Cobalt (III) oxides: Human health tier II assessment

27 November 2014

Chemicals in this assessment

Chemical Name in the Inventory	CAS Number
Cobalt oxide (Co2O3)	1308-04-9
Cobalt oxide (Co3O4)	1308-06-1

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 two oxides which contain cobalt in the 3+ (trivalent) oxidation state. 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+} and Co^{3+} cation. The (aqueous) Co^{3+} cation is unstable and reduces to Co^{2+} by oxidising water (Cotton & Wilkinson, 1988). Dicobalt trioxide (CAS No. 1308-04-9) is not a well characterised chemical and is related to tricobalt tetraoxide (CAS No. 1308-06-1). The majority of available data are for tricobalt tetraoxide (CAS No. 1308-06-1) which, being a source of the Co^{3+} ion, is a suitable analogue for dissolved fractions of dicobalt trioxide.

Import, Manufacture and Use

Australian

Safety data sheets (SDS) identify that tricobalt tetraoxide (CAS No. 1308-06-1) has commercial use as a component of construction materials.

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 and the US National Library of Medicine's Hazardous Substances Data Bank (HSDB).

The chemicals in this group have reported domestic use including in:

- cleaning and washing agents; and

- paints, lacquers and varnishes.

The chemicals in this group have reported commercial use including in paints, lacquers and varnishes.

The chemicals in this group have reported site-limited use including:

- as colourants in the formulation of pigments, stains, dyes and inks
- as process regulators; and
- in feedstocks.

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 chemicals are not listed on the Hazardous Substances Information System (HSIS) (Safe Work Australia).

Exposure Standards

Australian

No specific exposure standards are available.

International

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 cobalt and cobalt compounds—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

Toxicokinetics

Compared with cobalt (II) oxides (NICNASa), cobalt (III) oxides are relatively insoluble in water (1.56 and 5.1 mg/L at 20 and 37 °C respectively) (REACHa) and partially bioaccessible in artificial gastric fluid (CDI, 2014a).

Inhalation

Limited data on inhalation toxicokinetics are available. It has been reported that cobalt (II) oxide is cleared from the lungs at a faster rate than cobalt (II,III) oxide (WHO, 2006). A study conducted in beagle dogs following endotracheal instillation of cobalt (II) or cobalt (II,III) oxide reported the half lives of both compounds in the range of 6–80 days. Less than 10 % of either oxide was retained in the lungs; this fraction was estimated to have a biological half-life of 290–440 days (REACHa).

Oral

In a study conducted in male HMT (Harwell Mouth Tumour) rats, radiolabelled (^{57}Co) tricobalt tetraoxide (CAS No. 1308-06-1) (particle size 1.7 or 0.8 μm) was administered via a single oral gavage dose (0.5 mL). Rats were assessed daily over seven days. Greater than 90 % of the compound was excreted in the faeces, 0.29–3 % in the urine and up to 8 % was recovered from the carcass after termination of the study. Based on these results it was shown that absorption of the chemical was dependent on particle size; 0.51 and 2.85 % for particle sizes of 1.7 and 0.8 μm respectively (REACHa).

Dermal

No data are available for the chemicals in this group. However, based on the limited absorption of cobalt dichloride (REACHa), a soluble cobalt compound, and data that show low bioaccessibility of cobalt (II,III) oxide in artificial sweat (CDI, 2014a), the chemicals in this group are not expected to be bioavailable via dermal exposure.

Acute Toxicity

Oral

The chemicals in this group have low acute toxicity in animal tests following oral exposure. In a study conducted according to OECD Test guideline (TG) 40, the median lethal dose (LD50) in Sprague Dawley (SD) rats is greater than 5000 mg/kg bw for tricobalt tetraoxide (CAS No. 1308-06-1). There were no observed sub-lethal effects or noteworthy changes following necropsy (REACHa). Given the known oral toxicity of cobalt oxide (CAS No. 1307-96-6) (NICNASa), the lack of Co^{2+} mediated toxicity in this study is associated with the low bioavailability of cobalt tetraoxide (CDI, 2014).

Dermal

No data are available.

Given that the toxicokinetic data show low dermal absorption (REACHa; CoRC, 2014), acute toxicity via the dermal route is not expected.

Inhalation

The chemicals in this group have low acute toxicity in animal tests following inhalation exposure with no mortalities observed (median lethal concentration—LC50 is >5.06 mg/L).

A study conducted according to OECD TG 436 in Crj: CD(SD) rats showed that a four hour single exposure to tricobalt tetraoxide (CAS No. 1308-06-1) at a dose of 5.06 mg/L did not result in mortality. No effects were noted on necropsy in the main study, although a satellite study reported haemorrhagic lungs in all animals tested (REACHa). Given the known inhalation

toxicity of cobalt oxide (CAS No. 1307-96-6) (NICNASa), the lack of Co^{2+} mediated toxicity is associated with the low bioavailability of cobalt tetraoxide (CDI, 2014). (CDI, 2014).

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 tricobalt tetraoxide (CAS No. 1308-06-1) was applied to artificial human skin (EpiSkin kit) for 15 minutes. Based on a cell viability assay, it was concluded that the chemical is not a skin irritant under the conditions of this assay (REACHa).

Eye Irritation

The chemicals in this group are not eye irritants.

In a study conducted according to OECD TG 405, 0.1 g of the chemical was instilled briefly into one eye of New Zealand White rabbits. Animals were then observed at specific timepoints up to seven days. One hour after exposure, all animals were reported to have slight to moderate reddening of the eye which persisted to 72 hours after administration. Slight reddening and chemosis of the conjunctivae were noted one and 24 hours after instillation of the chemical. Slight ocular discharge was reported in all animals tested, one hour after instillation. All adverse effects were reported to resolve within the seven day observation period (REACHa).

In an in vitro test conducted according to OECD TG 437, 0.75 mL of a 20 % suspension of tricobalt tetraoxide (CAS NO. 1308-06-1) 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 (REACHa).

Sensitisation

Respiratory Sensitisation

There are no data available for the chemicals in this group. Considering the negligible release of the Co^{2+} ion into artificial alveolar fluid in bioaccessibility studies with cobalt tetraoxide (CAS No. 1308-06-1) (CDI, 2014), respiratory sensitisation is not expected for chemicals in this group.

Skin Sensitisation

The chemicals in this group are not skin sensitisers.

In a local lymph node assay (LLNA) assay conducted according to OECD TG 429, 25 μL of a suspension of tricobalt tetraoxide (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. Stimulation index of 0.9, 1.0 and 0.8 were reported for 12.5, 25 and 50 % suspensions of the chemical. An EC3 (estimated concentration needed to produce a stimulation index of three) value could not be calculated after linear interpolation of the results as all stimulation indices were well below 3. Based on the results of this study, tricobalt tetraoxide is not expected to be a skin sensitiser (REACHa).

Repeated Dose Toxicity

Oral

Data available on tricobalt tetraoxide (CAS No. 1308-06-1) suggest that chemicals in this group are unlikely to cause serious damage to health by prolonged exposure via the oral route.

In a recent OECD TG 422 (Combined Repeated Dose Toxicity Study with the Reproduction/Developmental Toxicity Screening Test) study, 0, 100, 300 or 1000 mg/kg bw/day tricobalt tetraoxide (CAS No. 1308-06-1) was administered by gavage to SD rats (10 animals/sex/dose) (CDI, 2014b). Male animals were dosed two weeks prior to mating, during mating and two weeks post mating. Female animals were dosed two weeks prior to mating and up to day 3 postpartum. No adverse effects related to the test substance were observed. Piloerection was observed in some female animals at a dose of 100 mg/kg bw/day and above, and at the highest dose in the males. The no observed adverse effect level was determined to be 1000 mg/kg bw/day.

Dermal

No data are available.

Given that the toxicokinetic data show low dermal absorption (ATSDR, 2004; REACHa; WHO, 2006; CoRC, 2014), repeated dose toxicity through the dermal route is not expected.

Inhalation

There are no data available for the chemicals in this group. Considering the negligible release of the Co^{2+} ion into artificial alveolar fluid and low release into artificial lysosomal fluid in bioaccessibility studies with cobalt tetraoxide (CAS No. 1308-06-1) (CDI, 2014), repeated dose toxicity via inhalation is not expected for chemicals in this group.

Genotoxicity

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

In Vitro

In a study conducted according to OECD TG 476, tricobalt tetraoxide (CAS No. 1308-06-1) incubated with mouse lymphoma L5178Y cells for 3 hours to a maximum concentration of 2408 μg/mL (with and without metabolic activation) did not induce mutations at the hypoxanthine-guanine phosphoribosyltransferase (hrpt) locus (REACHa).

In vivo

In a study conducted similarly to OECD TG 475, male and female SD rats were administered a single dose (500, 1000 or 2000 mg/kg bw) of tricobalt tetraoxide (CAS No. 1308-06-1) via oral gavage. Treatment had no effects on the mitotic index in the bone marrow, and there were no substantial increases in chromosome aberrations reported (REACHa).

Carcinogenicity

There are no specific carcinogenicity studies conducted on chemicals in this group.

Due to the negligible bioaccessibility of cobalt tetraoxide (CAS No. 1308-06-1) (CDI, 2014), the Co^{2+} ion is not expected to be biologically available. 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 determining if classification should be recommended.

Reproductive and Developmental Toxicity

Based on the information available, the chemical does not show specific reproductive or developmental toxicity.

In a recent OECD TG 422 (Combined Repeated Dose Toxicity Study with the Reproduction/Developmental Toxicity Screening Test) study, 0, 100, 300 or 1000 mg/kg bw/day tricobalt tetraoxide (CAS No. 1308-06-1) was administered by gavage to SD rats (10 animals/sex/dose) (refer ***Repeated dose toxicity-Oral*** section for full details) (CDI, 2014b). The chemical had no adverse effect on reproductive performance. The authors noted that while the viability index of the pups in the high dose group was significantly reduced compared to the controls, this was within the normal range of variability. In particular, the reduced viability was mainly due to the total loss of one litter. At the highest dose, pup weights were significantly reduced. Therefore, the NOAEL was determined to be 300 mg/kg bw/day for developmental toxicity. The reduced pup weights were not considered a sufficient basis for classification.

Risk Characterisation

Critical Health Effects

There are no critical health effects for risk characterisation. There are insufficient data to recommend classification for carcinogenicity.

Public Risk Characterisation

No domestic use of the chemicals in this group has been identified in Australia. Although the public may 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 not be bioavailable. Therefore the risk to the public is not considered to be unreasonable.

Occupational Risk Characterisation

During use of chemicals in this group, dermal, ocular and inhalation exposure of workers to the chemicals 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 that critical health effects were not identified, an unreasonable risk to workers is not expected.

NICNAS Recommendation

Current risk management measures are considered adequate to protect public and workers' health and safety, provided that all requirements are met under workplace health and safety, and poisons legislation as adopted by the relevant state or territory. No further assessment is required.

Regulatory Control

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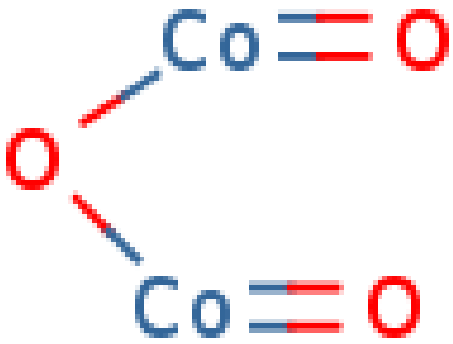
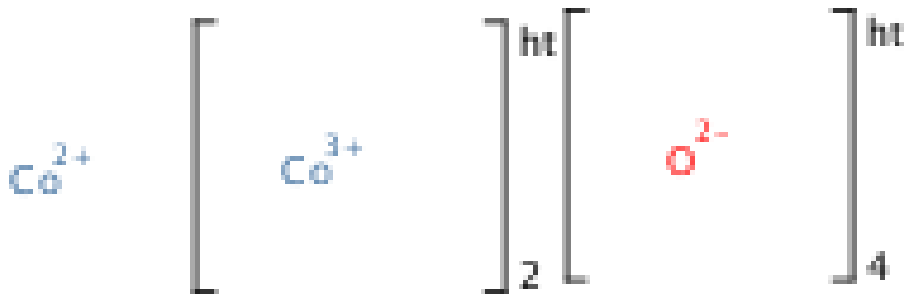
Last Update 27 November 2014

Chemical Identities

Chemical Name in the Inventory and Synonyms	**Cobalt oxide (Co2O3)** Cobalt (III) oxide Cobalt peroxide Cobalt trioxide Dicobalt trioxide Cobalt sesquioxide
CAS Number	1308-04-9

Structural Formula	
Molecular Formula	Co2O3
Molecular Weight	165.9

Chemical Name in the Inventory and Synonyms	**Cobalt oxide (Co3O4)** Cobaltous cobaltic oxide Cobalto-cobaltic tetroxide Tricobalt tetraoxide Cobaltosic oxide Cobalt (II,III) oxide
CAS Number	1308-06-1
Structural Formula	

	
Molecular Formula	Co3O4
Molecular Weight	240.8

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