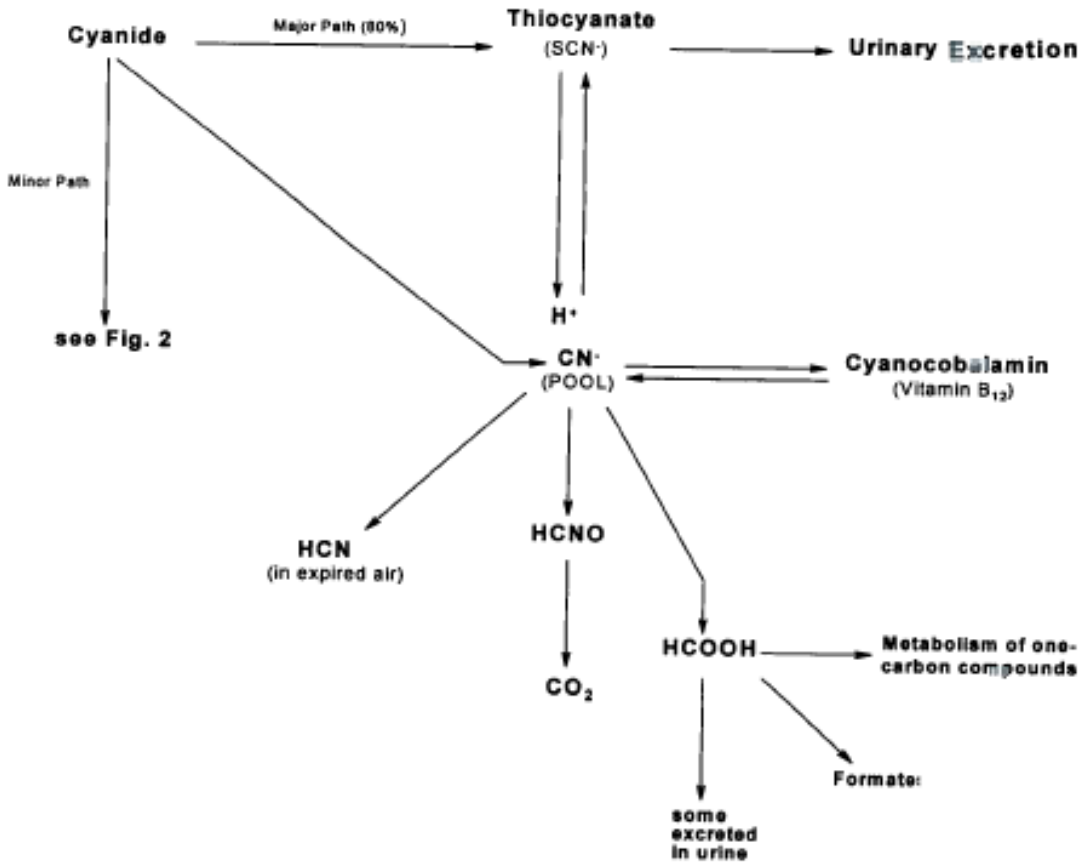

Fig 1: Basic processes involved in the metabolism of cyanide in mammals (Health Council of Netherlands, 2002)

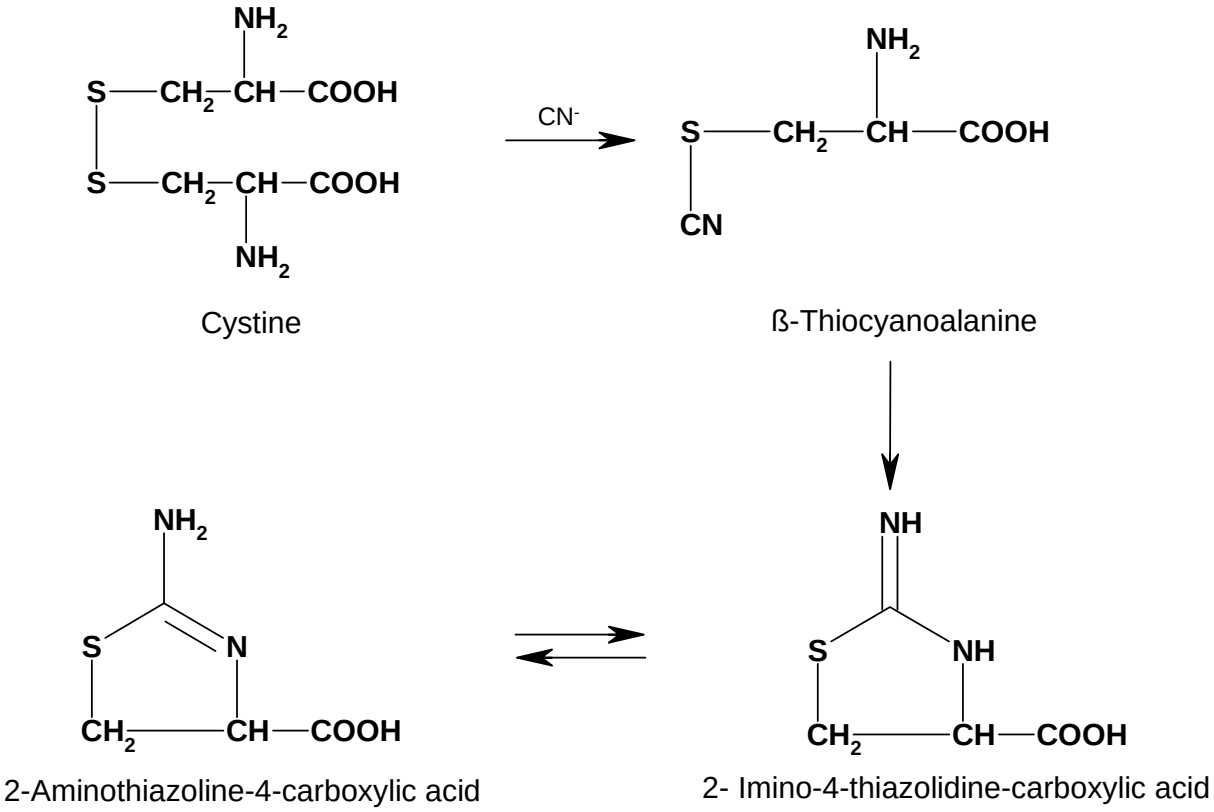

Fig 2: Minor path for the removal of cyanide from the body (Scheme based on Health Council of Netherlands, 2002)

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/m³ is immediately fatal, whereas a concentration of 150 mg/m³ is fatal after about 30 minutes and 10-20 mg/m³ 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/m³ (270 ppm)
Fatal after 10 min	200 mg/m³ (181 ppm)
Fatal after 30 min	150 mg/m³ (135 ppm)
Fatal after 0.5 – 1 h or later (or dangerous to life)	120-150 mg/m³ (110-135 ppm)
Tolerated for 20 min – 1 h (without immediate or late effects)	50-60 mg/m³ (45-54 ppm)
Slight symptoms after several hours	20-40 mg/m³ (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/m³/30 min. in the mouse, 151-173 mg/m³/30 min. in the rat and 208 mg/m³/35 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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