Cobalt oxide: Human health tier II assessment

27 November 2014

Chemicals in this assessment

Chemical Name in the Inventory	CAS Number
Cobalt oxide (CoO)	1307-96-6
Cobalt oxide	11104-61-3

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

This group of chemicals contains cobalt oxide (CAS No. 1307-96-6) and an unknown or variable composition, reaction product or biological (UVCB) form of cobalt oxide (CAS No. 11104-61-3). These compounds are grouped together as they are expected to have similar toxicity given that the health effects of exposure to these chemicals are driven by the Co^{2+} cation.

Import, Manufacture and Use

Australian

The chemical cobalt oxide (CAS No. 1307-96-6) has reported domestic and commercial use including:

- within nickel-metal hydride batteries; and
- as a colourant in glazes for arts and crafts.

International

The following international uses have been identified through European Union Registration, Evaluation, Authorisation and Restriction of Chemicals (EU REACH) dossiers; Galleria Chemica; Substances and Preparations in the Nordic countries (SPIN) database; the European Commission Cosmetic Ingredients and Substances (CosIng) database; and the US National Library of Medicine's Hazardous Substances Data Bank (HSDB).

The chemicals have reported domestic use including as a component (at <1 %) of glazes in arts and crafts.

The chemicals have reported commercial use including:

- as a colourant or dye;
- in pigments, paints and enamels; and
- as an agent for colouring glass.

The chemicals have reported site-limited use including in the:

- petroleum industry as a catalyst; and
- manufacture of pigments, paints and enamels.

Restrictions

Australian

Cobalt and its compounds are listed in Schedule 10 (prohibited carcinogens, restricted carcinogens and restricted hazardous chemicals) of the Work Health and Safety Regulations for restricted use in abrasive blasting at a concentration of greater than 0.1 % of cobalt (WHS, 2014).

International

No international restrictions have been identified.

Existing Worker Health and Safety Controls

Hazard Classification

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

Xn; R22 (Acute toxicity); and

R43 (Skin sensitisation).

Exposure Standards

Australian

No specific exposure standards are available.

International

The chemicals in this group generally fall under the group entry 'Cobalt and compounds'. The following exposure standards are identified (Galleria Chemica):

An exposure limit—time weighted average (TWA) of 0.05–0.1 mg/m^3 in different countries such as Germany (0.1 mg/m^3 inhalable fraction), Japan (0.05 mg/m^3, cobalt and compounds), and Switzerland (0.05 mg/m^3, cobalt and cobalt compounds as respirable dusts/aerosols).

Health Hazard Information

Limited data are available for specific toxicological endpoints (repeated dose toxicity, genotoxicity, carcinogenicity and reproductive and developmental toxicity) for the chemicals in this group. While published bioaccessibility data suggest that cobalt oxide releases the Co^{2+} cation in artificial gastric fluid at the same levels as soluble cobalt compounds (Stopford et al., 2003), unpublished data suggest that cobalt oxide releases the Co^{2+} cation at moderate levels compared to soluble cobalt compounds (CDI, 2014). In the absence of animal studies, considering that moderate (CDI, 2014) to high (Stopford et al., 2003) level of Co^{2+} ion release is expected through the oral route, the chemicals in this group will have a hazard profile ranging up to that for soluble cobalt compounds following oral exposure. Soluble cobalt compounds are assessed under the Inventory Multi-tiered Assessment and Prioritisation (IMAP) framework (NICNAS).

Toxicokinetics

Limited toxicokinetic data are available for the chemicals in this group.

The majority of data available are for cobalt (II, III) oxide, also referred to as tricobalt tetraoxide (Co_3O_4) (CAS No. 1308-06-1), a compound produced by heating cobalt oxide (CAS No. 1307-96-6) to 600–700 degrees Celsius resulting in a water insoluble form of cobalt oxide. Therefore, the toxicokinetic data cannot be compared with the slightly soluble cobalt oxide (3.27 mg/L at 37 degrees Celsius) (CAS No. 1307-96-6) described in this assessment (REACH). Bioaccessibility data indicate that the two chemicals in the current assessment release the Co^{2+} ion into artificial gastric and lysosomal fluids at different rates (Stopford et al., 2003; CoRC, 2014).

Inhalation

Inhaled particles of cobalt oxide are deposited in the respiratory tract and are absorbed through various mechanisms. The deposition of cobalt particles in specific areas of the lung is dependent on particle size. For example, particles of cobalt > 2 μm tend to deposit in the upper respiratory tract, while smaller particles are deposited in the lower respiratory tract (ATSDR, 2004). In humans, the deposition of cobalt oxide varied from approximately 50 % for particles with a mean diameter of 0.8 μm to 75 % for particles with a diameter of 1.7 μm (ATSDR, 2004). A study in humans using radioactive cobalt (^{57}Co) showed that cobalt oxide initially deposited in the lungs could be absorbed into the blood after dissolution, or transferred to the gastrointestinal tract by mucociliary action of the respiratory tract aided by swallowing (ATSDR, 2004). Further data indicate that in humans almost half of the cobalt oxide administered persisted in the lungs six months after exposure, while in rats, cobalt oxide was completely cleared after six months (WHO, 2006). In humans, the elimination of cobalt from the lungs is reported to follow three-phase kinetics. The first phase includes mucociliary clearance with a half-life of 2-44 hours. The second phase involves macrophage mediated clearance and has a half-life ranging from 10-78 days. The third phase is described to have a half-life in the order of several years (ATSDR, 2004).

Oral

Published bioaccessibility data indicate that cobalt oxide (CAS No. 1307-96-6) releases the Co^{2+} ion into artificial gastric fluid at a similar rate to cobalt sulfate heptahydrate (CAS No. 10026-24-1) (Stopford et al., 2003). Unpublished data suggest that the bioaccessibility of cobalt oxide is moderate in artificial gastric fluids (CDI, 2014). It is possible that different forms (sintered, calcined or precipitated) of cobalt oxide may have been used by Stopford et al., 2003 and the CDI, resulting in different gastric bioavailability.

The oral median lethal dose—LD50 value reported for cobalt oxide is 202 mg/kg bw, equivalent to 159 mg Co/kg bw. This can be compared to the LD50 value reported for cobalt sulfate heptahydrate (NICNASa) of 768 mg/kg bw; which is equivalent to 161 mg Co/kg bw. This comparison indicates that cobalt oxide (as used in the LD50 test) and cobalt sulfate heptahydrate have similar bioavailability to animals by oral exposure.

Dermal

No toxicokinetic data are available for the chemicals in this group. Considering that the absorption of soluble cobalt chloride was less than 1 % through intact guinea pig skin, it is not expected that cobalt oxide will be absorbed due to its lower solubility in water (ATSDR, 2004; REACH) and artificial sweat compared with cobalt chloride (CDI, 2014).

Acute Toxicity

Oral

Cobalt oxide (CAS No. 1307-96-6) is classified as hazardous with the risk phrase 'Harmful if swallowed' (Xn; R22) in HSIS (Safe Work Australia). The available data (median lethal dose—LD50—202 mg/kg bw) support this classification. Reported signs of toxicity include sedation, diarrhoea and a decrease in body temperature at the highest dose administered (1010 mg/kg bw) (REACH).

In a study conducted similarly to OECD Test Guideline (TG) 401, male and female Wistar rats were exposed to a single oral dose of cobalt oxide (CAS No. 1307-96-6) (200, 300, 450, 675 or 1010 mg/kg bw) and observed for 10 days. Based on the results, the LD50 for anhydrous cobalt oxide was reported as 202 mg/kg bw in male and female Wistar rats. Histopathological changes were reported (doses unspecified) in the heart (hyperaemia, haemorrhage, interstitial oedema and myocardial changes), liver (depletion of glycogen, vacuolisation, hyperaemia, necrotic foci and pale periportal cells) and kidneys (nephritis, hyperaemia, haemorrhage, tubular alterations and autolytic changes) (REACH).

Dermal

No data are available for the chemicals in this group. However, considering that the absorption of soluble cobalt chloride was less than 1 % through intact guinea pig skin, acute toxicity by the dermal route is not expected for chemicals in this group.

Inhalation

Cobalt oxide (CAS No. 1307-96-6) had very high acute toxicity in animal tests using acute inhalation exposure. The median lethal concentration (LC50) in rats was 0.06 mg/L. Observed sub-lethal effects were dose dependent and ranged from slight ataxia and dyspnoea at the lowest dose (0.05 mg/L) to moderate ataxia, tremor and reduced muscle tone at the highest dose (5.06 mg/L) (REACH).

In a study conducted according to OECD TG 436, male and female Crj: CD(SD) rats were exposed to a single inhalation concentrations of 0.11 and 0.53 mg/L cobalt oxide (CAS NO. 1307-96-6) (mass median aerodynamic diameter (MMAD) ranging from 3.3–3.7 μm) in the main study group for four hours, and then observed over 14 days and 0.05, 0.11, 0.53, 1.07 or 5.06 mg/L cobalt oxide in a satellite group, for four hours and observed for 24 hours. In the main study group, all animals exposed to concentrations of 0.11 and 0.53 mg/L died prematurely on days four and three of the observation period, respectively. In the satellite group observation only occurred for 24 hours and during this time mortality was reported at all concentrations above 0.05 mg/L (0.11 mg/L- 2/3 males and 0 females, 0.53mg/L- 3/3 males and 1/3 females, 1.07 mg/L 2/3 males and 3/3 females, 5.06 mg/L 3/3 males and 1/3 females). Sub-lethal effects reported in the main study included ataxia, tremor and dyspnoea across all exposure groups. In the satellite group, sub-lethal effects of ataxia, tremor, reduced muscle tone and dyspnoea were reported in animals exposed to the two highest concentrations (1.07 and 5.06 mg/L). Based on this study the LC50 was calculated to be 0.06 mg/L (REACH).

In a further study conducted according to OECD TG 403, male and female Wistar rats were exposed to a single exposure of 0.26 mg/L cobalt oxide (CAS No. unspecified) via inhalation for four hours and observed over a period of eight days. Mortality was reported in all animals within the eight day observation period. Sub-lethal effects reported included bradypnoea, decreased spontaneous activity, ventral recumbency and ruffled fur. Based on this study the LC50 was considered to be lower than 0.26 mg/L (REACH).

Corrosion / Irritation

Skin Irritation

The chemicals in this group are not skin irritants.

In an in vitro study conducted according to OECD TG 439, 10 mg of cobalt oxide (CAS No. 1307-96-6) was applied to artificial human skin (EpiSkin kit) for 15 minutes. Based on a cell viability assay, cobalt oxide was concluded not to be a skin irritant under the conditions of the assay (REACH).

Eye Irritation

Cobalt oxide (CAS No. 1307-96-6) is reported to be a slight eye irritant in animal studies. Effects were not sufficient to warrant a hazard classification.

In a study conducted according to OECD TG 405, 0.1 g of cobalt oxide (CAS No. 1307-96-6) was instilled into one eye of New Zealand White rabbits briefly. Animals were then observed at specific time points up to seven days. One hour after exposure, all animals were reported to have slight to moderate reddening of the eye which persisted until 72 hours after administration. Slight ocular discharge was reported in the male animal tested, one hour after instillation. All adverse effects were reported to resolve within the seven day observation period. Reported mean Draize scores for the cornea, iris and conjunctivae were 0, 0 and 1, respectively (REACH).

In an in vitro test conducted according to OECD TG 437, 0.75 mL of a 20 % suspension of cobalt oxide (CAS No. 1307-96-6) was applied to freshly isolated bovine eyes for 240 minutes. Based on the proposed INVITOX (UK) protocol no. 98 irritation scale, the chemical was evaluated as a mild eye irritant based on the average irritation score of 7.15 which lies in the mild eye irritant category (3.1–25) (REACH).

Sensitisation

Skin Sensitisation

Cobalt oxide (CAS No. 1307-96-6) is classified as hazardous with the risk phrase ‘May cause sensitisation by skin contact’ (R43) in HSIS (Safe Work Australia). The positive results reported in a local lymph node assay (LLNA) (EC3 is 37.5 %) support this classification (REACH).

In a LLNA assay conducted according to OECD TG 429, 25 µL of a suspension of cobalt oxide (CAS No. 1307-96-6) (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 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 is classified as a skin sensitiser (REACH).

Observation in humans

Respiratory sensitisation

Based on the available epidemiological evidence, the chemicals in this group are recommended for classification for sensitisation via the inhalation route of exposure (refer to **Observation in Humans**).

Several epidemiological studies conducted in cobalt-producing facilities support the findings that occupational exposure to inorganic cobalt compounds is associated with occupational asthma (ATSDR, 2004; WHO, 2006; CoRC 2014). Specifically, studies have show that there was a significant correlation between decreasing lung function tests (FEV1/VC ratio) and increasing concentrations of cobalt in the air and urine of occupationally exposed workers (CoRC, 2014).

Repeated Dose Toxicity

Oral

No data are available for the chemicals in this group. Bioaccessibility studies conducted with cobalt oxide indicate that the Co^{2+} ion is released at moderate (CDI, 2014) to high (Stopford et al., 2003) levels compared to soluble cobalt compounds (cobalt sulfate heptahydrate, CAS No. 10026-24-1) in artificial gastric fluid. Data available from the NICNAS assessment of soluble cobalt compounds, 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 compounds is polycythaemia (increased erythrocytes). However, this effect is reversible after cessation of exposure (NICNAS). The severity and/or reversibility of effects seen in these studies (NICNAS) do not meet the criteria for hazard classification.

Dermal

No data are available.

Given that the toxicokinetic data show low dermal absorption (ATSDR, 2004), repeated dose toxicity through the dermal route is not expected.

Inhalation

Limited data are available for the chemicals in this group. Bioaccessibility studies conducted with cobalt oxide indicate that while the Co^{2+} ion is released at low levels in artificial alveolar fluid, it is released at similar rates to soluble cobalt compounds (cobalt sulfate heptahydrate, CAS No. 10026-24-1) in artificial lysosomal fluid (Stopford et al., 2003). Considering the bioaccessibility studies in artificial lysosomal fluid, in the absence of sufficient data on the chemicals in this group, data on systemic toxicity may be read across from soluble cobalt compounds for repeated dose toxicity via the inhalation route.

It has been reported by Ortega et al., (2014) that phagocytosis followed by release of solubilised Co^{2+} and macrophage contents (for components bioavailable in lysosomal fluid) may be a route for toxicity. Considering that cobalt oxide is almost completely dissolved in artificial lysosomal fluid (Stopford et al., 2003) similarly to cobalt sulfate, it is prudent to read-across data from soluble cobalt compounds.

Furthermore, inhalation acute toxicity data strongly support classification for repeated dose toxicity via the inhalation route of exposure. Cobalt oxide had very high acute toxicity in animal tests following acute inhalation exposure with a LC50 in rats of 0.06 mg/L. Considering the level of toxicity from a single dose (i.e. 0.06 mg/L) meets the approved criteria for classifying hazardous substances (NOHSC, 2004) and GHS classification criteria for repeated dose toxicity via the inhalation route, chemicals in this group could cause serious damage to health by prolonged exposure through inhalation.

Cobalt oxide

A study conducted in Syrian Golden hamsters evaluated the effect of lifetime exposure to cobalt oxide (CAS No. 1307-96-6) at10 mg/L (seven hours a day, five days a week). Compared with controls, lifetime exposure to cobalt oxide did not affect survival, but induced pneumoconiosis (emphysema) (WHO, 2006).

Cobalt sulfate heptahydrate

The NTP conducted 13-week (NTP, 1991) and two-year studies (NTP, 1998) in male and female F344/N rats and B6C3F1 mice. In the 13-week study, rats and mice (10 animals/sex/species) were exposed to aerosols containing 0, 0.3, 1.0, 3.0, 10 or 30 mg/m^3 cobalt sulfate heptahydrate (CAS No. 10026-24-1) for six hours a day, five days a week for the duration of the study. Male rats exposed to any concentration of the chemical showed a significant increase in relative kidney weights. Histopathological examination of the kidneys did not indicate any increase in kidney lesions in rats or mice in the 13-week study, although in male rats there was a concentration-related increase in epithelial cells and granular casts observed in the urine, suggesting slight renal toxicity. There was also a significant increase in the relative lung weights of rats exposed to 0.3 mg/m^3 and higher for males, and 1 mg/m^3 and higher for females. In mice, this was observed in both sexes from 10 mg/m^3 and higher. Absolute and relative testis and epididymal weights were significantly decreased in male mice at 30 mg/m^3. Polycythaemia was observed in rats at 3 mg/m^3 and higher. Histopathological lesions were observed in the respiratory tract of both rats and mice at all exposure levels from the chemical. A LOAEC of 0.3 mg/m^3 was determined based on squamous metaplasia in the larynx (NTP, 1991).

Observation in humans

There are no data available specifically for cobalt oxide. 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. In particular, 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 the 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). Further data on the risk of lung cancer and cobalt exposure is summarised in the **Carcinogenicity** section of this report.

Genotoxicity

Based on the available data, the chemicals in this group do not have mutagenic or genotoxic potential.

In an in vitro study conducted according to OECD TG 476, cobalt oxide (CAS No. 1307-96-6) was incubated with mouse lymphoma L5178Y cells up to a maximal concentration of 120 μg/mL with and without metabolic activation. There were no significant increases in mutation frequency with or without metabolic activation. Also, the chemical did not induce mutation at the hypoxanthine-guanine phosphoribosyltransferase (hrpt) locus of the lymphoma cells tested (REACH).

In an in vivo study carried out similarly to OECD TG 475, SD rats were given a single dose of cobalt oxide (CAS No. 1307-96-6) (100, 300 or 1000 mg/kg bw) via oral gavage. The results concluded that under the conditions of the study the chemical is not mutagenic with respect to the induction of chromosome aberrations in the bone marrow of the animals studied (REACH).

Carcinogenicity

Limited data are available for the chemicals in this group. Cobalt oxide (CAS No. 1307-96-6) was assessed by the International Agency for Research on Cancer (IARC) as having sufficient evidence (presented below) for carcinogenicity in experimental animals (IARC, 1991), although it is not clear if the IARC classification is carried across to the most up to date IARC report published in 2006 (IARC, 2006).

The available carcinogenicity data are inappropriate for interpreting the hazard classification due to the non-physiologically relevant exposure routes used, absence of guideline laboratory studies and confounding in epidemiological studies arising from mixed exposure to cobalt oxide with other cobalt compounds and metals (nickel, arsenic, tungsten carbide). The mechanisms of carcinogenicity for cobalt compounds found to be carcinogenic by IARC (IARC, 2006) have not been clearly identified, making read across for compounds of different solubility difficult. Further studies are required to investigate the specific mode of action prior to classification.

Animal studies

Cobalt oxide

In a study conducted in Syrian Golden hamsters (51 animals per group), exposure to cobalt oxide (10 mg/m^3) with or without co-exposure to tobacco smoke for seven hours a day, five days a week for a lifetime was not associated with an increase in pulmonary tumours when compared with controls. Exposure to tobacco smoke alone was associated with 14 occurrences of pulmonary tumours compared with 11 cases in animals exposed to both cobalt oxide and cigarette smoke (WHO, 2006).

In a further study, SD rats were administered cobalt oxide via intratracheal instillation at 2 or 10 mg/kg bw/day every two weeks for 18 weeks, followed by every four weeks from the 19th treatment to the 30th treatment (total of two years). Two benign pulmonary tumours were reported in the low dose group (2 mg/kg bw/day) and two benign and four malignant tumours in the high dose group (10 mg/kg bw/day) (WHO, 2006).

In a further study, 10 SD rats were subcutaneously exposed to either five 2 mg/kg bw injections or 1 x 10 mg/kg bw injection once a week for the duration of their lives. The rats were reported to develop local malignant tumours (5/10 and 4/10 in the low and high dose groups, respectively) (WHO, 2006). In a similar study, SD rats exposed intraperitoneally to three injections of 200 mg/kg bw of cobalt oxide resulted in the development of malignant peritoneal tumours in 14/20 animals exposed (WHO, 2006).

Epidemiological studies

There are no specific studies which have been conducted on cobalt oxide alone. The majority of studies published describe occupational exposure (mainly in the 'hard metal' or cobalt extraction industry) to 'cobalt and cobalt compounds' or 'cobalt dust'.

An initial cohort study of workers occupationally exposed to cobalt compounds in an electrochemical plant showed a significant excess of lung cancer—standardised mortality ratio (SMR) of 4.66 in workers involved in the production of cobalt. Further analysis taking into account other factors (exposure to arsenic and nickel and smoking) did not support the initial SMR, which was reassessed as being 0.85 (De Boeck et al., 2003). A further retrospective cohort study showed that a cohort of Swedish workers in the 'hard metal industry' who had worked in the industry for more than 10 years, and exposed to cobalt compounds, had a significant increased SMR for lung cancer (2.78) compared to a SMR of 0.96 in the total cohort of 3000 workers (De Boeck et al., 2003).

A further study of workers in the 'hard metal industry' exposed to cobalt compounds in France showed an increased SMR of 2.13 for lung cancer. The SMR rose to 5.03 in the highest exposure group. Further follow up studies of this cohort in France have consistently shown significantly elevated SMRs for lung cancer associated with exposure to cobalt compounds in the 'hard metal industry'. Smoking was not considered a significant confounder alone or in combination with cobalt exposure (De Boeck et al., 2003).

Reproductive and Developmental Toxicity

No data are available for the chemicals in this group. On weight of evidence, data indicate that cobalt oxide (CAS No. 1307-96-6) has moderate (CDI, 2014) to high (Stopford et al., 2003) bioaccessibility and bioavailability (refer to **Toxicokinetics Oral section**) in artificial gastric fluid. On the basis of reproductive effects reported at the lowest dose tested (25 mg/kg bw/day) of cobalt chloride (CAS No. 7646-79-9) (NICNASb), soluble cobalt compounds (including cobalt sulfate heptahydrate) are classified as hazardous, Category 2 substances toxic to reproduction, with the risk phrase ‘May impair fertility’ (T; R60) in HSIS (Safe Work Australia). Based on the bioaccessibility and bioavailability of cobalt oxide in gastric fluid, classification for this group of chemicals is recommended.

Risk Characterisation

Critical Health Effects

The critical health effects for risk characterisation include a systemic long-term effect (reproductive toxicity), systemic acute effect (acute toxicity from oral and inhalation exposure) and local effects (skin sensitisation and respiratory sensitisation). The chemicals may also cause toxic effects following repeated exposure through inhalation. There are insufficient data to enable classification for carcinogenicity.

Public Risk Characterisation

Both overseas and in Australia, cobalt oxide is available as a component of glazes for arts and crafts. While these products are available to the public, the concentration of cobalt oxide in these products appears to be low (<1 %). The public may also come into contact with articles/coated surfaces containing these chemicals; it is expected that the chemicals will be bound within the article/coated surface and hence will have low bioavailability. Therefore, in both cases the risk to the public is not considered to be unreasonable.

Occupational Risk Characterisation

Commercial use of cobalt oxide (CAS No. 1307-96-6) has been identified in Australia. During use of chemicals in this group, dermal, ocular and inhalation exposure of workers to the chemical may occur, particularly where manual or open processes are used. These may include transfer and blending activities, quality control analysis, and cleaning and maintaining equipment. Worker exposure to the chemicals at lower concentrations may 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.

Given the critical systemic long-term, acute and local health effects, the chemicals in this group may pose an unreasonable risk to workers unless adequate control measures to minimise dermal and inhalation exposure to the chemicals are implemented. These chemicals should be appropriately classified and labelled to ensure that a person conducting a business or undertaking (PCBU) at a workplace (such as an employer) has adequate information to determine appropriate controls. The data available support an amendment to the hazard classification in HSIS (refer to **Recommendation** section).

Considering the concentration of 0.3 mg/m^3 cobalt sulfate heptahydrate (CAS No. 10026-24-1) identified in the inhalation repeated dose toxicity studies (refer **Repeated Dose Toxicity** section) at which adverse effects are observed, there is a concern that the absence of exposure controls in the HSIS may not adequately protect workers' health.

NICNAS Recommendation

A Tier III assessment may be required to assess the relationship between cobalt oxide exposure and carcinogenicity should relevant data become available.

A Tier III assessment may be necessary to provide further information to determine the adequacy of protection to workers under the current exposure control framework.

All other risks are considered to have been sufficiently assessed at the Tier II level, subject to implementing any risk management recommendations, and provided that all requirements are met under workplace health and safety and poisons legislation as adopted by the relevant state or territory.

Regulatory Control

Work Health and Safety

The chemical is recommended for classification and labelling under the current approved criteria and adopted GHS as below. This assessment does not consider classification of physical hazards and environmental hazards.

The classifications proposed below for respiratory sensitisation, repeat dose toxicity and reproductive toxicity are based on read-across principles (OECD, 2014). The classifications should be used as a default for all members of this group. If empirical data become available for any member of the group indicating that a lower (or higher) classification is appropriate for the specific chemical, these may be used to amend the default classification for that chemical.

Hazard	Approved Criteria (HSIS)[a]	GHS Classification (HCIS)[b]
Acute Toxicity	Harmful if swallowed (Xn; R22) Very toxic by inhalation (T+; R26)	Toxic if swallowed - Cat. 3 (H301) Fatal if inhaled - Cat. 2 (H330)
Sensitisation	May cause sensitisation by inhalation (Xn, R42) May cause sensitisation by skin contact (Xi; R43)*	May cause allergy or asthma symptoms or breathing difficulties if inhaled - Cat. 1 (H334) May cause an allergic skin reaction - Cat. 1 (H317)
Repeat Dose Toxicity	Toxic: danger of serious damage to health by prolonged exposure through inhalation (T; R48/23)	Causes damage to organs through prolonged or repeated exposure through inhalation - Cat. 1 (H372)
Reproductive and Developmental Toxicity	Repro. Cat 2 - May impair fertility (T; R60)	May damage fertility - Cat. 1B (H360F)

[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 industry

Control measures

Control measures to minimise the risk from oral, dermal and inhalation exposure to the chemical(s) 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 chemical is used. Examples of control measures which may minimise the risk include, but are not limited to:

- using closed systems or isolating operations;
- using local exhaust ventilation to prevent the chemical from entering the breathing zone of any worker;
- health monitoring for any worker who is at risk of exposure to the chemical if valid techniques are available to monitor the effect on the worker's health;
- 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 chemical.

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 assist with meeting 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 chemical 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 the chemicals has not been undertaken as part of this assessment.

References

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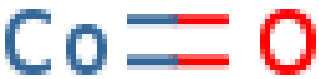
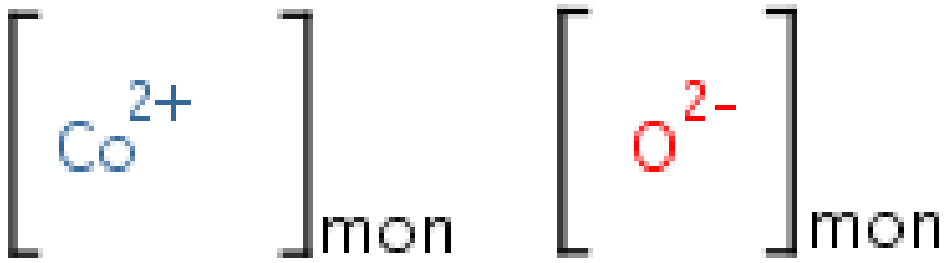
Last Update 27 November 2014

Chemical Identities

Chemical Name in the Inventory and Synonyms	**Cobalt oxide (CoO)** Cobalt monoxide Cobaltous oxide C.I. 77322 C.I. Pigment Black 13 Cobalt black
CAS Number	1307-96-6
Structural Formula	

	
Molecular Formula	CoO
Molecular Weight	74.9

Chemical Name in the Inventory and Synonyms	**Cobalt oxide**
CAS Number	11104-61-3
Structural Formula	

	
Molecular Formula	Unspecified
Molecular Weight	74.9

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