Australian Government
Department of Health and Aged Care
Australian Industrial Chemicals Introduction Scheme

Cobalt sulfide (CoS)

Assessment statement (CA09958)

13 March 2025

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AICIS assessment (CA09958)

Chemical in this assessment

Name	CAS registry number
Cobalt sulfide (CoS)	1317-42-6

Reason for the assessment

An application for an assessment certificate under section 31 of the *Industrial Chemicals Act 2019* (the Act).

Certificate application type

AICIS received the application in a Health and Environment Focus type.

Defined scope of assessment

The chemical has been assessed:

- as imported into Australia at up to 2 tonnes once during a five-year period
- as imported in finished end use products (solid form) at up to 3% concentration as a component of a processing agent (catalyst) for use in the petroleum refining industry (production of fuels)
- for use by industrial and professional workers only

Summary of assessment

Summary of introduction, use and end use

The assessed chemical will not be manufactured, reformulated, or re-packaged in Australia. It will be imported into Australia at up to 2 tonnes once during a five-year period, packed in sealed 200L steel drums. The imported end use products (solid form) containing the assessed chemical at up to 3% concentration will be transported from the port to the refinery by road. It may be temporarily stored at this site in an isolated area until further deployment into the refinery reactors.

The products containing the assessed chemical at up to 3% concentration will not be available to the public and will only be used by specialised catalyst loading contractors at one industrial site as a processing agent for use in the production of fuels.

Human health

Summary of health hazards

The submitted toxicological data on the assessed chemical and analogue chemicals (see **Supporting information Section**) indicate that the assessed chemical is:

- of low acute oral toxicity (LD50 >5,000 mg/kg bw in rats)
- of low acute dermal toxicity (LD50 >2,000 mg/kg bw in rats)
- of low acute inhalation toxicity (LC50 >5.09 mg/L in rats)
- not irritating to the skin
- slightly irritating to the eye
- a skin sensitiser
- not considered to be genotoxic

In a 28-day repeated dose inhalation toxicity study, rats were exposed (nose-only) to an aerosol of an analogue chemical (Tricobalt tetraoxide) at 0, 5, 20 and 80 mg/m^3, for 6 hours/day, 5 days/week for 4 weeks, with a 90-day recovery period group for all groups. Based on several adverse effects noted, a no observable adverse effect concentration (NOAEC) of 5 mg/m^3 for the analogue chemical was established for both male and female rats. The assessed chemical, based on the adverse effects reported in this study is classified as hazardous for prolonged or repeated exposure through inhalation (H372: causes damage to organs through prolonged or repeated exposure through inhalation), according to GHS Criteria.

No information on respiratory sensitisation of the assessed chemical or analogue chemical was provided by the applicant. However, several epidemiological studies conducted on cobalt compounds were associated with occupational asthma providing the basis of classification for respiratory sensitisation via the inhalation route of exposure (ATSDR, 2004; WHO, 2006; CoRC, 2014; NICNAS IMAP report, 2014). Therefore, the assessed chemical is classified as a respiratory sensitiser (H334: May cause allergy or asthma symptoms or breathing difficulties if inhaled), according to GHS Criteria.

In a combined repeated dose oral toxicity study on the assessed chemical with the reproduction/developmental toxicity screening, the no observed adverse effect level (NOAEL) was determined to be 1,000 mg/kg bw/day (the highest tested dose) for no adverse effects reported in F_0 generation and reproductive toxicity. Therefore, under the conditions of this study, the assessed chemical does not require hazard classification for reproductive/developmental toxicity, according to GHS criteria.

The International Agency for Research on Cancer (IARC) classified the assessed chemical, cobalt(II) sulfide in Group 3: Not classifiable as to its carcinogenicity to humans (IARC monograph, 2023).

Hazard classifications relevant for worker health and safety

Based on the data provided by the applicant and other information available to AICIS, the assessed chemical satisfies the criteria for classification according to the *Globally Harmonized System of Classification and Labelling of Chemicals* (GHS) (UNECE 2017) for hazard classes relevant for worker health and safety as adopted for industrial chemicals in Australia.

Health hazards	Hazard category	Hazard statement
Skin Sensitisation	Category 1	H317: May cause an allergic skin reaction
Respiratory Sensitisation	Category 1	H334: May cause allergy or asthma symptoms or breathing difficulties if inhaled
Specific target organ toxicity (repeated exposure)	Category 2	H372: Causes damage to organs through prolonged or repeated inhalation exposure

Summary of health risk

Public

The products containing the assessed chemical at up to 3% concentration will not be available for use by the public. When introduced and used in the proposed manner, it is unlikely that the public will be exposed to the assessed chemical.

This assessment does not identify any risks to the public health that require specific risk management measures.

Workers

Limited occupational exposure is expected to the assessed chemical at 3% concentration during use in the production of fuels, including handling at the end of usable life (approximately 5 years). According to the applicant, specialised catalyst loading contractors, special engineering controls and the personal protective equipment (PPE) will be used during these procedures.

Considering the adverse health effects possible through exposure to the assessed chemical, control measures to minimise inhalation, dermal and ocular exposure are needed to manage the risk to workers (see **Means for managing risk** section).

Environment

Summary of environmental hazard characteristics

As the assessed chemical is inorganic, it is excluded from categorisation under the Australian Environmental Criteria for Persistent, Bioaccumulative and/or Toxic Chemicals (DCCEEW, 2022).

Environmental hazard classification

A dissolution test conducted on the assessed chemical following OECD 105 Shake flask method coupled with spectroscopy determination showed that soluble cobalt was detected. Therefore, the hazard classification for the assessed chemical is based on soluble cobalt data. Accordingly, the assessed chemical satisfies the criteria for classification according to the GHS (UNECE, 2017) as Acute Category 1 (H400) and Chronic Category 1 (H410).

Environmental Hazard	Hazard Category	Hazard Statement
Hazardous to the aquatic environment (acute / short-term)	Aquatic Acute 1	H400: Very toxic to aquatic life
Hazardous to the aquatic environment (long-term)	Aquatic Chronic 1	H410: Very toxic to aquatic life with long lasting effects

Summary of environmental risk

The assessed chemical will be introduced into Australia as a component of a processing agent (catalyst) for use in the petroleum refining industry (production of fuels).

No environmental exposures of the assessed chemical are expected during use or end of life disposals.

A Risk Quotient (PEC/PNEC) for the aquatic compartment was not calculated as the currently available information indicates the assessed chemical will not be released to the environment, untreated. Therefore, it is expected that the environmental risk from the introduction of the assessed chemical can be managed.

Means for managing risk

Recommendation to Safe Work Australia

- It is recommended that Safe Work Australia (SWA) update the *Hazardous Chemical Information System* (HCIS) to include classifications relevant to work health and safety (see **Hazard classifications relevant for worker health and safety**).

Information relating to safe introduction and use

The information in this statement, including recommended hazard classifications, should be used by a person conducting a business or undertaking at a workplace (such as an employer) to determine the appropriate controls under the relevant jurisdiction Work Health and Safety laws.

The following control measures could be implemented to manage the risk arising from exposure to the assessed chemical during loading and unloading:

- Use of engineering controls such as
  - Enclosed and automated systems
  - Adequate workplace ventilation to avoid accumulation of dust or mist
- Use of safe work practices to
  - Avoid contact with skin and eyes
  - Avoid inhalation of dusts or mist
- Use of personal protective equipment (PPE)
  - Impervious gloves
  - Protective clothing
  - Eye protection
  - Respiratory protection

- The storage of the assessed chemical should be in accordance with the Safe Work Australia *Code of Practice for Managing Risks of Hazardous Chemicals in the Workplace* (SWA 2023) or relevant State or Territory Code of Practice.

- As the assessed chemical is a respiratory and skin sensitiser, the control measures may need to be supplemented with health monitoring for any worker who is at significant risk of exposure to the chemical, if valid techniques are available to monitor the effect on the worker's health.

- A copy of the Safety Data Sheet (SDS) should be easily accessible to workers.

Conclusions

The Executive Director is satisfied that the risks to human health or the environment associated with the introduction and use of the industrial chemical can be managed.

Note:

1. Obligations to report additional information about hazards under s 100 of the *Industrial Chemicals Act 2019* apply.
2. You should be aware of your obligations under environmental, workplace health and safety and poisons legislation as adopted by the relevant state or territory.

Supporting information

Chemical identity

CAS number	1317-42-6
CAS name	Cobalt sulfide (CoS)
Molecular formula	CoS
Associated names	Cobalt monosulfide Cobalt(2+) sulfide Cobalt(II) sulfide
Molecular weight (g/mol)	91.00
SMILES (canonical)	S=[Co]
Representative structure	

Relevant physical and chemical properties

Physical form	Grey solid powder
Melting point	>1,100 °C
Density	5,450 kg/m^3 at 20 °C
Water solubility	3.05 - 15 mg/L at 20 °C
Particle Size	Inhalable fraction (<100 µm): 14.8% Respirable fraction (<10 µm): 0.2%
Ionisable in the environment	Yes
log K_D	4.43 (Vesley et al., 2001)

Human exposure

Workers

At the refinery reactors, the solid products containing the assessed chemical at up to 3% concentration will be loaded from the steel drums into enclosed reactors. According to the applicant, this process will be completed by specialised catalyst loading contractors using refilling equipment under an inert atmosphere with sufficient personal protections as per the well documented site procedures. Special engineering controls such as isolated, automated, specialised processes, inert atmospheric environment, and atmospheric monitoring will be in

place. The specialised loading contractors will use the PPE including hazmat life support suits and self-contained respiratory systems during handling of the assessed chemical to minimise worker exposure to the assessed chemical.

Once the assessed chemical is loaded into the reactors, the assessed chemical at up to 3% concentration is expected to remain in enclosed systems over a period of approximately five years and will not be available for exposure during the intended use. At the end of usable life, the used product containing the assessed chemical will be unloaded into appropriate containers by specialised contractors using gravity and maintained under inert atmosphere. The used product will then be sent offsite for regeneration or disposed of according to relevant Commonwealth, state, territory and local government legislation. Fresh product containing the assessed chemical at up to 3% concentration will be reloaded into the reactor.

Exposure to the assessed chemical at up to 3% concentration in solid form may be possible during opening of the steel drums containing the assessed chemical at up to 3% concentration, loading to reactor vessels using refilling equipment, bale packing of used bags and cleaning and maintenance processes. However, as mentioned above, exposure to the assessed chemical at up to 3% concentration will be minimised through the use of specialised catalyst loading contractors, special engineering controls and the use of PPE.

Health hazard information

Acute toxicity

Oral

In an acute oral toxicity study (OECD TG 425), two groups of females Sprague-Dawley (SD) (n=3/dose) were administered a single dose of the assessed chemical in distilled water at 5,000 and 11,000 mg/kg bw by oral gavage. All animals were observed for mortality, signs of gross toxicity, and behavioural changes at least twice daily for 14 days after dosing. All animals survived, gained body weight and appeared active and healthy over the 14-day observation period: only a reduced faecal volume noted for one animal at 11,000 mg/kg bw. No signs of gross toxicity, adverse pharmacologic effects, or abnormal behaviour, and gross abnormalities were noted at necropsy at day 14 in both dose groups. Therefore, under the conditions of this study, the acute oral median lethal (LD50) of the assessed chemical is >5,000 mg/kg bw in female rats.

In a non-guideline acute oral toxicity study, SD rats (n=5/sex) were administered the assessed chemical at a single dose of 5,000 mg/kg bw in corn oil by oral gavage. The animals were observed for pharmacotoxicity signs and mortality three times on the day of administration and twice daily thereafter for a total of 15 days. All animals survived and appeared normal throughout the observation period. A weight gain was also observed, and no remarkable visceral findings were observed at necropsy. The acute oral median lethal dose (LD50) was reported to be >5,000 mg/kg bw in both males and females.

Dermal

In an acute dermal toxicity study (OECD TG 402), an analogue chemical (Cobalt resinate) was applied at a single dose of 2,000 mg/kg bw to the skin of SD rats (n=5/sex) by a semi-occlusive dressing for 24 hours. The animals were observed for 14 days following application. All animals survived until the end of the 14-day study period and no clinical signs were observed during the study. While a slightly lower body weight gain was noted in 2/5 males over the study, the overall body weight gain of other animals was similar to the historical control animals. No

apparent abnormalities were observed at necropsy in any animal. Under the conditions of this study, the acute dermal median lethal dose (LD50) of the analogue chemical was determined to be >2,000 mg/kg bw in rats.

In another acute dermal toxicity study (OECD TG 402), another analogue chemical (Cobalt resinate) was tested with the identical study design and at 2,000 mg/kg bw. All animals survived until the end of the 14-day study period and no clinical signs were observed during the study. While a slight lower body weight gain was noted in 2/5 males and in 1/5 females between day 8 and 15, the overall body weight gain of the other animals was not affected by treatment with the analogue chemical. No apparent abnormalities were observed at necropsy in any animal. Under the conditions of this study, the acute dermal LD50 of the analogue chemical was determined to be >2,000 mg/kg bw in rats.

Based on the above studies, the assessed chemical is considered to be of low acute dermal toxicity (LD50 >2,000 mg/kg bw in rats).

Inhalation

In an acute inhalation toxicity study (OECD TG 436), SD rats (Crl: CD(SD)) (n=3/sex/group) were exposed to a dry aerosol of the assessed chemical (nose-only exposure) at a gravimetrically determined concentration of 5.09 ± 0.06 mg/L air for 4 hours (14-day sacrifice) and with a satellite animal group for 24 hour sacrifice. The generated aerosol particulates of the main study and satellite animals had a mass median aerodynamic diameter (MMAD) of 4.004 and 4.418 µm, respectively.

There was no death during the study and the clinical signs observed were considered by the authors to be an overall clinical sign of general toxicity common to dust exposure, but not necessarily associated with the inhalation of the assessed chemical. Discolouration of the lungs in 2/3 male and 3/3 female animals (at 14-day sacrifice) and in all animals of the satellite study (at 24-hour sacrifice) was noted. As no significant pathologically findings were noted during the detailed histopathology of the respiratory tract, it is likely that the assessed chemical is not considered to be irritating to the respiratory system. Mild morphological changes in form of an inflammatory reaction were observed in the nose and lungs. The changes observed had almost recovered 14 days after exposure. The minimal lympho-histological infiltrations in the lungs, nose, trachea and larynx, and the pneumonic foci in the lungs were considered by the study authors as accidental findings or normal immunological reaction in healthy rats. Under the conditions of this study, the study authors determined the 4-hour inhalation medium lethal concentration (LC50 inhalation) for the assessed chemical to be > 5.09 mg/L air. Therefore, the assessed chemical is considered to be of low acute toxicity via inhalation.

Corrosion/Irritation

Skin irritation

The skin irritation potential of the assessed chemical was tested using an *in vitro* skin irritation test using the reconstructed human epidermis tissue model (EpiSkin™) (OECD TG 439). Human skin model tissues (EpiSkin) were treated with either the assessed chemical, the negative control or the positive control for 15 minutes. The relative mean viability of the assessed chemical treated tissues, after the 15-Minute exposure period (followed by the 42-hours post-exposure incubation period) was 106.90% (vs negative control of 100%).

Under the conditions of the study, the assessed chemical was not considered to be irritating to the skin and does not require classification as a skin irritant, according to GHS criteria.

Eye irritation

The eye irritation potential of the assessed chemical was determined using Bovine Corneal Opacity and Permeability (BCOP) test (OECD TG 437). A 0.75 mL of a 20% (w/v) suspension of assessed chemical was applied into the anterior part of each bovine cornea and incubated for 240 minutes. An *In vitro* Irritation Score (IVIS) was calculated, with an IVIS greater than 55 being indicative of risk of serious damage to eyes (OECD TG 437). The assessed chemical, relative to the negative control, did not cause any increase of the corneal opacity or permeability, the IVS was determined to be 0.12. Therefore, under the conditions of this study, the assessed chemical is not corrosive or irritating to the eyes and does not require classification as an eye irritant, according to GHS criteria.

In an *in vivo* eye irritation study (OECD TG 405), undiluted assessed chemical (0.1g) was instilled into the conjunctival sac of left eye of one male and 2 female NZ White rabbits and animals were observed for 7 days. Slight to moderate reddening of the conjunctivae was noted in all animals up to 48 hours and persisted as slight in two animals at the 72-hour observation. Slight reddening of the sclerae was noted in two animals at 24 hours. All eye reactions were reversible within 7 days following instillation. No abnormal findings were observed for the cornea or for the iris light reflex or any corrosion/staining of the treated eyes. The individual mean scores for corneal opacity, iris light reflex and conjunctival chemosis were 0.00 for all three animals. The individual mean scores for reddening of the conjunctivae were 0.67, 1.33 and 1.33, for 24, 48, and 72-hour observations, respectively. The assessed chemical did not induce any significant or irreversible damage to the rabbit eye. Therefore, under the conditions of this test, the assessed chemical was a slight eye irritant in rabbits and does not require hazard classification, according to GHS criteria.

Sensitisation

Skin sensitisation / Observation in humans

The applicant has not provided any study on skin sensitisation for the assessed chemical.

In a local lymph node assay (LLNA) (OECD TG 429), 25 mL of a suspension of an analogue chemical (cobalt oxide, CAS No. 1307-96-6) at 50, 25 or 12.5 % in acetone/olive oil was applied to the dorsal area of each ear of CBA female mice once daily for three consecutive days. Based on the LLNA study results, stimulation indexes of 1.8, 2.6 and 3.4 were reported for 12.5, 25 and 50 % suspensions of the analogue chemical. After linear interpolation of the results, an EC3 (estimated concentration needed to produce a stimulation index of three) value of 37.5 % was reported. Based on the results of this study, cobalt oxide was classified as a skin sensitiser (NICNAS IMAP report, 2014).

Several epidemiological studies conducted in cobalt-producing facilities support the findings that occupational inhalation exposure to inorganic cobalt compounds is associated with occupational asthma (ATSDR, 2004; WHO, 2006; CoRC, 2014; NICNAS IMAP report, 2014) and provide the basis of classification for sensitisation via the inhalation route of exposure. Specifically, studies have shown that there was a significant correlation between decreasing lung function tests (FEV1/FVC ratio) and increasing concentrations of cobalt in the air and in the urine of occupationally exposed workers (CoRC, 2014; NICNAS IMAP report, 2014).

In a study conducted in human volunteers, skin patch tests showed a positive reaction in 286/4034 patients to 1 % cobalt chloride (CAS No. 7646-79-9) in petroleum jelly 24 hours after exposure (REACH; NICNAS IMAP report, 2014). In another two patch test studies, 225/1415 patients and 24/373 patients showed a positive reaction to cobalt chloride when applied to the upper back using occlusive patches (REACH; NICNAS IMAP report, 2014). There appears to

be an increased incidence of positive reactions in females compared with males in all tests (REACH; NICNAS IMAP report, 2014). In an occupational study with 853 hard metal workers patch tested with an initial dose of 1 % cobalt chloride (CAS No. 7646-79-9), 62 % showed a positive skin sensitisation reaction (REACH; NICNAS IMAP report, 2014). In another study, flaring of eczema was observed following an oral administration with 1 mg of cobalt sulfate (CAS No. 10124- 43-3) in cobalt-sensitised people, with exposure once a week over a duration of three weeks. The allergic dermatitis reported was considered a positive allergic response to cobalt (ATSDR, 2004; NICNAS IMAP report, 2014).

Based on the above data on analogue chemicals, the assessed chemical has the potential to cause skin sensitisation and allergy or asthma symptoms or breathing difficulties if inhaled. Therefore, the assessed chemical is classified as hazardous for skin sensitisation H317: Category 1, May cause an allergic skin reaction) and for respiratory sensitiser (H334: May cause allergy or asthma symptoms or breathing difficulties if inhaled), according to GHS criteria.

Repeat dose toxicity

Oral

As unpublished data show moderate to high bioaccessibility and bioavailability in artificial gastric fluid, data from soluble cobalt compounds are read-across (OECD, 2014; NICNAS IMAP report, 2014). Data available from the NICNAS assessment of soluble cobalt compounds (NICNAS IMAP report, 2014), particularly data available for cobalt sulfate heptahydrate (CAS No. 10026-24-1) and cobalt chloride hexahydrate (CAS No. 7791-13-1) show that the main effect after repeated oral exposure to soluble cobalt compounds is polycythaemia (increased erythrocytes). However, this effect is reversible after cessation of exposure (NICNAS IMAP report, 2014).

In a combined repeated dose oral toxicity study with the reproduction/developmental toxicity screening (OECD TG 422), the assessed chemical was administrated to Crl:CD (SD) rats (n=10/sex/group) via oral gavage doses of 0 (vehicle), 100, 300 and 1,000 mg/kg bw/day. The assessed chemical was administered to males 2 weeks before mating (pre-mating) and continue during the mating period and approximately 2 weeks post mating until the minimum total dosing period of 28 days was completed (up to and including the day before sacrifice). The assessed chemical was administered to females 2 weeks before mating, during mating, gestation and lactation periods until day 3 post-partum or the day before sacrifice.

During the F_0 generation, there were no treatment-related effects on survival, body weight, food consumption, drinking water consumption, neurological screening (observation screening and functional observation), haematology and clinical biochemistry. Furthermore, no treatment related effects were noted at macroscopic/microscopic examination and on the sperm stages or interstitial testicle cell structure. The only treatment related non-adverse findings was piloerection noted in few male and female rats in all treatment groups.

Based on the above information, the NOAEL was determined to be 1,000 mg/kg bw/day (the highest tested dose) for no adverse effects observed on F_0 generation (parental generation). Therefore, based on the above information, the assessed chemical does not require hazard classification for repeated exposure via oral route, according to GHS criteria.

Inhalation

In a 28-day repeated dose inhalation toxicity study (OECD TG 412), Wistar rats Crl:WI (Han) (n=10/sex/dose) were exposed (nose-only) to an aerosol of an analogue chemical (Tricobalt tetraoxide) (grey-black powder) at 0 (clean air), 5, 20 and 80 mg/m^3, for 6 hours/day, 5 days/week for 4 weeks, with a 90-day recovery period group for all groups (n=10/sex/dose). The target concentrations were achieved at all doses. The mean mass-median-aerodynamic diameters (MMAD) were 1,81, 98, and 2.14 µm at 5, 20, and 80 mg/m^3, respectively. Bronchoalveolar lavage (BAL) was performed in 5 male and 5 female rats per group after end of exposure (day 1) and following end of recovery period (day 91).

No mortalities were observed during the study. There was no treatment related adverse effects on body weight, food and water consumption, haematology and clinical chemistry. At necropsy, there were no treatment-related adverse macroscopic findings.

Absolute and relative lung weights (lung weight/body weight), compared to concurrent control, were significantly increased in male and female animals in the high dose groups at day 1 following end of exposure. Following the recovery period at day 91, significantly increased lung weights (absolute and relative) persisted in the high dose groups up to day 91. Similar results were observed at lungs used for BAL. At day 1 following end of exposure, significant increases of polymorphonuclear neutrophils (PMN) were noted in the mid dose group (19%/13% in males/females) and in the high dose group (31%/35% in males/females). Furthermore, significant increases of lactic dehydrogenase and total protein were also observed in the mid dose males and lactic dehydrogenase, ß-glucuronidase and total protein in the high dose males and female animals. Furthermore, a clear dose-dependency effects were observed for cytokine concentrations.

Adverse histopathological findings were observed in lungs at day 1 following end of exposure. The findings included: the alveolar infiltration of granulocytic cells, the interstitial mononuclear cell infiltration at the terminal bronchus, the lipoproteinosis, and interstitial fibrosis in some mid-dose animals and all high dosed animals. Histopathological changes observed at day 1 following end of exposure, were also observed after 91 days of recovery but only in the high dose animals.

Under the conditions of this study and based on several adverse effects noted as above at mid dose (20 mg/m^3) a NOAEC of 5 mg/m^3 for the analogue chemical was established for both male and female rats. Therefore, based on the above adverse effects, the assessed chemical is classified as hazardous for repeated exposure through inhalation (H372: causes damage to organs through prolonged or repeated exposure through inhalation), according to GHS criteria.

Observation in humans

A survey conducted in workers exposed to 'cobalt dusts' consisting of cobalt oxides, cobalt salts or cobalt metal (average concentration of 0.125 mg/m^3) concluded that exposure to these compounds interfered with thyroid metabolism and induced respiratory disorders. Workers exposed to 'cobalt dusts' frequently complained of difficulty in breathing (dyspnoea and wheezing), compared with the control group. This was supported by a statistically significant relationship (logistic regression analysis) between the dustiness of the workplace, the level of cobalt in the urine and symptoms of dyspnoea in workers. Also, there was a significant dose-effect relationship between a reduction in measures of lung function (FEV1/FVC ratio) to the intensity of 'cobalt dust' exposure as measured in the air and measured as cobalt in the urine of workers (Swennen et al., 1993; NICNAS IMAP report, 2014). Further data on the risk of lung cancer and cobalt exposure are summarised in the Carcinogenicity section of this report.

Cobalt-induced cardiac failure was attributed to 50 patients who had ingested, over a period of years, an average of 0.2 to 0.7 mg/kg bw/day of cobalt sulfate heptahydrate (CAS No. 10026-24-1) that was added to stabilise foam in beer. The first signs of beer–cobalt cardiomyopathy were gastrointestinal effects including nausea, vomiting and diarrhoea. Beer–cobalt cardiomyopathy and alcoholic cardiomyopathy have similar symptoms, although the onset of beer–cobalt cardiomyopathy was found to be very abrupt. These patients had protein-poor diets and consumed significant quantities of alcohol, which might affect the symptoms of cardiomyopathy, pulmonary rales and pulmonary oedema that were observed (ATSDR, 2004; NICNAS IMAP report, 2014). In an occupational study of 237 workers from a cobalt refinery, no dose-effect relationships were observed between cobalt exposure and incipient signs of cardiomyopathy (Lantin et al., 2013; NICNAS IMAP report, 2014). Polycythaemia (increase in erythrocytes) and an increase in haemoglobin levels were observed in all subjects in another study where six volunteers were exposed to a daily dose of 150 mg/day of cobalt chloride (CAS No. 7646-79-9) for up to 22 days. Erythrocyte counts returned to normal in all subjects 15 days after treatment (ATSDR, 2004; NICNAS IMAP report, 2014). Cobalt has been previously used therapeutically to treat anaemia due to its ability to increase haemoglobin levels. In a series of studies, patients with impaired kidney function were treated with 0.65–4.0 mg/kg/day of cobalt chloride (CAS No. 7646-79-9), daily for 3–32 weeks. The increase in erythrocytes resulted in a decreased need for blood transfusions (ATSDR, 2004; NICNAS IMAP report, 2014). In another series of studies, sickle-cell anaemia patients receiving cobalt therapy showed enlargement and hyperplasia of the thyroid gland, which were reversible upon cessation of cobalt therapy (ATSDR, 2004; NICNAS IMAP report, 2014). When pregnant women were treated for 90 days with 2–2.4 mg/kg/day of cobalt chloride (CAS No. 7646-79-9), it did not prevent the common occurrence of decreasing levels of haemoglobin and haematocrit levels observed during pregnancy. There were also no effects observed on the heart, in liver function or obvious birth defects (ATSDR, 2004; NICNAS IMAP report, 2014).

Genotoxicity

Limited data are available on the assessed chemical.

Various analogues of the assessed chemical were found to be non-mutagenic in a bacterial reverse mutation assays, with or without metabolic activation (S9-mix), using *Salmonella typhimurium* strains (OECD TG 471): TA97a (cobalt dichloride, tested up to the top cytotoxic concentration of 3,160 pg/plate), TA100 (cobalt sulphate, tested up to the top concentration of 5,000 pg/plate), TA98 (cobalt metal powder, tested up to the cytotoxic concentration of 1,000 pg/plate), TA97a (cobalt dichloride hexahydrate, tested up to the top concentration of 5,000 pg/plate).

Therefore, based on the above results, the assessed chemical is expected to be non-mutagenic in bacterial reverse mutation assay, with or without metabolic activation (S9-mix), using *Salmonella typhimurium* strains.

Data on the *in vitro* genotoxicity for an analogue chemical (Cobalt(II) hydroxide) are of limited relevance due to its low solubility in culture medium. Under *in vivo* conditions, solubilisation of the chemical in biological fluids, including acidic gastric juices, precedes the delivery of cobalt to the cells. Based on the high solubility of the chemical after ingestion, genotoxicity data can be read-across from the NICNAS assessment of soluble cobalt compounds (NICNAS IMAP report, 2014). It was concluded that effective protective processes exist in vivo to prevent genotoxicity in human (OECD, 2014; NICNAS IMAP report, 2014) and hence, no classification is required for genotoxicity (NICNAS IMAP report, 2014).

The assessed chemical was tested for its ability to induce mutation at the hypoxanthine-guanine phosphoribosyl transferase (hprt) locus (6 -thioguanine [6TG] resistance) in mouse

lymphoma cell line L5178Y, using a fluctuation protocol (OECD TG 476). The study consisted of two independent cytotoxicity experiments. In the mutation experiments, no statistically significant increases in mutant frequency were observed following treatment with the assessed chemical at concentration ranging from 50 to 922 µg/mL in the absence of S-9. Therefore, it is concluded that the assessed chemical did not induce mutation at the *hprt* locus of L5178Y mouse lymphoma cells when tested up to toxic concentrations for 24 hours exposure in the absence of metabolic activation.

Based on the above information, the assessed chemical is not considered to be genotoxic.

Carcinogenicity

No data were submitted on the assessed chemical for AICIS to conduct an assessment of this health end point.

AICIS notes that the IARC has recently classified cobalt(II) sulfide (the assessed chemical) in Group 3: Not classifiable as to its carcinogenicity to humans (IARC monograph, 2023).

The IARC Group 3 conclusion for the assessed chemical was based on inadequate evidence regarding cancer in humans, limited evidence for cancer in experimental animals, and on inadequate mechanistic evidence. High incidence of malignant neoplasms noted in a single experiment in rat was taken into consideration for indication as limited evidence for cancer in experimental animals.

Reproductive and development toxicity

In a combined repeated dose oral toxicity study with the reproduction/developmental toxicity screening (OECD TG 422), the assessed chemical was administrated to Crl:CD (SD) rats (n=10/sex/group) via oral gavage doses of 0 (vehicle), 100, 300 and 1,000 mg/kg bw/day (as discussed above).

There was no treatment-related effect related on fertility and reproduction parameters such as pre-coital time, gestation length, number of corpora lutea, implantation sites, number and sex of pups, runts or malformed pups, birth index, live birth, preimplantation loss, post-implantation loss and sperm number, viability and morphology at any tested dose levels. During the F_1 generation, there was no test substance related deaths or abnormal behaviour in pups or on the growth and development of the offspring from conception until sacrifice on lactation day 4 post-partum or shortly thereafter at any tested dose. No test substance related effect was noted on the mean and total litter weight or on external abnormalities in any pups examined at any of the tested dose levels.

Based on the above information, the NOAEL was determined to be 1,000 mg/kg bw/day (the highest tested dose) for no adverse effects observed on reproductive toxicity. Therefore, under the conditions of this study, the assessed chemical does not require hazard classification for reproductive/developmental toxicity, according to GHS criteria.

Environmental exposure

Exposures to the environment during manufacturing, reformulation or re-packaging processes are not expected. The catalysts containing the assessed chemical will be imported into Australia as fully finished products containing the assessed chemical and will be transported

from port to the refinery by road. It may be temporarily stored at refinery sites until it is deployed into refinery reactors. No environmental release is expected during these processes.

In the unlikely event of accidental spills or leaks during storage, transport, activation and loading, the assessed chemical is expected to be collected for re-use or metal reclamation to the extent practicable.

Environmental exposures during loading the catalyst containing the assessed chemical into reactors is also expected to be minimal, as specialised procedures will be in place during these processes.

Once the catalysts are loaded into the reactors, the assessed chemical is expected to remain in the enclosed systems over a period of approximately 5 years and is not expected to have any environmental release during use.

The used catalysts will be sent offsite for regeneration or disposed of according to relevant Commonwealth, state, territory and local government legislation, or exported for metal reclamation processes. Any potential disposal to landfill requires prior consent from appropriate local, State and Federal government authorities.

Environmental fate

Dissolution, speciation and partitioning

The behaviour of the cobalt(II) is strongly dependent on the chemistry of the environmental compartment into which it is released.

In the environment, cobalt exists primarily as Co(II) and Co(III). Co(II) is more soluble as compared to Co(III). At neutral to acidic pH, Co(II) is soluble in water and available for uptake by organisms. At pH above 7 and high concentrations, cobalt may precipitate as cobalt hydroxide, cobalt carbonate, cobalt oxide and cobalt sulfide. At high pH, cobalt solubility also decreases due to strong retention by sediments and soils (McLaughlin and Batley, 2010).

The cobalt sulfide is expected to be significantly more soluble than other metal sulfides such as copper, nickel and lead. Therefore, in environments where metal sulfides co-occur, the assessed chemical is expected to be displaced from sediments (Simpson et al., 2000) and may become mobilised.

Degradation

No information on the degradation of the assessed chemical was provided. The assessed chemical is inorganic, and therefore excluded from persistence classification.

Bioaccumulation

Conventional measures of bioaccumulation as applied to organic chemicals are not appropriate for metal ions. Cobalt is an essential element for nitrogen fixation by bacteria, blue-green algae, and in root nodules of leguminous plants. It is also an essential micro-nutrient for animals and is an integral component of cobalamin or vitamin B12 and is required by several enzymes involved in nitrogen fixation (IPCS 2006; Mathews et al. 2008; Metian et al. 2009; Hu et al., 2021). Hence, cobalt will naturally be taken up and may be accumulated by certain species of organisms. However, the available data indicate that biomagnification of cobalt does not occur in natural food webs (Environment Canada, 2017).

Predicted environmental concentration (PEC)

The predicted environmental concentration (PEC) has not been calculated as release of the assessed chemical to the aquatic environment is not expected based on its assessed use patterns.

Environmental effects

Effects on aquatic Life

Acute toxicity

The following median lethal concentration (LC50) and effect concentration (EC50) values for model organisms were supplied for dissolvable Co in solution.

Taxon	Endpoint	Method
Fish	96 h LC50 = 0.8 mg Co/L	*Oncorhynchus mykiss* (Rainbow trout) OECD TG 203 Flow-through conditions Mean measured concentration
Invertebrate	48 h LC50 = 0.777 mg Co/L	*Ceriodaphnia dubia* (Water flea) Immobility/other effect OECD TG 202 Static conditions Mean measured concentration
Algae	72 ErC50 = 144 µg Co/L	*Raphidocelis subcapitata* (Green algae) Growth rate, OECD TG 201, Static conditions, Mean measured concentration
Aquatic plants	7 d ErC10 = 90.1 µg Co/L	*Lemna minor* (Duckweed), Vegetative growth test (Heijerick, 2007)

Chronic toxicity

The following chronic toxicity values including no effect concentrations (NOEC) and effect concentration (EC10) values for model organisms were supplied for dissolvable Co in solution.

Taxon	Endpoint	Method
Fish	30 d NOEC = 0.488 mg Co/L	*Oncorhynchus mykiss* (Rainbow trout) Mortality OECD TG 203 Flow-through conditions Mean measured concentration
Algae	72 ErC10 = 23 µg Co/L	*Raphidocelis subcapitata* (Green algae) Growth rate, OECD TG 201, Static conditions, Mean measured concentration
Aquatic plants	7 d ErC10 = 4.9 µg Co/L	*Lemna minor* (Duckweed), Vegetative growth test (Heijerick, 2007)

Predicted no-effect concentration (PNEC)

Default guideline values are published for cobalt in the Australian and New Zealand Guidelines for Fresh and Marine Water Quality. These values represent thresholds above which further assessment of potential toxicity may be required to ensure environmental quality. For marine ecosystems, a high reliability guideline value for protection of 95% of marine species has been determined to be 1 µg Co/L (ANZECC, 2000).

Categorisation of environmental hazard

As the assessed chemical is inorganic, it is excluded from categorisation under the Australian Environmental Criteria for Persistent, Bioaccumulative and/or Toxic Chemicals (DCCEEW, 2022).

Environmental risk characterisation

As the assessed chemical is inorganic, it is excluded from categorisation under the Australian Environmental Criteria for Persistent, Bioaccumulative and/or Toxic Chemicals (DCCEEW, 2022).

A Risk Quotient (PEC/PNEC) for the aquatic compartment was not calculated as the currently available information indicates the assessed chemical will not be released to the environment, untreated. Therefore, the risk from the assessed chemical can be managed.

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