



Crystalline silica: Human health tier II assessment

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Chemicals in this assessment

Chemical Name in the Inventory	CAS Number
Silica	7631-86-9
Cristobalite (SiO₂)	14464-46-1
Quartz (SiO₂)	14808-60-7
Fumes, silica	69012-64-2

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

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ACRONYMS & ABBREVIATIONS

Grouping Rationale

The chemicals in this group include three crystalline forms of silicon dioxide (SiO₂) (CAS No. 7631-86-9, 14464-46-1 and 14808-60-7) and one form of silica that is not clearly defined to be non-crystalline (CAS No. 69012-64-2). These chemicals can be grouped together for risk assessment purposes due to their similar physico-chemical properties, related end uses and toxicity (OECD, 2014). This group of crystalline silica should not be considered analogous to amorphous (polymorphic) form(s) of silicon dioxide, especially with respect to their toxicity; the key physico-chemical difference being that crystalline silica has a regular repeating 3-dimensional pattern that is not present in amorphous forms of silica (IARC, 2012; Environment & Health Canada, 2013).

Import, Manufacture and Use

Australian

The chemicals fumes, silica (CAS No. 69012-64-2), silica (CAS No. 7631-86-9) and quartz (CAS No. 14808-60-7) are listed on the 2006 High Volume Industrial Chemicals List (HVICL) with total reported volumes between 1000 and 1000000 tonnes.

The following Australian industrial uses were reported for the chemicals under previous mandatory and/or voluntary calls for information.

Silica (CAS No. 7631-86-9) has reported cosmetic use as an adhesive and/or binding agent.

Silica (CAS No. 7631-86-9), quartz (CAS No. 14808-60-7) and fumes, silica (CAS No. 69012-64-2) have reported domestic and commercial use including as additives in construction materials.

Silica (CAS No. 7631-86-9) and quartz (CAS No. 14808-60-7) have reported site-limited use including:

- as process regulators in the paper and pulp industry;
- in mining and metal extraction; and
- as vulcanising agents.

International

The following international uses have been identified through the Organisation for Economic Cooperation and Development Screening Information Dataset Initial Assessment Report (OECD SIAR); Galleria Chemica; Substances and Preparations in the Nordic countries (SPIN) database; the European Commission Cosmetic Ingredients and Substances (CosIng) database; United States (US) Personal Care Product Council International Nomenclature of Cosmetic Ingredients (INCI) dictionary and the US National Library of Medicine's Hazardous Substances Data Bank (HSDB).

Silica (CAS No. 7631-86-9) has reported cosmetic uses as:

- an abrasive agent (also quartz, CAS No. 14808-60-7);
- an absorbent;
- an anticaking agent;
- a bulking agent; and
- a viscosity controlling agent.

Silica (CAS No. 7631-86-9), cristobalite (CAS No. 14464-46-1) and quartz (CAS No. 14808-60-7) have reported domestic uses including:

- as adhesive and binding agents;
- as cleaning and washing agents;
- as colouring agents;
- as corrosion inhibitors;
- as fertilisers;
- in construction materials (also fumes, silica CAS No. 69012-64-2);
- as fillers (also fumes, silica CAS No. 69012-64-2);
- as flame retardants;
- as insulating agents; and
- in paints, lacquers and varnishes (also fumes, silica CAS No. 69012-64-2).

Silica (CAS No. 7631-86-9), cristobalite (CAS No. 14464-46-1) and quartz (CAS No. 14808-60-7) have reported commercial uses including:

- as anti-adhesive agents;
- as anti-static agents;
- as conductive agents;

- in construction materials (also fumes, silica CAS No. 69012-64-2);
- in cutting fluids;
- as viscosity adjusters;
- as reprographic agents;
- as welding and soldering agents;
- in electromechanical components; and
- in colouring and dye applications.

Silica (CAS No. 7631-86-9), cristobalite (CAS No. 14464-46-1) and quartz (CAS No. 14808-60-7) have reported site-limited uses including as:

- complexing and flocculating agents;
- electroplating agents;
- manufacturing intermediates;
- stabilisers; and
- vulcanising agents.

The chemicals in this group have non-industrial uses including as:

- pharmaceuticals (silica, CAS No. 7631-86-9; quartz, CAS No. 14808-60-7); and
- pesticides and preservatives (quartz, CAS No. 14808-60-7).

Restrictions

Australian

Free silica (crystalline silicon dioxide) is listed in Schedule 10 (prohibited carcinogens, restricted carcinogens and restricted hazardous chemicals) of the Work Health and Safety Regulations (WHS, 2011) for restricted use in abrasive blasting at a concentration of greater than 1 %.

International

No known restrictions have been identified.

Existing Worker Health and Safety Controls

Hazard Classification

Some of the chemicals in this group (CAS No. 14464-46-1 and 14808-60-7) are listed on the Hazardous Substances Information System (HSIS) (Safe Work Australia) under a common entry for 'Silica – crystalline', with 'Health' as the hazard type. There are no specific risk phrases for human health.

The chemicals silica (CAS No. 7631-86-9) and fumes, silica (CAS No. 69012-64-2) are not specifically listed on the HSIS (Safe Work Australia).

Exposure Standards

Australian

The following Australian exposure standards are identified in the HSIS (Safe Work Australia) under a common entry for 'Silica – Crystalline':

- cristobalite (respirable dust) (CAS No. 14464-46-1) and quartz (respirable dust) (CAS No. 14808-60-7) have an exposure standard of 0.1 mg/m³ time weighted average (TWA)
- silica (CAS No. 7631-86-9) is listed as 'Fumed silica (respirable dust)' with an exposure standard of 2 mg/m³ TWA—although the CAS No. used for this entry is the same as the crystalline form, it refers to the amorphous form of the chemical.

No specific exposure standards are available for fumes, silica (CAS No. 69012-64-2).

International

The following international exposure standards are identified (Galleria Chemica):

- an occupational exposure limit (OEL) of 0.025–0.15 mg/m³ time weighted average (TWA) for cristobalite (CAS No. 14464-46-1) in different countries such as the USA (Hawaii, Tennessee and Vermont), Canada (Alberta, British Columbia, Ontario, Quebec and Saskatchewan), France, Iceland, Netherlands, Norway, Spain, South Africa and Sweden
- an OEL of 0.025–0.1 mg/m³ TWA for quartz (CAS No. 14808-60-7) in different countries such as the USA (Hawaii, Tennessee and Vermont), Canada (Alberta, British Columbia, Quebec and Saskatchewan), South Africa and Spain.

Health Hazard Information

There is ubiquitous exposure of humans to silica, including quartz (sand) and silica food additives from dermal and oral routes. Silica is regarded as GRAS (generally recognised as safe) for food use (FDA, 2013). Acute toxicity, repeated dose toxicity, irritation and sensitisation from oral and dermal exposure are not considered relevant for risk assessment in this report. Amorphous forms of silica were considered to have a low hazard potential and were assessed at Tier I under the IMAP programme (NICNAS). However, exposure of humans to respirable dusts (i.e. dust particles small enough to penetrate deep into the respiratory system) of crystalline silica in industrial applications have been associated with irreversible toxicity in the lungs, including carcinogenicity secondary to lung damage. This assessment will only consider inhalation toxicity of crystalline silica.

Toxicokinetics

Crystalline silica dust is largely insoluble in bodily fluids, but can form silicic acid, which is readily excreted via the kidneys (US EPA, 1996; HSDB). After inhalation exposure, crystalline silica can accumulate in the lungs as a result of disruption in macrophage-mediated mechanical clearance. This is because crystalline silica is cytotoxic towards macrophages (SCOEL, 2003). Where there is high levels of crystalline silica dust, macrophage-mediated clearance will be limited and thus lead to accumulated dust in the lungs (SCOEL, 2003). This phenomenon is often referred to as 'particle overload' (WHO, 2000). The implications of particle overload are not characterised in humans, although they are reported to initiate an inflammatory response in the rodent lung (WHO, 2000).

Inhalation exposure

Male Fischer 344 (F344) rats exposed to crystalline silica (3 mg/m^3) for six hours a day, five days a week for 13 weeks had lung burdens of crystalline silica of 335.6 ± 28.3 and $819 \pm 83.3 \text{ } \mu\text{g SiO}_2/\text{lung}$ after 6.5 and 13 weeks of exposure, respectively. After 13 weeks of exposure, the rats underwent a recovery phase where they were exposed to 12 and 32 weeks of clean air. Lung burdens of SiO_2 were marginally reduced to 657.6 ± 28 and $643.0 \pm 14.5 \text{ } \mu\text{g SiO}_2/\text{lung}$ after 12 and 32 weeks of recovery time, respectively (Johnston et al., 2000).

Scanning electron microscopy (SEM) of rat lungs (strain not specified) exposed to crystalline silica (109 mg/m^3 quartz for three hours) showed that crystalline silica was deposited on bronchiolar and alveolar duct surfaces. Twelve hours after exposure, 72 % of macrophages in lavage fluid contained silica; these levels were maintained 24 days after exposure (HSDB). Within 24 hours after exposure, 82 % of the particles were cleared from the alveolar duct surfaces and were suggested to have been translocated to the interstitium and then to the lymph nodes (HSDB).

In a further study, the disposition of crystalline silica was assessed in alveolar fluid, free cells, lung tissue and lymph nodes after inhalation exposure in rats (strain unspecified) to $11\text{--}65 \text{ mg/m}^3$ of quartz and cristobalite for seven hours a day, for eight days. The data showed that the relative toxicity of quartz and cristobalite was attributed to the toxicity of these compounds to lung macrophages, impairing their movement in response to a chemical signal (chemotactic response) and hence resulting in impaired clearance of the chemical from the lungs. However, substantial transfer of quartz to the lymph nodes up to 150 days after exposure stopped was noted (HSDB).

Oral exposure

The majority (95 %) of orally administered crystalline silica to rodents (species unspecified) was not absorbed then excreted unmetabolised in the faeces. A small proportion was excreted through the urine (4 %), and 1 % was reported to remain in tissues (HSDB).

Dermal exposure

No data are available.

Acute Toxicity

Inhalation

No guideline studies have been conducted to assess the acute inhalation exposure to crystalline silica. Studies conducted using a single intratracheal instillation of crystalline silica in rodents have shown significant lung pathology such as the formation of silicotic nodules and lung fibrosis (WHO, 2000). However, these studies are not directly relevant for human exposure.

A single intratracheal instillation of quartz (50 mg, particle size $<5 \text{ } \mu\text{m}$ in diameter) in male rats (strain unspecified) resulted in a three-fold increase in water, protein and phospholipid content in lungs within 28 days of administration (WHO, 2000). In another study, 12 mg of quartz (particle size $<5 \text{ } \mu\text{m}$ in diameter) was administered to male and female rats (strain unspecified) using a single intratracheal instillation. Discrete silicotic granulomas in the lungs of both sexes were observed 21–30 days after instillation (WHO, 2000).

Repeated Dose Toxicity

Inhalation

Based on the available data in animals and humans (see **Observation in humans** below), the chemicals are considered to have repeated dose inhalation toxicity, warranting hazard classification (see **Recommendation** section). The reported lowest observed adverse effect concentration (LOAEC) for adverse pulmonary effects in various rat and mice studies ranged between $1\text{--}5 \text{ mg/m}^3$ (US EPA, 1996). Non-neoplastic adverse effects specific to the lungs of rodents included granulomatous lesions in

the walls of the large bronchi, pulmonary fibrosis, hyperplasia of the alveolar compartment and increases in lung collagen content.

In one study, male and female F344 rats were exposed to 1 mg/m³ crystalline silica (quartz, mass median aerodynamic diameter (MMAD)–1.3 µm) for six hours a day, five days a week for 24 months. No treatment-related effects on survival were reported. Non-neoplastic effects included extensive subpleural and peribronchiolar fibrosis, increase (doubling) of the lung collagen content, lipoproteinosis, cholesterol clefts, enlargement of lymph nodes and a granulomatous response in the walls of bronchi. Lung tumours were first reported after 21 months of exposure to the chemical (see **Carcinogenicity** section) (US EPA, 1996).

In another study, 62 female F344 rats were exposed to 12 mg/m³ of crystalline silica dust (quartz, MMAD of 2.24 ± 0.2 µm) for six hours a day, four days a week, for 83 weeks. There were no significant effects on survival, with 54/60 animals surviving the 83-week exposure period. Adverse effects reported in surviving animals included pronounced pulmonary fibrosis (characterised by granulomas and collagenous connective tissue) often accompanied with emphysema and alveolar proteinosis in animals with advanced fibrosis (US EPA, 1996).

In a further study, 144 F344 rats/sex were exposed to 50 mg/m³ of crystalline silica (quartz, MMAD ranging from 1.7–2.5 µm) for six hours a day, five days a week, for up to 24 months. The mean survival time for rats exposed to quartz was decreased (539 days) compared with controls (688 days). Rats exposed to quartz had lower body weights after 12 months of exposure and increased lung weights and volume. Pathological changes were reported at four months after exposure and included grossly enlarged lungs with diffuse spotting, brown-purple discolouration and grey-white subpleural foci. These changes were reported to worsen with time and histopathology revealed an increase in the number of alveolar macrophages, alveolar proteinosis, alveolar epithelial metaplasia, pulmonary adenomatosis, interstitial lesions and lymphoreticular hyperplasia (US EPA, 1996).

In a study conducted in female BALB/c mice, groups of six mice were exposed to approximately 5 mg/m³ of crystalline silica (MMAD–2 µm) for six hours a day, five days a week for 3, 9, 15, 27, 33 or 39 weeks. At these time points, the mice were challenged with an *Escherichia coli* antigen administered as an aerosol. Mice exposed to crystalline silica had reduced immunity indicated by an impaired physiological response of splenic lymphocytes to the antigen. The spleen/body weight ratio of exposed animals at weeks 15, 21 and 27 were significantly higher than controls. Also, the lung tissue of mice exposed to crystalline silica from weeks 3–21 showed varying degrees of lymphocyte infiltration. At week 24 and beyond, histological analysis showed silica-filled macrophages, and by week 39, fibrotic nodules of collagen, fibroblasts, lymphocytes and silica-filled macrophages were reported (US EPA, 1996).

Observation in humans

Dermal

Long-term (3–34 years) occupational dermal exposure to silica dusts are reported to be associated with connective tissue diseases with a potential to produce progressive systemic scleroderma. While there is debate about a true cause and effect relationship, there is evidence to show a link between scleroderma and lung silicosis in occupational settings (Thomas et al., 2000).

Inhalation

In humans, inhaled particles of crystalline silica can be transported to other parts of the body through the lymphatic system (US EPA, 1996; Thomas et al., 2000). Two forms of silicosis—accelerated (develops 5–10 years after initial exposure) and chronic (develops 10 years after initial exposure)—have been reported after repeated occupational exposure to crystalline silica dust, mainly that from quartz (US EPA, 1996; WHO, 2000). In a study of 67 gold mine workers in Canada, there was a significant linear relationship between lung quartz concentration and the severity of silicosis. While there were other particles detected in the lung tissue, quartz was the only significant indicator of silicosis severity (WHO, 2000).

Epidemiological studies show that the prevalence of radiographic silicosis (as defined by categories 1/0 or 1/1 under the International Labour Organisation (ILO) classification system) increases with average exposure to crystalline silica (WHO, 2000). For example, exposure to <0.05 mg/m³ was associated with a 10 % prevalence of silicosis, whereas exposure to >0.05-

0.10 mg/m³ caused silicosis, with a prevalence of 22.5 %, and at exposure concentration >0.10 mg/m³ the prevalence of silicosis was 48.6 % (WHO, 2000).

Further epidemiological data also indicate an exposure-response relationship between respirable crystalline silica (quartz) dust and silicosis in various occupational exposure settings (gold mining, stone/granite industries, brick workers and diatomaceous earth industries). Also, there are data which indicate that exposure to crystalline silica (quartz) dust can increase the risk of developing tuberculosis (TB). However, the relationship between exposure to crystalline silica (quartz) dust and TB risk in the absence of radiographically classified silicosis has not been substantiated through epidemiological studies (WHO, 2000).

Acute silicosis or silico-proteinosis is a rare and fatal condition arising from over exposure to respirable-sized, high quartz content dust over a short period of time. This condition is clinically similar to pulmonary oedema with the symptoms including shortness of breath and fluid accumulation in the upper and middle areas of the lungs. This condition has only been reported in historical case reports such as during the building of the Gauley Bridge hydroelectric tunnel in West Virginia, USA (1930–31). In this case, out of 2000 construction workers digging through high-silica rock without any respiratory protection, 400 workers died on site and 1500 workers were disabled with acute silicosis (US EPA, 1996).

Genotoxicity

In vitro studies with chemicals in this group gave both positive and negative results. The majority of positive genotoxicity assay results can be explained by the generation of reactive oxygen species (OECD, 2011) resulting in DNA damage. Since DNA damage is secondary to crystalline silica-induced oxidative damage, a direct genotoxic effect is not expected. Based on this information, it is not expected that chemicals in this group directly induce heritable mutations in human germ cells. Therefore, the available data do not warrant hazard classification.

In vitro data

Crystalline silica (type not specified) tested positive for genotoxicity in 2/3 micronuclei tests in Syrian hamster embryo cells and Chinese hamster lung fibroblast cells (Environment & Health Canada, 2013). Crystalline silica also tested positive for genotoxicity in 4/4 cell transformation assays conducted in various cell lines (BALB/3T3/31-1-1 mouse cells, Syrian hamster embryo cells and foetal rat lung epithelial cells). Also, crystalline silica tested positive for genotoxicity in 1/2 hypoxanthine-guanine phosphoribosyltransferase (HPRT) assays conducted in rat RLE-6TN alveolar epithelial cells (Environment & Health Canada, 2013).

The majority of in vitro genotoxicity studies using cells of human origin were positive. In a micronucleus assay, human embryonic lung Hel 299 cells and human lymphoblast cells gave positive results for genotoxicity. A sister chromatid exchange assay conducted with human lymphocytes was negative for genotoxicity. Tests for oxidative DNA damage (8-OHdG assay) and DNA strand breaks were all positive for genotoxicity when conducted using extracts of human lung epithelial cells (Environment & Health Canada, 2013).

In vivo animal data

Crystalline silica (type unknown unless specified) tested both positive and negative in various in vivo assays of genotoxicity. For example, crystalline silica tested positive for genotoxicity in 4/5 oxidative DNA damage tests in lung tissue from rats exposed to silica (Environment & Health Canada, 2013). However, it has been demonstrated that DNA strand breaks were inhibited when a reactive oxygen species scavenger was included in the test. This suggests that DNA damage was not a direct effect but secondary to the result of DNA damage as a result of reactive oxygen species generation (Environment & Health Canada, 2013).

HPRT assays conducted in alveolar epithelial cells of rats exposed to crystalline and amorphous silica (3 and 50 mg/m³ respectively) via inhalation exposure for 13 weeks showed that mutation frequency was significantly increased in rats exposed to crystalline silica but not amorphous silica (Government of Canada, 2013). In an assay conducted to assess DNA damage—the 8-OHdG (8-hydroxy-2'-deoxyguanosine) assay, female rats were exposed to a single intratracheal instillation of 0, 0.3, 1.5 or 7.5 mg quartz. A statistically significant increase in DNA oxidation was observed in rats exposed to ≥1.5 mg of quartz, 90 days after exposure. In a parallel in vitro study, 8-OHdG and DNA strand breaks were observed at concentrations ≥10 µg/m³ in rat lung epithelial cells (Environment & Health Canada, 2013). Similarly to the previously summarised study, DNA damage was a result of reactive oxygen species production, secondary to crystalline silica administration.

Human data

Genotoxicity assays were conducted on blood samples collected from 50 workers occupationally exposed to stone dust containing 50–60 % silica. After taking smoking status into consideration, the frequency of sister chromatid exchanges was significantly higher in the non-smoking workers exposed to stone dust when compared with matched controls. In a second genotoxicity assay conducted using the same study protocol as above, the observed increased incidence of chromosome aberrations was only statistically significant in the smokers in the cohort (Environment & Health Canada, 2013).

DNA damage was assessed in peripheral blood lymphocytes using the Comet assay in a study of foundry and pottery workers occupationally exposed to crystalline silica. No correction for smoking status or other carcinogens was made. DNA damage was reported to be higher in pottery or foundry workers when compared with matched controls (Environment & Health Canada, 2013).

In a further study, the presence of micronuclei was evaluated in peripheral blood lymphocytes and nasal epithelial cells from workers occupationally exposed to crystalline silica dust from grinding, bagging and sandblasting jobs. The frequency of micronuclei in exposed workers was three-fold higher in nasal epithelial cells and two-fold higher in peripheral blood lymphocytes compared with matched controls (Environment & Health Canada, 2013). However, no direct correction for smoking status or exposure to other potential carcinogens was considered (Environment & Health Canada, 2013).

Carcinogenicity

The International Agency for Research on Cancer (IARC) has classified the chemical as 'Carcinogenic to humans' (Group 1), based on sufficient evidence for carcinogenicity in humans and experimental animals. Based on the data below, the respirable fraction of chemicals in this group is recommended for classification (see **Recommendation** section).

Epidemiological data

The strongest evidence supporting the carcinogenicity of crystalline silica in the lung comes from pooled data and meta-analyses of available data (IARC, 2012). IARC concluded that crystalline silica is a confirmed human carcinogen based largely on nine studies of cohorts in four industry sectors that were considered to be least influenced by confounding factors, including gold mining, quarries and granite works, ceramic/pottery/refractory brick industries and the diatomaceous earth industry (IARC, 2012). Analysis from numerous epidemiology studies indicated that lung cancer tended to increase with the following parameters: cumulative exposure; duration of exposure; peak intensity of exposure; and presence of silicosis (Environment & Health Canada, 2013).

In a cohort study of 2266 diatomite workers employed in the United States (U.S) between 1942–87, lung cancer mortality was compared with controls from the general population. Based on cumulative exposure to crystalline silica (modelled data), the overall risk of mortality from lung cancer was significantly increased and reported as a standardised mortality ratio (SMR) of 1.41 although, after correcting for exposure to asbestos, the SMR was not statistically significant for crystalline silica-associated lung cancer mortality (Checkoway et al., 1996).

In a further study of 1022 Italian brick workers, the cause of mortality of workers employed for six months or more was compared with the general male population. The workers were reported to be exposed to between 0.2–0.5 mg/m³ of dust with a silica content between 30–65 %. The reported SMR for lung cancer was 1.51 and increased to 2.01 for workers employed for 19 years or more (Merlo et al., 1991).

In a further study, the relationship between lung cancer and exposure to crystalline silica (quartz) in a cohort of 5408 men in manufacturing plants or quarries between 1950–82 was assessed (men were followed up until 1996). Workers who worked for more than 30 years, or who were followed up for at least 40 years, showed the highest SMRs for lung cancer. No adjustment for smoking status was made in this study (Graham et al., 2004). In a further cohort study, the standardised risk ratios (SRR) for lung cancer in 6266 brick workers exposed to crystalline silica from 11 refractory plants in China were assessed. The overall SRR for lung cancer was 1.49 across all workers. This study further assessed the SSR for lung cancer with respect to silicosis and smoking status. The SRR for lung cancer was 2.1 and 1.1 for workers with and without silicosis, respectively. In smokers with silicosis, the SRR for lung cancer was 2.34 and in smokers without silicosis the SRR for lung cancer was 1.2. In non-smokers with silicosis the SRR for lung cancer was 2.13 and in non-smokers without silicosis the SRR for lung cancer was 0.85 (Dong et al., 1995). The authors of this study also noted that the rates of lung cancer increased with the latency and severity of silicosis (Dong et al., 1995).

Three further key studies (pooled cohort studies) have identified an exposure-response relationship between crystalline silica and lung cancer (Steenland & Sanderson, 2001; Cassidy et al., 2007; Vida et al., 2010). Briefly, in a cohort of 4626 workers exposed to respirable silica through various occupations, the odds ratio (OR) for developing lung cancer (2.26) was significantly elevated at an exposure concentration of $>0.065 \text{ mg/m}^3$ (Steenland & Sanderson, 2001). In the second study, the role of crystalline silica dust in lung cancer was assessed in 2852 cases and compared with 3104 matched controls. The overall OR for lung cancer after exposure to crystalline silica across all occupations was significant at 1.37. There was also a significant increase in the lung cancer OR in relation to the duration of exposure in years (OR ranged from 1.25 in the shortest duration group to 1.73 in the longest duration group); in hours (OR range 1.16–1.88); and overall cumulative exposure (OR range 1.07–2.08) (Cassidy et al., 2007). In the third study, two case control studies were pooled to assess the association of exposure to crystalline silica and lung cancer. The overall OR for lung cancer from exposure to crystalline silica was 1.31 and increased to 1.67 in the 'substantial exposure' group (exposure details not specified) (Vida et al., 2010).

Laboratory animal data

The positive results from human data are also supported by studies conducted in experimental animals where clear and consistent increases in lung tumours have been noted after chronic inhalation exposure (Environment & Health Canada, 2013).

In a low-dose exposure study, groups of 50 rats (F-344) per sex were exposed for six hours a day, five days a week for 24 months to filtered air or 1 mg/m^3 of quartz through whole-body exposure. In the exposed group, 18 animals developed tumours (12 tumours in females and six tumours in males). The majority (10/18) of the tumours observed were adenocarcinomas in the lung. In a group of 50 animals exposed to 5 mg/m^3 of titanium dioxide as a negative control, only three exhibited tumours (Muhle et al., 1989).

Although most carcinogenicity studies use inhalation exposure, quartz-induced lymphoma incidence was also increased in several studies in rats following intrapleural administration, and in one study in mice, after subcutaneous administration (IARC, 2012).

In a carcinogenicity study, rats received a single intratracheal instillation of 12 or 20 mg quartz and 12 mg of cristobalite, suspended in saline. Rat lungs showed a clear progression of effects starting with an initial inflammatory response leading to a marked hyperplasia and hypertrophy of alveolar cells after one month. At six months, hyperplasia was evident and at 11 months after instillation, lung tumours were observed with a 17 % and 42 % incidence in males and females, respectively. Seventeen months after instillation, incidences of lung tumour were 32 % in males rats and 59 % in females. No lung tumours were found in ferric oxide-treated rats (negative controls) (Saffiotti et al., 1992).

Risk Characterisation

Critical Health Effects

The critical health effects for risk characterisation include local long-term effects (carcinogenicity) and harmful effects following repeated exposure through inhalation (silicosis).

Public Risk Characterisation

The public may be exposed to chemicals in this group through potential cosmetic and domestic uses. However, given that inhalation is the major route of concern, the available cosmetic and domestic formulations containing crystalline silica are not expected to be dusty and therefore not expected to be a concern to the public. Therefore this group of chemicals is not considered to pose an unreasonable risk to public health.

Occupational Risk Characterisation

Given the critical local long-term and acute health effects, the chemicals might pose an unreasonable risk to workers unless adequate control measures to minimise inhalation exposure to the chemicals are implemented. The 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 (see **Recommendation** section).

Internationally, the Scientific Committee on Occupational Exposure Limits' (SCOEL) assessment of crystalline silica concludes that there is sufficient evidence from epidemiological studies to indicate that silicosis, the main effect in humans after occupational inhalation of respirable silica dust, is associated with the development of lung cancer. Therefore, preventing the onset of silicosis is likely to reduce the risk of lung cancer (SCOEL, 2003). According to the SCOEL assessment of crystalline silica, a dose-response curve for silicosis indicates that maintaining the respirable exposure below 0.05 mg/m³ would reduce the prevalence of silicosis in exposed individuals. Therefore the SCOEL committee has recommended that the occupational exposure limit (OEL) is below 0.05 mg/m³ of respirable silica dust (SCOEL, 2003).

Based on the available epidemiological data for crystalline silica, there is a concern that the current occupational exposure standard (0.1 mg/m³—respirable fraction) for quartz (CAS No. 14464-46-1) and cristobalite (CAS No. 14808-60-7) in HSIS might not be sufficiently protective to workers' health. There is also currently no recommended exposure standard for crystalline silica (CAS No. 7631-86-9) or fumes, silica (CAS No. 69012-64-2).

NICNAS Recommendation

A Tier III assessment might be necessary to provide further information whether the current exposure controls are appropriate to offer adequate protection to workers.

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 chemicals in this group are 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 below apply only to the respirable fractions of chemicals in this group.

Hazard	Approved Criteria (HSIS) ^a	GHS Classification (HCIS) ^b
Repeat Dose Toxicity	Toxic: danger of serious damage to health by prolonged exposure through inhalation (T; R48/23)	Causes damage to lungs through prolonged or repeated exposure through inhalation - Cat. 1 (H372)
Carcinogenicity	Carc. Cat 1 - May cause cancer by inhalation (T; R49)	May cause cancer - Cat. 1A (H350i)

^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 and inhalation exposure to the chemicals should be implemented in accordance with the hierarchy of controls. Approaches to minimise risk include substitution, isolation and engineering controls. Measures required to eliminate or minimise risk arising from storing, handling and using a hazardous chemical depend on the physical form and the manner in which the 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;
- air monitoring to ensure control measures in place are working effectively and continue to do so;
- minimising manual processes and work tasks through automating processes;
- work procedures that minimise splashes and spills;
- regularly cleaning equipment and work areas; and
- using protective equipment that is designed, constructed, and operated to ensure that the worker does not come into contact with the 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.

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Chemical Identities

Chemical Name in the Inventory and Synonyms	Silica silicon dioxide silicon oxide diatomaceous earth, calcined
CAS Number	7631-86-9
Structural Formula	



Molecular Formula	O ₂ Si
Molecular Weight	60.1

Chemical Name in the Inventory and Synonyms	Cristobalite (SiO₂) silicon dioxide alpha-cristobalite metacristobalite Belcron B 6000 Crysvarl
CAS Number	14464-46-1
Structural Formula	



Molecular Formula	O ₂ Si
Molecular Weight	60.1

Chemical Name in the Inventory and Synonyms	Quartz (SiO₂) silicon oxide, di- (sand) silica dust crystalline silica quartz fibrous glass Aventurine
CAS Number	14808-60-7
Structural Formula	



Molecular Formula	O ₂ Si
Molecular Weight	60.1

Chemical Name in the Inventory and Synonyms	Fumes, silica fumed silica, crystalline
CAS Number	69012-64-2
Structural Formula	

No Structural Diagram Available

Molecular Formula	Unspecified
Molecular Weight	Unspecified

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