Sodium and potassium cyanides: Human health tier II assessment

01 September 2015

Chemicals in this assessment

Chemical Name in the Inventory	CAS Number
Sodium cyanide	143-33-9
Potassium cyanide (K(CN))	151-50-8

Preface

This assessment was carried out by staff of the National Industrial Chemicals Notification and Assessment Scheme (NICNAS) using the Inventory Multi-tiered Assessment and Prioritisation (IMAP) framework.

The IMAP framework addresses the human health and environmental impacts of previously unassessed industrial chemicals listed on the Australian Inventory of Chemical Substances (the Inventory).

The framework was developed with significant input from stakeholders and provides a more rapid, flexible and transparent approach for the assessment of chemicals listed on the Inventory.

Stage One of the implementation of this framework, which lasted four years from 1 July 2012, examined 3000 chemicals meeting characteristics identified by stakeholders as needing priority assessment. This included chemicals for which NICNAS already held exposure information, chemicals identified as a concern or for which regulatory action had been taken overseas, and chemicals detected in international studies analysing chemicals present in babies' umbilical cord blood.

Stage Two of IMAP began in July 2016. We are continuing to assess chemicals on the Inventory, including chemicals identified as a concern for which action has been taken overseas and chemicals that can be rapidly identified and assessed by using Stage One information. We are also continuing to publish information for chemicals on the Inventory that pose a low risk to human health or the environment or both. This work provides efficiencies and enables us to identify higher risk chemicals requiring assessment.

The IMAP framework is a science and risk-based model designed to align the assessment effort with the human health and environmental impacts of chemicals. It has three tiers of assessment, with the assessment effort increasing with each tier. The Tier I assessment is a high throughput approach using tabulated electronic data. The Tier II assessment is an evaluation of risk on a substance-by-substance or chemical category-by-category basis. Tier III assessments are conducted to address specific concerns that could not be resolved during the Tier II assessment.

These assessments are carried out by staff employed by the Australian Government Department of Health and the Australian Government Department of the Environment and Energy. The human health and environment risk assessments are conducted and published separately, using information available at the time, and may be undertaken at different tiers.

This chemical or group of chemicals are being assessed at Tier II because the Tier I assessment indicated that it needed further investigation.

For more detail on this program please visit:**www.nicnas.gov.au**

Disclaimer

ACRONYMS & ABBREVIATIONS

Grouping Rationale

Sodium cyanide (NaCN) (CAS No. 143-33-9) and potassium cyanide (KCN) (CAS No. 151-50-8) are simple salts. The chemicals both contain the cyanide anion (CN^-) and have similar physico-chemical properties, resulting in similar toxicological properties.

Import, Manufacture and Use

Australian

Sodium cyanide is listed on the 2006 High Volume Industrial Chemicals List (HVICL) with a total reported volume of 10,000–99,999 tonnes.

The following Australian uses have been identified through:

- Australian HVICL;
- NICNAS priority existing chemical assessment report—sodium cyanide (2010); and
- the National Pollutant Inventory (NPI).

The chemicals have reported site-limited use including:

- as flotation agents in mining and metal extraction (sodium cyanide);
- in electroplating metals; and
- in synthesising other chemicals.

The chemicals have reported non-industrial uses, including as insecticides.

International

The following international uses have been identified through:

- the European Union (EU) Registration, Evaluation Authorization and Restriction of Chemicals (REACH) dossiers;
- Galleria Chemica;
- the Substances and Preparations in the Nordic countries (SPIN) database;
- the Organisation for Economic Co-operation and Development (OECD) High Production Volume chemical program (OECD HPV); and
- the United States (US) National Library of Medicine's Hazardous Substances Data Bank (HSDB).

The chemicals have reported site-limited uses including:

- in extracting gold and silver from ores;
- in electroplating metals;
- as flux agents for casting;
- in synthesising other chemicals;
- in metal hardening;
- in soil fertilisation (potassium cyanide (CAS No. 151-50-8)); and
- in manufacturing dyes, pigments, nylon intermediates and chelate compounds (sodium cyanide (CAS No. 143-33-9)).

The chemicals have reported non-industrial uses including:

- as insecticides; and
- in manufacturing pharmaceuticals.

Restrictions

Australian

These chemicals are listed in the *Poisons Standard—the Standard for the Uniform Scheduling of Medicines and Poisons* (SUSMP) in Schedule 7 (SUSMP, 2015).

Schedule 7 chemicals are described as ‘Substances with a high potential for causing harm at low exposure and which require special precautions during manufacture, handling or use. These poisons should be available only to specialised or authorised users who have the skills necessary to handle them safely. Special regulations restricting their availability, possession, storage or use may apply’ (SUSMP, 2015).

International

The chemicals are listed on the following (Galleria Chemica):

- EU Cosmetics Regulation 1223/2009 Annex II—List of substances prohibited in cosmetic products;

- New Zealand Cosmetic Products Group Standard—Schedule 4: Components cosmetic products must not contain;
- Health Canada List of prohibited and restricted cosmetic ingredients (The Cosmetic Ingredient 'Hotlist'); and
- The Association of Southeast Asian Nations (ASEAN) Cosmetic Directive Annex II Part 1: List of substances which must not form part of the composition of cosmetic products

Existing Worker Health and Safety Controls

Hazard Classification

The chemicals are classified as hazardous, with the following risk phrases for human health in the Hazardous Substances Information System (HSIS) (Safe Work Australia):

- T+; R26/R27/R28 (acute toxicity)
- Xi; R38 (irritation)

Exposure Standards

Australian

Cyanides, including the chemicals in this group, have an exposure standard of 5 mg/m^3 time weighted average (TWA) (Safe Work Australia).

International

The following exposure standards are identified for cyanide salts (Galleria Chemica):

An exposure limit of 3–5 mg/m^3 TWA and 10 ppm short-term exposure limit (STEL) in different countries such as the USA, Canada, the United Kingdom and Japan.

Health Hazard Information

Sodium cyanide (CAS No. 143-33-9) has been the subject of a NICNAS priority existing chemical report (NICNAS, 2010), but this addressed only the environmental risks of the chemical. Sodium cyanide and potassium cyanide (CAS No. 151-50-8) are soluble in water and readily dissociate into the cyanide anion and their respective metal cation. The cyanide ion (CN^-) is considered to be the main driver of toxicity associated with these chemicals. The potassium and sodium cations released upon dissociation in solution are not expected to contribute to the toxicity of these chemicals.

Sodium and potassium cyanide salts liberate hydrogen cyanide (HCN) (CAS No. 74-90-8) gas at the acidic pH levels of the stomach and lower gastrointestinal tract (ATSDR, 2006) as well as when in contact with water. Where appropriate, data for these chemicals may be 'read across' from HCN.

Toxicokinetics

Exposure to sodium cyanide and potassium cyanide is measured in the body as detectable levels of dissociated CN^- or HCN. The form of cyanide to which the body is exposed, whether it be the simple salts or HCN, does not influence the distribution,

metabolism or excretion from the body (REACHa).

Absorption

Potassium cyanide and sodium cyanide are absorbed rapidly following inhalation or oral exposure, but more slowly following dermal exposure (ATSDR, 2006).

Data indicate that absorption of cyanide decreases with increasing dose levels. Absorption was estimated at 19.5, 18.1, and 15.7 % in people estimated to have ingested 297, 557, and 1450 mg HCN, respectively, in reported suicide attempts (US EPA IRIS, 2005).

A case has been documented involving an 80 kg male who ingested an estimated 15–25 mg CN^-/kg (as potassium cyanide) in a suicide attempt. Based on a concentration of 200 mg hydrogen cyanide/L in the blood two hours after ingestion, it was estimated that the person had 1.2 g hydrogen cyanide in the blood, with approximately 2.3 g CN^- in the body, after two hours (WHO, 2004; ATSDR, 2006). The validity of these data is unclear, given that the volume of cyanide in the body seemingly exceeds the total volume of cyanide reported to be ingested by this individual.

A study performed in dogs studied the gastrointestinal absorption of hydrogen cyanide following administration of lethal doses of the chemical in solution. The animals, dosed by oral gavage with 1.6, 4.4 or 8.4 mg HCN/kg, died 155, 21, and eight minutes after treatment and had absorbed 72, 24 and 17 % of the administered dose, respectively (ATSDR, 2006; NICNAS, 2010).

Distribution

Absorbed cyanide is quickly distributed and is typically found in high levels in the liver, lungs, blood and brain (WHO, 2004). A study has also shown that following dosing by oral gavage in rats, cyanide is distributed with the highest concentration in the liver, followed by the lungs and blood (Yamamoto et al., 1982).

Organ levels of CN^- in a case of fatal poisoning were reported as follows, in mg: stomach contents, 160; spleen, 3.77; blood, 2.39; liver, 1.62; brain, 1.2; kidney, 0.61; and urine, 0.06 (Ansell & Lewis, 1969).

Combined data from studies in which rats that died 3.3 and 10.3 minutes following oral administration of 7 or 21 mg CN^-/kg (as sodium cyanide), demonstrated mean tissue concentrations of cyanide (in µg/g) of: liver, 8.9; lung, 5.8; blood, 4.9; spleen, 2.1; and brain, 1.5 (NICNAS, 2010)

Metabolism

In a 1951 study, cases of human cyanide poisoning were used to study the metabolism of cyanide following exposure. Two key metabolic pathways for the breakdown of cyanide were reported. In the first, cyanide is converted to its main metabolite, thiocyanate, by rhodanese (found ubiquitously in the body) or 3-mercaptopyruvate sulfur transferase. The second pathway involves cyanide combining with cysteine to form β-thiocyanoalanine, resulting in production of 2-iminothiazolidine-4-carboxylic acid and 2-aminothiazoline-4-carboxylic acid (REACHb).

The majority of cyanide metabolism occurs within tissues in animals. In rats, after a single oral dose, the blood elimination half-life for potassium cyanide was 14.1 minutes (WHO, 2004).

Excretion

Absorbed cyanide is excreted primarily as thiocyanate in the urine following oral administration. Traces of cyanide can also be excreted unchanged or as metabolites in sweat, saliva or exhaled air (NICNAS, 2010).

A study found that rats administered radiolabelled potassium cyanide orally (equivalent to 2 mg CN^-/kg bodyweight (bw)) excreted 47 % of the dose in the urine within 24 hours of dosing (Farooqui & Ahmed, 1982).

Acute Toxicity

Oral

The chemicals are classified as hazardous with the risk phrase 'Very toxic if swallowed' (T+; R28) in the HSIS (Safe Work Australia). The available data (median lethal doses (LD50) 1.4–56 mg/kg bw) support this classification.

The acute toxicity of potassium cyanide was assessed in male rats. Five animals per group were administered a single oral dose of the chemical at 3.4, 12, 17, and 26 mg/kg bw (range-finding experiment) and 10 and 20 mg/kg bw (LD50 experiment). Two out of five animals died at the 10 mg/kg dose and 5/5 animals died at the 20 mg/kg dose. An LD50 of 11.3 mg/kg bw was calculated. Sublethal effects of exposure included hyperaemia, chewing, unresponsiveness, increased respiration and increased urine excretion (ECETOC, 2007; REACHb).

Male Crl:CD rats (10/group) were dosed orally with potassium cyanide at 5, 8, 10 or 15 mg/kg bw. Under these test conditions, the oral LD50 was 10 mg/kg bw. Sub-lethal effects included convulsions, tremors, lethargy, gasping, and slight weight loss (REACHb).

Oral acute toxicity data for potassium cyanide and sodium cyanide were reviewed by the European Centre for Ecotoxicology and Toxicology of Chemicals (ECETOC) task force. They validated and presented the following, lowest reported, LD50 values:

- 7.49 mg/kg bw in female rats (potassium cyanide);
- 1.4 mg/kg bw in dogs (potassium cyanide); and
- 5.09 mg/kg bw in female rats (sodium cyanide) (ECETOC, 2007).

In a study conducted according to OECD test guideline (TG) 401 (acute oral toxicity), Crl:CD rats (10/sex/dose) were administered sodium cyanide at 30, 50, or 70 mg/kg bw by oral gavage. Animals were observed for 14 days following treatment. Under these test conditions, an LD50 of 56 mg/kg bw was determined. Sub-lethal effects included excess salivation and lethargy (REACHa).

Dermal

The chemicals are classified as hazardous with the risk phrase 'Very toxic in contact with skin' (T+; R27) in the HSIS (Safe Work Australia). The available data (LD50s of 11.83–22.33 mg/kg bw (solution/moistened material on intact skin)) support this classification.

In a comprehensive non-guideline study, the abraded and intact skin of female rabbits (nine/group) was exposed to sodium cyanide as a dry or moistened powder, or in solution. The following LD50 values were reported for sodium cyanide (ECETOC, 2007; REACHa).

Intact skin:

- 200 mg/kg bw (dry powder);
- 11.83 mg/kg bw (moistened powder); and
- 14.63 mg/kg bw (in solution).

Abraded skin:

- 7.35 mg/kg bw (dry powder); and
- 11.28 mg/kg bw (in solution).

In a non-guideline study, the abraded and intact skin of female rabbits (nine/group) was exposed to potassium cyanide in solution. Sublethal effects of exposure included transient difficulty with breathing and occasional retrocolic spasms, weakness and unsteadiness of movement. Under these test conditions, the dermal LD50 was 22.33 mg/kg bw (intact skin) and 14.29 mg/kg bw (abraded skin) (ECETOC, 2007; REACHb).

These data indicate that the chemicals are highly acutely toxic from dermal exposure.

Inhalation

The chemicals are classified as hazardous with the risk phrase 'Very toxic by inhalation' (T+; R26) in the HSIS (Safe Work Australia).

No inhalation exposure studies are available for these chemicals, which are not volatile but can occur in dusts. There are data available for hydrogen cyanide gas, which is liberated from both potassium cyanide and sodium cyanide salts when in contact with water.

Inhalation median lethal concentration (LC50) values of hydrogen cyanide (CAS No. 74-90-8) in rats ranged from 143 ppm (60 minutes exposure) to 3417 ppm (10 seconds exposure). Similar LC50 values have been generated in mouse studies. The LC50 values of hydrogen cyanide in rabbits ranged from 2200 ppm (45 seconds exposure) to 118 ppm (30 minutes exposure) (ATSDR, 2006; NICNAS, 2010).

Observation in humans

Numerous incidences of cyanide poisoning in humans have been documented.

Oral

An early paper reported four cases of lethal cyanide poisoning. The investigators were able to calculate the absorbed dose in these cases by evaluating the combined tissue levels and unabsorbed amount of the chemical in the stomach. Absorbed doses between 0.5 and 3 mg CN^-/kg bw were determined. The minimum lethal absorbed dose was 0.5 mg CN^-/kg bw, and the average fatal dose 1.4 mg CN^-/kg bw. The specific forms of cyanide in these cases of poisoning were not given (Gettler & Baine, 1938).

Dermal

Numerous reports exist of humans being exposed to cyanide salts dermally; however, reliable data are difficult to obtain with regard to the concentrations or doses involved.

An average LD50 value for dermal exposure of 100 mg CN^-/kg as hydrogen cyanide has been estimated for humans (ATSDR, 2006).

In one instance, a 38-year-old female was exposed to potassium cyanide after using it to remove silver dye staining on her hands. She experienced vertigo and fainted. She vomited later in the evening and developed cyanosis of the lips, hands and fingers, but recovered in 72 hours (ECETOC, 2007).

Fatal reports involving the cyanide salts are typically a result of the solid material reacting with water. For example, a study described an accident in which a man was killed when the potassium cyanide he was carrying spilled into a puddle of water. The boiling solution splashed into his face. He became unconscious and died three hours later. In another instance, a worker was accidently splashed with an 80 % solution of sodium cyanide. The liquid struck the man's head and shoulders and he died in less than one hour (ECETOC, 2007).

Inhalation

As mentioned previously, HCN gas is liberated from sodium cyanide and potassium cyanide when in contact with water.

Inhalation of sufficient concentrations of hydrogen cyanide can rapidly lead to death in humans. An average fatal concentration has been estimated as 546 ppm with an exposure time of 10 minutes. Non-lethal exposures to hydrogen cyanide typically cause upper respiratory irritation, cough, altered olfactory sense, nasal congestion, nosebleeds, haemoptysis (coughing up blood) and shortness of breath (ATSDR, 2006).

Corrosion / Irritation

Skin Irritation

The chemicals are classified as hazardous with the risk phrase 'Irritating to skin' (Xi; R38) in the HSIS (Safe Work Australia).

No data are available to support this classification. However, dermal toxicity of cyanides is sufficiently high (see **Acute dermal toxicity** section) such that death or systemic toxicity are likely to occur before local inflammatory irritation effects in the skin develop (ECETOC, 2007; NICNAS, 2010). As a result, no standard skin irritation studies have been conducted on sodium cyanide or potassium cyanide.

Eye Irritation

The dermal toxicity of the chemicals is sufficiently high (see **Acute dermal toxicty** section) such that death or systemic toxicity are likely to occur at levels at which eye irritation is observed.

A non-guideline study was conducted to assess the potential for sodium cyanide to cause ocular irritation. The chemical (as a powder) was instilled into the conjunctival sac of New Zealand White rabbits (10 animals/dose) at 3.18–9.96 mg/kg bw. Irritation was immediately observed, consisting of lacrimation, moderate conjunctival hyperaemia and mild chemosis. In survivors, the conjunctival hyperaemia became progressively more severe and, by 24 hours post-instillation, there was mild to moderate corneal opacification and mild iritis. Conjunctival hyperaemia and lacrimation resolved slowly after 24 hours but mild inflammation was present for seven days following instillation. In addition to ocular effects, observed signs of toxicity include ataxia, convulsions and coma, with deaths occurring within four to 12 minutes (NICNAS, 2010).

Sensitisation

Skin Sensitisation

No data are available.

Repeated Dose Toxicity

Oral

In a 90-day repeated dose toxicity study, male and female Fischer 344 (F344) rats (10/group) were administered sodium cyanide in the diet at 0, 3, 10, 30, 100 and 300 ppm. Histopathology, clinical chemistry, haematology, urine chemistry and clinical signs were assessed. No significant adverse effects on body weights, organ weights, histopathology or clinical pathology parameters were observed. Under these test conditions, a no observed adverse effect level (NOAEL) of 300 ppm (equivalent to 12.5 mg CN^-/kg bw/day) was established. The investigators also reported that the chemical did not have any thyrotoxic or neurotoxic effects at doses that caused no clinical signs of toxicity (REACHa).

In a 90-day repeated dose toxicity study, male Sprague Dawley (SD) rats (10/group) were administered potassium cyanide in their drinking water at 40, 80 and 140 mg/kg bw/day. At the conclusion of the study, the animals were euthanised and organs weighed and examined histopathologically. Dosing with the chemical resulted in reduced food and water intake in the highest dose group. Reduced weight gain in the two highest dose groups was observed. There were also reductions in organ weights (adrenals, heart, kidneys, lungs and thymus) in the two highest dose groups. No treatment-related change was observed in ophthalmology, hearing or dentition. There were no significant changes in haematology parameters. Proteinuria was dose dependent. Gross pathological findings included haemorrhagic centres in the stomach in the high dose group (REACHb). Deaths of treatment group animals were reported. However, no further details were provided regarding the number of mortalities per dose group. While a NOAEL of 40 mg/kg bw/day is reported for this study, it is unclear whether deaths occurred at this dose.

In a 280-day oral repeated dose toxicity study, male New Zealand White rabbits (six/group) were fed a diet containing potassium cyanide at 702 ppm (equivalent to 17–24 mg CN^-/kg bw/day). Numerous parameters were assessed including food consumption, body weight change, clinical chemistry, enzyme activity and histopathology on selected tissues. Body weight gain was reduced, despite increased food consumption. Kidney and liver function were affected and histopathological changes (congestion and necrosis) were seen in these organs. As a result of these findings, no NOAEL was established.

In an oral repeated dose toxicity study, rats were fed a diet containing potassium cyanide at 1,500 mg/kg for 11.5 months (equivalent to doses of 30 mg CN^-/kg bw/day). The chemical caused a consistent reduction in weight gain and decreased thyroid activity in young rats. At necropsy, thyroids were enlarged. On the basis of these changes, a lowest observed effect level (LOEL) was established as 30 mg/kg bw/day (WHO, 2004).

Male Wistar rats were administered potassium cyanide in drinking water at 0.3, 0.9, 3.0 and 9.0 mg/kg bw/day, for 15 days, in a repeated dose toxicity study. The 0.3, 0.9 and 3 mg/kg groups consisted of 10 animals, whereas the highest dose group had six animals. A statistically significant reduction in weight gain was observed in the highest dose group. Histopathological findings included thyroid, liver and renal effects in the two highest dose groups. Liver enzyme levels were altered in all groups except the 0.3 mg/kg bw/day group. On the basis of these findings, a NOAEL of 0.3 mg/kg bw/day for potassium cyanide was determined (REACHb).

Dermal

No data are available.

Inhalation

No data are available.

Genotoxicity

Based on the weight of evidence from the available in vitro and in vivo genotoxicity studies, the chemicals are not considered to be genotoxic.

In vitro

In a US Environmental Protection Agency (EPA) guideline study, an Ames bacterial reverse mutation assay was used to assess sodium cyanide's genotoxic potential. The chemical was tested on *Salmonella typhimurium* strains TA 98, TA 100, TA 1535 and TA 1537 at 0, 1.0, 3.3, 10.0, 33.0, 100.0 or 300.0 µg/plate, in the presence or absence of a metabolic activation system. Under these test conditions, sodium cyanide was non-mutagenic in any of the strains tested at any of the concentrations assessed (REACHa).

Potassium cyanide was assessed in a mammalian cell gene mutation assay using Chinese hamster lung fibroblasts (V79). Cells were incubated with the chemical at 400, 800, 1000, 2000 or 3000 µg/mL (without metabolic activation) and 1000, 2000, 3000, 4000, 6000, 8000 or 10000 µg/mL (with metabolic activation) for 24 hours. The mutation frequencies in cells treated with potassium cyanide were within the range of experimental and historical controls. Under these test conditions, potassium cyanide was found not to be mutagenic, in the presence or absence of metabolic activation (REACHb).

In vivo

In a non-guideline in vivo study, the potential for potassium cyanide to induce chromosomal aberrations in bone marrow cells was assessed. Male Swiss-Webster mice were administered the test chemical at 5.5 mg/kg bw (via intraperitoneal injection). Under these test conditions, potassium cyanide failed to induce statistically significant chromosomal aberrations in bone marrow cells harvested from treated mice (REACHb).

Carcinogenicity

No carcinogenicity studies are available for potassium or sodium cyanide. The following data are read across from a carcinogenicity study using hydrogen cyanide.

Carworth farm rats (10/sex/group) were fed HCN-fumigated diets at 0, 100 or 300 ppm/day for two years. There were no differences in survival, weight gain, food intake and behaviours between test groups and controls. Absolute and relative organ weights (organs assessed: liver, kidneys, spleen, brain, heart, adrenals, testes and ovaries) were also comparable with controls. No treatment-related histopathological changes were observed. No tumours were observed in rats fed a diet containing hydrogen cyanide. On the basis of these findings an NOAEL of 300 ppm (equivalent to 7.9 mg CN^-/kg bw/day) was determined (REACHa).

Reproductive and Developmental Toxicity

Based on the available data, the chemicals in this group are not expected to cause reproductive or developmental toxicity at dose levels at which maternal toxicity is not observed.

The following reproductive toxicity data are taken from a study described previously (See **Repeated dose toxicity** section):

Sodium cyanide was administered to male and female F344 rats for 13 weeks in their diet at 0, 3, 10, 30, 100 and 300 ppm. Various reproductive organs were assessed in this study. No histopathological changes in the testes, epididymides or ovaries were observed. At all dose levels, caudal epididymis weights were significantly reduced and sperm motility was also decreased. Proestrus and dioestrus time was increased in female rats in the two highest dose groups. According to the authors, these effects cannot unequivocally be attributed to cyanide exposure as they were not dose-dependent. An NOAEL of 100 ppm for rats (equivalent to 4.9 mg CN^-/kg bw/day) was determined (REACHa).

The following reproductive toxicity data are also taken from a study described previously (See **Repeated dose toxicity** section):

Male SD rats (10/group) were fed potassium cyanide in water at 40, 80 and 140 mg/kg bw/day for 13 weeks. The absolute weight of the testes was reduced in the 80 and 140 mg/kg bw group, but only statistically significantly in the latter group. No major histopathological changes in the testes were seen. Under these test conditions, an NOAEL of 80 mg/kg bw/day (equivalent to 32 mg CN^-/kg bw/day) was determined (REACHb). These values are considerably higher than reported LD50s for the chemical, indicating there could have been a reporting error in this study.

Developmental toxicity

A study was performed similarly to OECD TG 414 (prenatal developmental toxicity study) to assess the developmental toxicity of potassium cyanide. Female Wistar rats (10/sex/dose) were administered the chemical in drinking water from gestation day (GD) 6 to 20, and consumed doses of either 1, 3 or 30 mg/kg bw/day. There was no change in the number of corpora lutea, preimplantation loss, postimplantation loss, foetal and placental weight or foetal length. No dams showed total litter resorptions. However, there was a statistically significant increase in the incidence of visceral alterations in litters from mothers in the 30 mg/kg bw/day group. Microscopic alterations in the foetal liver and brain were also observed in the two highest dose groups. As there were also higher incidences of similar lesions in the dams, no specific sensitivity of the foetus to cyanide could be determined. An NOAEL of 3 mg/kg bw/day was reported for developmental toxicity (REACHb).

In a developmental toxicity study in pigs, pregnant sows were administered potassium cyanide in their diet from the third week of pregnancy until the final day of gestation, at 2, 4 or 6 mg/kg bw/day. Foetuses were screened for malformations by ultrasound on GD 21, 35, 45, 55 and 65. Piglets delivered normally were evaluated daily until they were 120 days old. Histopathological evaluation of sows revealed degenerative vacuolar lesions in the liver, pancreas, thyroid and central nervous system. Histopathological evaluation of piglets revealed degenerative vacuolar lesions in the thyroid and lungs. No foetal abnormalities were reported (REACHb).

Risk Characterisation

Critical Health Effects

The critical health effects for risk characterisation are the systemic acute effects (acute toxicity from oral, dermal and inhalation exposure).

Public Risk Characterisation

Given the uses identified for these chemicals, it is unlikely that the public will be exposed. Hence, the public risk from the industrial uses of these chemicals is not considered to be unreasonable.

Occupational Risk Characterisation

During product formulation, dermal, oral and ocular exposure might occur, particularly where manual or open processes are used. These could include transfer and blending activities, quality control analysis, and cleaning and maintaining equipment. Worker exposure to the chemicals at lower concentrations could also occur while using formulated products containing the chemicals. The level and route of exposure will vary depending on the method of application and work practices employed.

NICNAS Recommendation

Assessment of these chemicals are considered to be sufficient, provided that the recommended amendment to the classification is adopted, and labelling and all other requirements are met under workplace health and safety and poisons legislation as adopted by the relevant state or territory.

Regulatory Control

Public Health

Products containing the chemicals should be labelled in accordance with state and territory legislation (SUSMP, 2015).

Work Health and Safety

The chemicals are recommended for classification and labelling under the current Approved Criteria and adopted GHS as below. This assessment does not consider classification of physical and environmental hazards.

Hazard	Approved Criteria (HSIS)[a]	GHS Classification (HCIS)[b]
Acute Toxicity	Very toxic by inhalation, in contact with skin and if swallowed (T+; R26/27/28)*	Fatal if swallowed - Cat. 2 (H300) Fatal in contact with skin - Cat. 1 (H310) Fatal if inhaled - Cat. 2 (H330)
Irritation / Corrosivity	Irritating to skin (Xi; R38)*	Causes skin irritation - Cat. 2 (H315)
Other Health Effects	Contact with water liberates toxic gas (R29) Contact with acids liberates very toxic gas (R32)	Contact with water liberates toxic gas (AUH029) Contact with acid liberates very toxic gas (AUH032)

[a] Approved Criteria for Classifying Hazardous Substances [NOHSC:1008(2004)].

[b] Globally Harmonized System of Classification and Labelling of Chemicals (GHS) United Nations, 2009. Third Edition.

[*] Existing Hazard Classification. No change recommended to this classification

Advice for consumers

Products containing the chemicals should be used according to the instructions on the label.

Advice for industry

Control measures

Control measures to minimise the risk from oral, dermal, ocular and inhalation exposure to the chemicals should be implemented in accordance with the hierarchy of controls. Approaches to minimise risk include substitution, isolation and engineering controls. Measures required to eliminate, or minimise risk arising from storing, handling and using a hazardous chemical depend on the physical form and the manner in which the chemicals are used. Examples of control measures which could minimise the risk include, but are not limited to:

- using closed systems or isolating operations;
- using local exhaust ventilation to prevent the chemicals from entering the breathing zone of any worker;
- health monitoring for any worker who is at risk of exposure to the chemicals, if valid techniques are available to monitor the effect on the worker's health;
- air monitoring to ensure control measures in place are working effectively and continue to do so;
- minimising manual processes and work tasks through automating processes;
- work procedures that minimise splashes and spills;
- regularly cleaning equipment and work areas; and
- using protective equipment that is designed, constructed, and operated to ensure that the worker does not come into contact with the chemicals.

Guidance on managing risks from hazardous chemicals are provided in the *Managing risks of hazardous chemicals in the workplace—Code of practice* available on the Safe Work Australia website.

Personal protective equipment should not solely be relied upon to control risk and should only be used when all other reasonably practicable control measures do not eliminate or sufficiently minimise risk. Guidance in selecting personal protective equipment can be obtained from Australian, Australian/New Zealand or other approved standards.

Obligations under workplace health and safety legislation

Information in this report should be taken into account to help meet obligations under workplace health and safety legislation as adopted by the relevant state or territory. This includes, but is not limited to:

- ensuring that hazardous chemicals are correctly classified and labelled;
- ensuring that (material) safety data sheets ((M)SDS) containing accurate information about the hazards (relating to both health hazards and physicochemical (physical) hazards) of the chemicals are prepared; and
- managing risks arising from storing, handling and using a hazardous chemical.

Your work health and safety regulator should be contacted for information on the work health and safety laws in your jurisdiction.

Information on how to prepare an (M)SDS and how to label containers of hazardous chemicals are provided in relevant codes of practice such as the *Preparation of safety data sheets for hazardous chemicals—Code of practice* and *Labelling of workplace*

hazardous chemicals—Code of practice, respectively. These codes of practice are available from the Safe Work Australia website.

A review of the physical hazards of these chemicals has not been undertaken as part of this assessment.

References

Agency for Toxic Substances & Disease Registry (ATSDR) 2006. Toxicological profile for cyanide. Accessed February 2015 at **http://www.atsdr.cdc.gov/toxprofiles/tp8.pdf**

Ansell, M.,& Lewis, F. A. (1969). A review of cyanide concentrations found in human organs. A survey of literature concerning cyanide metabolism, 'normal', non-fatal, and fatal body cyanide levels. Journal of forensic medicine, 17(4), 148-155.

European Centre for Ecotoxicology and Toxicology of Chemicals - Joint Assessment of Commodity Chemicals Report No. 3. Sodium and Potassium, and Acetone Cyanohydrin (CAS Nos. 74-90-8, 143-33-9, 151-50-8 and 75-86-5). Accessed February 2015 at **http://members.ecetoc.org/Documents/Document/JACC%20053%20Vol%20I.pdf**

Farooqui, M. Y. H.,& Ahmed, A. E. (1982). Molecular interaction of acrylonitrile and potassium cyanide with rat blood. Chemico-biological interactions, 38(2), 145-159.

Galleria Chemica. Accessed February 2015 at **http://jr.chemwatch.net/galleria/**

Gettler, A. O.,& Baine, J. O. (1938). The Toxicology of Cyanide. The American Journal of the Medical Sciences, 195(2), 182-197.

Hazardous Substances Data Bank (HSDB). National Library of Medicine. Accessed February 2015 at **http://toxnet.nlm.nih.gov**.

National Industrial Chemicals Notification and Assessment Scheme (NICNAS) 2006. Australian High Volume Industrial Chemicals List (AHVICL). Accessed January 2015 at **http://www.nicnas.gov.au/__data/assets/pdf_file/0019/6661/NICNAS_AHVICL_2006_PDF.pdf**

National Pollutant Inventory (NPI). Accessed February 2015 at **http://www.npi.gov.au/index.html**

NICNAS (2010) Priority Existing Chemical Report for Sodium Cyanide (CAS No. 143-33-9), February 2010. Electronic version for the web, accessed January 2015 at **http://www.nicnas.gov.au/__data/assets/pdf_file/0018/4392/PEC_31_Sodium-Cyanide_Full_Report_PDF.pdf**

Organisation for Economic Co-operation and Development (OECD), The 2007 OECD List of High Production Volume (HPV) Chemicals (2007). Accessed January 2015 at **http://www.oecd.org/officialdocuments/publicdisplaydocumentpdf/?cote=env/jm/mono%282009%2940&doclanguage=en**

REACH Dossier for Potassium Cyanide (CAS No. 151-50-8), accessed January 2015 at **http://echa.europa.eu/information-on-chemicals/registered-substances**

REACH Dossier for Sodium Cyanide (CAS No. 143-33-9), accessed January 2015 at **http://echa.europa.eu/information-on-chemicals/registered-substances**

Substances in Preparations in Nordic Countries (SPIN). Accessed January 2015 at **http://188.183.47.4/dotnetnuke/Home/tabid/58/Default.aspx**

The Poisons Standard (the Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP)) 2015.Accessed April 2015 at **http://www.comlaw.gov.au/Details/F2015L00128**

U.S Environmental Protection Agency (EPA) (2005). Toxicological Review of Hydrogen Cyanide and Cyanide Salts. In Support of Summary Information on the Integrated Risk Information System (IRIS). Accessed February 2015 at **http://www.epa.gov/iris/toxreviews/0060tr.pdf**

World Health Organisation (WHO) 2004. Hydrogen Cyanide and Cyanides: Human Health Aspects. Concise International Chemical Assessment Document; 61. Accessed February 2015 at

http://www.who.int/ipcs/publications/cicad/en/cicad61.pdf

Yamamoto, K., Yamamoto, Y., Hattori, H.,& Samori, T. (1982). Effects of routes of administration on the cyanide concentration distribution in the various organs of cyanide-intoxicated rats. The Tohoku journal of experimental medicine, 137(1), 73-78.

Last Update 01 September 2015

Chemical Identities

Chemical Name in the Inventory and Synonyms	**Sodium cyanide** hydrocyanic acid, sodium salt cyanide of sodium
CAS Number	143-33-9
Structural Formula	
Molecular Formula	CNNa
Molecular Weight	49.008

Chemical Name in the Inventory and Synonyms	**Potassium cyanide (K(CN))** hydrocyanic acid, potassium salt cyanide of potassium

CAS Number	151-50-8
Structural Formula	
Molecular Formula	CKN
Molecular Weight	65.116

Share this page