Screening Assessment for the Challenge

Quartz
Chemical Abstracts Service Registry Number
14808-60-7

Cristobalite
Chemical Abstracts Service Registry Number
14464-46-1

Environment Canada
Health Canada

June 2013

Synopsis

Pursuant to section 74 of the *Canadian Environmental Protection Act, 1999* (CEPA 1999), the Ministers of the Environment and of Health have conducted a screening assessment of quartz, Chemical Abstracts Service Registry Number[1] 14808-60-7 and cristobalite, Chemical Abstracts Service Registry Number 14464-46-1. These substances were identified as a high priority for screening assessment and included in the Challenge initiative under the Chemicals Management Plan. Quartz and cristobalite were identified as high priorities as they were considered to pose greatest potential for exposure of individuals in Canada and their respirable forms are classified by the International Agency for Research on Cancer as carcinogenic to humans (quartz and cristobalite) and by the National Toxicology Program as known human carcinogens (crystalline silica). These substances met the ecological categorization criteria for persistence, but not for bioaccumulation potential or inherent toxicity to aquatic organisms.

According to information reported under Section 71 of CEPA 1999 for the year 2006, over 10 000 000 kg of quartz were manufactured, imported and used in Canada. Based on the results of the same survey, over 10 000 000 kg of cristobalite were manufactured and between 1 000 000 and 10 000 000 kg were imported and used in the year 2006.

It should be noted that this quantity does not represent the total quantities of quartz and cristobalite in the market in Canada because response to the mandatory section 71 Notice was required only if the substance or product, mixture or manufactured item containing the substance, was composed of more than 5% respirable crystalline silica and was intended for use within a residence. The major uses of quartz and cristobalite are in construction related activities such as road building and sanding in winter, and as a cement additive. Other uses include the manufacture of glass fibres and ceramics, as a filler and extender in rubber and coatings, and as an abrasive.

Quartz and cristobalite are both naturally occurring. Quartz is found abundantly in many types of rock formations while cristobalite can be found in the ashes of volcanic eruptions. Cristobalite is less prevalent than quartz as its presence is limited to specific geographic regions and rock types.

Quartz and cristobalite were qualitatively found to be very persistent because they are extremely resistant to chemical weathering. Also, quartz and cristobalite were qualitatively found to not bioaccumulate in aquatic organisms since they are expected to have very limited potential for uptake through for example the gill or gut of fish. Respirable fractions may physically accumulate in the lung tissues of terrestrial organisms. Results from available experimental toxicity studies indicate that quartz and cristobalite are not highly hazardous to aquatic organisms. In mammals however, these crystalline phases can cause harm to the lung (e.g., silicosis) depending on the severity

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and duration of exposure.

Quartz and cristobalite meet the criteria for persistence, but do not meet the criteria for bioaccumulation, as set out in the *Persistence and Bioaccumulation Regulations*. A risk quotient analysis at eight Canadian sites, integrating conservative to very conservative estimates of exposure via inhalation with a predicted no-effect concentration resulted in risk quotients below one, indicating the current estimated exposure concentrations of quartz and cristobalite in air are unlikely to cause harm to terrestrial fauna. On the basis of this evidence, it is concluded that these substances do not meet the criteria in paragraphs 64*(a)* and *(b)* of CEPA 1999, as they are not entering the environment in a quantity or concentration or under conditions that have or may have an immediate or long-term harmful effect on the environment or its biological diversity or that constitute or may constitute a danger to the environment on which life depends.

Concentrations of silicon in respirable particulate matter in Canada were identified and used to estimate inhalation exposure to quartz and cristobalite for the general population. The major anthropogenic releases of airborne respirable quartz and cristobalite are expected to come from dust generated due to agriculture, construction activity, and vehicle traffic on unpaved and paved roads.

The International Agency for Research on Cancer (IARC) has classified respirable quartz and cristobalite from occupational exposure as Group 1 carcinogens (*carcinogenic to humans*). The U.S. National Toxicology Program classified crystalline silica of respirable size as known to be a human carcinogen. The basis for these classifications is sufficient evidence from human studies indicating a causal relationship between exposure to respirable crystalline silica in the workplace and increased lung cancer rates in workers. While the mode of induction of lung tumours is not fully elucidated, sufficient data exists to demonstrate that a threshold approach to risk characterization is appropriate.

On the basis of the adequacy of the margins between conservative estimates of the exposure to quartz and cristobalite from ambient air and critical effect levels in experimental animals and humans, it is concluded that quartz and cristobalite do not meet the criteria in paragraph 64*(c)* of CEPA 1999, as they are not entering the environment in a quantity or concentration or under conditions that constitute or may constitute a danger in Canada to human life or health.

Based on the information available, it is concluded that quartz and cristobalite do not meet any of the criteria set out in section 64 of CEPA 1999.

These substances will be considered for inclusion in the *Domestic Substances List* inventory update initiative. In addition and where relevant, research and monitoring will support verification of assumptions used during the screening assessment.

Introduction

The *Canadian Environmental Protection Act, 1999* (CEPA 1999) (Canada 1999) requires the Minister of the Environment and the Minister of Health to conduct screening assessments of substances that have met the categorization criteria set out in the Act to determine whether these substances present or may present a risk to the environment or to human health.

Based on the information obtained through the categorization process, the Ministers identified a number of substances as high priorities for action. These include substances that

- met all of the ecological categorization criteria, including persistence (P), bioaccumulation potential (B) and inherent toxicity to aquatic organisms (iT), and were believed to be in commerce in Canada; and/or
- met the categorization criteria for greatest potential for exposure (GPE) or presented an intermediate potential for exposure (IPE) and had been identified as posing a high hazard to human health based on classifications by other national or international agencies for carcinogenicity, genotoxicity, developmental toxicity or reproductive toxicity.

The Ministers therefore published a notice of intent in the *Canada Gazette*, Part I, on December 9, 2006 (Canada 2006), that challenged industry and other interested stakeholders to submit, within specified timelines, specific information that may be used to inform risk assessment, and to develop and benchmark best practices for the risk management and product stewardship of those substances identified as high priorities.

The substances quartz and cristobalite were identified as high priorities for assessment of human health risk because they were considered to present GPE and had been classified by other agencies on the basis of carcinogenicity. The Challenges for these substances were published in the *Canada Gazette* on December 26, 2009 (Canada 2009a, 2009b). A substance profile was released at the same time. The substance profiles presented the technical information available prior to December 2005 that formed the basis for categorization of these substances. As a result of the Challenges, submissions of information pertaining to the substances were received.

Although quartz and cristobalite were determined to be a high priority for assessment with respect to human health and also met the ecological categorization criteria for persistence, they did not meet the criteria for bioaccumulation or inherent toxicity to non-human organisms.

Screening assessments focus on information critical to determining whether a substance meets the criteria as set out in section 64 of CEPA 1999. Screening assessments examine

scientific information and develop conclusions by incorporating a weight-of-evidence approach and precaution[2].

Quartz and cristobalite were grouped together in this screening assessment as they have many similarities including a common chemical composition as well as environmental fate and hazard properties. Where there are relevant differences, these are discussed in the text. This screening assessment includes consideration of information on chemical properties, hazards, uses and exposure, including the additional information submitted under the Challenge. Data relevant to the screening assessment of these substances were identified in original literature, review and assessment documents, stakeholder research reports and from recent literature searches, up to August 2010 for the ecological and human health sections. Key studies were critically evaluated; modelling results have also been used to reach conclusions. The ecological component of this screening assessment focuses on respirable fractions of dust from sources such as roads, agricultural, mining, power plants, quarries and construction sites. Quartz is typically a major component of sand that can contribute to eutrophication of aquatic systems when deposited in large amounts. The specific contributions of quartz to this process are not considered in this assessment because there are existing Canadian regulations in place to manage the dumping of substances such as sand into aquatic systems.

Evaluation of risk to human health involves consideration of data relevant to estimation of exposure (non-occupational) of the general population, as well as information on health hazards (based principally on the weight-of-evidence assessments of other agencies that were used for prioritization of the substance). Decisions for human health are based on the nature of the critical effect and/or margins between conservative effect levels and estimates of exposure, taking into account confidence in the completeness of the identified databases on both exposure and effects, within a screening context. The final screening assessment does not represent an exhaustive or critical review of all available data. Rather, it presents a summary of the critical information upon which the conclusion is based.

This final screening assessment was prepared by staff in the Existing Substances Programs at Health Canada and Environment Canada and incorporates input from other programs within these departments as well as comments from Denmark, France, Japan, Netherlands, United Kingdom and United States of America.

The ecological and human health portions of this assessment have undergone external written peer review/consultation. Comments on the technical portions relevant to human health were received from scientific experts selected and directed by Toxicology Excellence for Risk Assessment including Dr. Pam Williams (E Risk Sciences), Dr. John

[2] A determination of whether one or more of the criteria of section 64 are met is based upon an assessment of potential risks to the environment and/or to human health associated with exposures in the general environment. For humans, this includes, but is not limited to, exposures from ambient and indoor air, drinking water, foodstuffs, and the use of consumer products. A conclusion under CEPA 1999 on the substances in the Chemicals Management Plan (CMP) Challenge Batches 1-12 is not relevant to, nor does it preclude, an assessment against the hazard criteria specified in the Controlled Products Regulations, which is part of regulatory framework for the Workplace Hazardous Materials Information System [WHMIS] for products intended for workplace use. Similarly, a conclusion based on the criteria contained in section 64 of CEPA 1999 does not preclude actions being taken under other sections of CEPA or other Acts.

Christopher (CH2M Hill) and Dr. Irene Abraham (Toxicology Excellence for Risk Assessment). Additionally, the draft of this screening assessment was subject to a 60-day public comment period. Approaches used in screening assessments under the Challenge have been reviewed by an independent Challenge Advisory Panel. Although external comments were taken into consideration, the final content and outcome of the screening assessment remain the responsibility of Health Canada and Environment Canada.

The critical information and considerations upon which the final assessment is based are summarized below.

Substance Identity

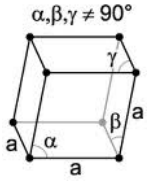
Substances Name

For the purposes of this document, the substances considered in this evaluation will be referred to as quartz and cristobalite. Their identities are presented in Table 1a and Table 1b, respectively. The basis for their grouping is that quartz and cristobalite share a common chemical composition and very similar environmental fate and hazard properties (e.g.: OECD 2007a; Table 1a, 1b, and 2).

The silicon dioxide group represents a polymorphic category containing a large number of forms identical in composition but with different atomic arrangements that afford different chemical properties. There are two sub-categories within this group: crystalline silica, to which the present substances quartz and cristobalite belong, and non-crystalline or amorphous silica (Cotton and Wilkinson 1988; Moore 1999). The key distinction between these sub-categories is that in crystalline substances, the building blocks are arranged in regular, repeating 3-dimentional pattern having long range order, whereas amorphous materials do not display long range order. In all forms of silica, (crystalline and non-crystalline), the silicon atom is tetrahedral and bound to four neighbouring oxygen atoms. Polymorphic crystal structures arise from the different orientation and position of these tetrahedral subunits. Cristobalite is a polymorph of quartz and a temperature exceeding 900°C is required for this crystal conversion (Cotton and Wilkinson 1988; Clark and Peakor 1992; Moore 1999). However, this mineral may also have a biogenic origin that may not require heat for formation (Murata and Nakata 1974).

Table 1a. Substance identity for quartz

Chemical Abstracts Service Registry Number (CAS RN)	**14808-60-7**
DSL name	**Quartz**
National Chemical Inventories (NCI) names[a]	*Quartz (SiO2) (TSCA, EINECS, ENCS, AICS, ECL, PICCS, ASIA-PAC, NZIoC); crystalline silica (PICCS); quartz (PICCS); silica crystalline (PICCS); crystalline silica quartz (PICCS, REACH); quartz, white (sand) (PICCS)*
Other names	*a-Quartz; 1FX; Aventurine; Aventurine (quartz); CMC 12S; CRS 1101-17; Crystalite 5K; Crystalite 5X; Crystalite A 1; Crystalite A 2; Crystalite AA; Crystalite C; Crystalite CRS; Crystalite SS; Crystalite VX-S; Crystalite VX-S 2; Crystalite VX-SR; Crystalite VX-X; DQ 12; E 600; E 600 (quartz); EQ 906; HHH; Inducarb 0.5-1; IOTA 4; Iota 6; KP 3; KP 3 (quartz); LAD; LAD (mineral); LM 300; M 10; M 4; M 4 (quartz); Marshalite; Mikrosil LM 300; Mikrosil SP 10; Mikrosil SP 3; Millisil W 12; Millisil W 3; Millisil W 6; Millisil W 6EST; Plastorit; Rock crystal; SF 35; Sibelco M 10; Siderite (SiO2); Sifraco C 10; Sifraco C 600; Sikron 3000; Sikron 500; Sikron 600; Sikron F 100; Sikron F 600; Sikron H 200; Sikron*

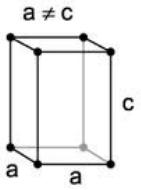
	H 500; Sikron H 600; Sikron SF 300; Sikron SF 600; Sikron SF 6000; Sikron SF 800; Silbond 600EST; Silbond FW 600EST; Silbond FW 61EST; Silbond VP 810-10/1EST; Silcron F 600; Silverbond 200; Silverbond 325; Sircon 200; SP 3; SP 3 (quartz); TGL 16319; Tiger-eye; VX-S 2; W 12; W 12MST.
Chemical group (DSL Stream)	Inorganics
Major chemical class or use	Silicon dioxide group
Major chemical sub-class	Crystalline silica
Chemical formula	SiO_2
Crystal conformation	Trigonal symmetry 
SMILES[b]	O=[Si]=O
Molecular mass	60.08 g/mol

[a] National Chemical Inventories (NCI). 2009: AICS (Australian Inventory of Chemical Substances); ASIA-PAC (Asia-Pacific Substances Lists); ECL (Korean Existing Chemicals List); EINECS (European Inventory of Existing Commercial Chemical Substances); ENCS (Japanese Existing and New Chemical Substances); NZIoC (New Zealand Inventory of Chemicals); PICCS (Philippine Inventory of Chemicals and Chemical Substances); REACH (Registration, Evaluation, Authorisation and Restriction of Chemicals**)** and TSCA (Toxic Substances Control Act Chemical Substance Inventory).

[b] Simplified Molecular Input Line Entry System

Table 1b. Substance identity for cristobalite

Chemical Abstracts Service Registry Number (CAS RN)	**14464-46-1**
DSL name	**Cristobalite**
National Chemical Inventories (NCI) names[a]	*Cristobalite (SiO2) (TSCA, ENCS, AICS, PICCS, ASIA-PAC, NZIoC); Cristobalite (EINECS, ECL, PICCS, REACH)*
Other names	*α-Cristobalite; α-Crystobalite; 43-63C; Belcron B 6000; Cristoballite; Crystobalite; Crystoballite; Crysvarl; Metacristobalite; SF 4000; Sibelco B 0012; Sibelite M 3000; Sibelite M 4000; Sibelite M 6000; Silbond 006MST; W 006; WGL 300; XPF 6*
Chemical group (DSL Stream)	Inorganics
Major chemical class or use	Silicon dioxide group

Major chemical sub-class	Crystalline silica
Chemical formula	SiO_2
Crystal conformation	Tetragonal symmetry 
SMILES[b]	O=[Si]=O
Molecular mass	60.08 g/mol

[a] National Chemical Inventories (NCI). 2009: AICS (Australian Inventory of Chemical Substances); ASIA-PAC (Asia-Pacific Substances Lists); ECL (Korean Existing Chemicals List); EINECS (European Inventory of Existing Commercial Chemical Substances); ENCS (Japanese Existing and New Chemical Substances); NZIoC (New Zealand Inventory of Chemicals); PICCS (Philippine Inventory of Chemicals and Chemical Substances); REACH (Registration, Evaluation, Authorisation and Restriction of Chemicals) and TSCA (Toxic Substances Control Act Chemical Substance Inventory).

[b] Simplified Molecular Input Line Entry System

Physical and Chemical Properties

The estimated and experimental physical and chemical properties of quartz and cristobalite that are relevant to their environmental fate are described in Table 2. Quantitative structure-activity relationships (QSAR) model results are not available for most inorganic compounds, including the present substances, because inorganic compounds fall outside of most QSAR application domains and their structures are not compatible with the estimation methods of these models. Therefore, Table 2 does not include any QSAR-based estimates. Most of the numerical values of Table 2 have been obtained from chemistry handbooks and peer-reviewed databases. The very similar physico-chemical properties of quartz and cristobalite reflect their closely related crystal forms.

The water solubility of crystalline silicates decreases as a function of silica tetrahedral packing density and long-range crystal order (Wilding et al. 1977). For example, cristobalite has a more open framework structure than does quartz (Wilding et al. 1977) and its density is lower; therefore, its solubility is higher (Table 2). The solubility of these minerals is also function of temperature, pH, particle size, and the presence of a disrupted surface layer. This may explain the variability of solubility values reported by many authors. Wilding et al. (1977) suggest that the most probable solubility value for quartz is approximately 3.8 mg Si/L, or 6.4 mg/L expressed as the SiO_2 species, while the solubility of cristobalite is approximately 8.7 mg Si/L or 18 mg SiO_2/L. The kinetics of dissolution of these substances is slow owing to the high activation energy required to hydrolyse the Si-O-Si bond (e.g., Brady and Walther 1990). Wilding et al. (1977) report that concentrations of less than 3 mg Si/L can exist for months in aqueous solution in contact with quartz.

Table 2. Physical and chemical properties for quartz and cristobalite

Substance	Type	Value[a]	Tempera-ture (°C)	Reference
Physical state				
Quartz	Experimental	Colourless, white or variable black, purple, green crystals	--	NIOSH 1997a
Cristobalite		Colourless or white crystals	--	NIOSH 1997b
Melting point (°C)				
Quartz	Experimental	1,610	--	NIOSH 1997a

Substance	Type	Value[a]	Temperature (°C)	Reference
		1,400-2,000	--	European Commission 2000a
Cristobalite		1,713	--	NIOSH 1997b
		1,718-1,728	--	European Commission 2000b
Boiling point (°C)				
Quartz	Experimental	2,230	--	NIOSH 1997a
		2,230	--	European Commission 2000a
Cristobalite		2,230	--	NIOSH 1997b
		2,230	--	European Commission 2000b
Density (kg/m^3)				
Quartz	Experimental	2,600 (Relative density: 2.6)	--	NIOSH 1997a
		2,500-2,700	20	European Commission 2000a
		2,650	--	Wilding et al. 1977
Cristobalite		2,300 (Relative density: 2.3)	--	NIOSH 1997b
		2,324-2,325 (2.324-2.325 g/cm^3)	--	European Commission 2000b
		2,320-2,380	--	Wilding et al. 1977
Vapour pressure (Pa)				
Quartz	Experimental	Negligible	Not indicated	NIOSH 1997a

Substance	Type	Value[a]	Tempera-ture (°C)	Reference
Cristobalite	Estimated	Negligible	Not indicated	Moore 1999[b]
Henry's Law constant ($Pa \cdot m^3/mol$)				
Quartz	Estimated	Negligible	--	Expert judgment
Cristobalite		Negligible	--	Expert judgment
Water solubility (mg/L)				
Quartz	Experimental	6 (soluble SiO_2)	Room temperatures	Krauskopf 1956 Schleyer and Blumberg 1982
	Experimental	6.6 [c] (soluble SiO_2)	Not indicated	Gardner 1938
	Experimental	3.8 [d] (soluble Si)	Room temperature	Wilding et al. 1977
	Experimental	Insoluble	Environmen-tally relevant atmospheric temperatures	Moore 1999
	Experimental	Insoluble (none)	Not indicated	NIOSH 1997a
	Experimental	Insoluble	Not indicated	European Commission 2000a
Cristobalite	Extrapolated from experimental data	8.7 [d] (soluble Si)	Room temperature	Wilding et al. 1977
	Experimental	Insoluble (none)	Not indicated	NIOSH 1997b
Log K_{OW} (octanol-water partition coefficient); (dimensionless)				
Not applicable				
Log K_{OC} (organic carbon-water partition coefficient); (dimensionless)				

Substance	Type	Value[a]	Tempera-ture (°C)	Reference
Not applicable				

[a] Values and units in brackets represent those originally reported by the authors.

[b] Moore (1999) considers quartz and cristobalite close analogues because of their crystalline forms identical in chemical composition and their closely related crystal structures.

[c] Colometric test for the amount of soluble silica liberated in un-buffered sodium chloride isotonic solution.

[d] Concentration calculated from a diagram of soluble silicon in mg/L as a function of time in Wilding et al. (1977).

Sources

Natural Sources

In Canada, quartz naturally occurs in many types of rock formations. Those with high silicon dioxide content (95% SiO_2 or more) include vein and massive intrusion bodies, silica sand, sandstone and quartzite (Dumont 2006). Sandstone is a sedimentary rock mostly composed of quartz grains cemented by a bonding material such as clay, calcite or iron oxide. Quartzite is a hard, compact, metamorphosed sandstone made of grains of quartz firmly bonded with a siliceous cement. Commercial mineral aggregates (e.g., sand and gravel) have variable silicon dioxide content (Panagapko 2006). Quartz is also found as crystals, aggregates or discrete particles in certain igneous rocks (e.g., granites and pegmatites), soils, sediments, air and surface water (Wilding et al. 1977, IARC 1997, Dumont 2006). This omnipresence is consistent with the fact that silicon is the second most abundant chemical element on Earth. Its concentration in the upper continental crust has been determined to range from 30.3 to 30.8% (Reimann and de Caritat 1998).

Cristobalite occurs naturally in the ashes of volcanic eruptions. It may be produced by combustion metamorphism which is a local phenomenon of spontaneous combustion of naturally occurring substances such as bituminous rocks, coal or oil (Clark and Peacor 1992, Baxter et al. 1999). It may furthermore be found in cavities in volcanic rocks and in thermally metamorphosed sandstones (Deer et al. 1967) and may also be a transient stage in the diagenesis of diatomaceous shale with the result that soils made of these geologic formations may be rich in cristobalite (Murata and Nakata 1974). Unlike quartz, the natural occurrence of cristobalite is limited to specific geographic regions and rock types (Wilding et al. 1977), such as near Princeton, British Columbia where it occurs associated with bentonite deposits (Kiely and Jackson 1964).

Anthropogenic Sources

Natural quartz is isolated from ore via beneficiation, which involves milling or grinding the material into particles that are separated into the desired mineral and waste. The materials obtained are either used directly or further purified. In Canada, in 2006, 2.146×10^{9} kg of pure quartz were mined, and 2.385×10^{11} kg of sand and gravel aggregates were produced (Statistics Canada 2008). The proportion of quartz in silica

sand deposits will vary from one site to another. Sand and gravel aggregates contain various quantities of diverse substances, including crystalline silica (Statistics Canada 2008).

Cristobalite can form from silica melts during the preparation of silica glass; quartz is not obtained from melts but is manufactured at elevated temperature and pressure via a hydrothermal process (Armington 2000). Cristobalite also forms during the calcination of diatomaceous earth (IARC 1997).

The quantities of quartz and cristobalite manufactured, imported, and used in Canada, as reported in surveys conducted under section 71 of CEPA 1999 for the year 2006, are presented in Table 3. It should be noted that this quantity does not represent the total quantities of quartz and cristobalite in the market in Canada because response to the mandatory section 71 Notice was required only if the substance or product, mixture or manufactured item containing the substance, was composed of more than 5% respirable crystalline silica and was intended for use within a residence.

Table 3: Quantities of quartz and cristobalite manufactured, imported and used in Canada for the year 2006, according to section 71 survey conducted under CEPA 1999

Substance	CAS number	Quantity reported (kg)		
		Manufactured	Imported	Used
Quartz	14808-60-7	>10 000 000	>10 000 000	> 10 000 000
Cristobalite	14464-46-1	>10 000 000	1 000 000–10 000 000	1 000 000–10 000 000

Uses

The focus of this assessment is on quartz and cristobalite. Uses of non-crystalline forms, including amorphous forms, which, as detailed in the Substance Identity, are distinct substances with unique CAS RNs, are not described in this assessment. Non-crystalline silicas are commonly used as anti-caking agents in dry powders, foods, and cosmetics (Villota et al. 1986).

Consistent with oxygen and silicon being the two most abundant elements in the Earth's crust, silicon-oxide minerals, including quartz, are ubiquitous in the natural environment. In particular, as a component of sand, quartz may find use in a diverse array of applications. Several high volume uses include, but are not limited to, the use of sand as a filling material for the construction of roads and in general building activities, the use of sand and gravel aggregates as abrasives on roads in winter and the use of fly-ash, which may contain 4-14% quartz and 0.5-1% cristobalite, as a cement additive (Moore 1999; Environment Canada 2009). These abrasives used on winter roads are usually mixed with road salts and may be sand only, stone dust, sand and gravel aggregates, or pre-treated sand. They are used mainly by rural municipalities or in areas where cold temperatures diminish the efficiency of salts for de-icing. Quantities of abrasives used in Canada were

5.73×10^9 kg, 4.59×10^9 kg, and 4.93×10^9 kg for 2007, 2008 and 2009, respectively (August 2010, personal communication from Products Division, Environmental Stewardship Branch, Environment Canada, to Ecological Assessment Division, Science and Technology Branch, Environment Canada; unreferenced).

Industrial sand is a term normally applied to high purity silica sand products with closely controlled sizing; it is a more precise product than common concrete and asphalt gravels. Industrial sands expected to contain quartz and cristobalite include lump silica (2-3mm up to 15 cm or more), silica sand (75µm to 2-3mm) and silica flour (less than 75µm) (2010 email from Minerals and Metals Sector, Natural Resources Canada to Existing Substances Risk Assessment Bureau, Health Canada, unreferenced). Lump silica may be used in the production of silicon alloys, silica bricks, and the linings of certain types of pulverizers (eg. ball mills and tube mills). Silica sand may be used in the manufacture of glass and glass fibres, silicate chemicals and silicon carbide, the hydraulic fracturing of wells, foundry moulding, and for sandblasting. Silica flour may find use in the ceramics and cement industries, as a filler and extender in rubber and coatings, and as an abrasive in soaps (2010 email from Minerals and Metals Sector, Natural Resources Canada to Existing Substances Risk Assessment Bureau, Health Canada, unreferenced).

Natural clays, such as bentonite and fuller's earth, are used in cat litters (HPD 2010) for their high absorbance capacities and, in the case of sodium bentonite, since liquid waste causes swelling and the formation of a hard clump that can be removed (Murray 2002). Quartz is a natural component of these clays; consequently, it may be present in cat litter products.

High purity α-quartz is a piezoelectric material, which means that application of a voltage induces a distortion in the crystal shape and vice versa (Schwartz 2000). This ability to interconvert electrical and mechanical energy has led to the use of quartz crystals in electronic devices requiring precise timing control, for example telephones, radios, watches and computers (Armington 2000).

According to information received in response to section 71 surveys, in Canada, quartz and cristobalite are also used in abrasives, adsorbents, filter products (diatomaceous earth), grout and cement (Environment Canada 2009). These substances reportedly also find use as fillers, which add bulk and improve wear resistance, in paints and coatings, adhesives, sealants, polymer films, caulking, epoxy resins and silicones (Environment Canada 2009). In paints and coatings the substances are used to form a matte finish (Uhrlandt 2006); the small particles impart a roughness to the coating's surface, which scatters light, thus reducing gloss.

The Pest Management Regulatory Agency of Health Canada confirmed that quartz and cristobalite are present in pest control products in materials used as formulants; 49 products contain cristobalite and 278 products contain quartz. The active ingredient diatomaceous earth contains less than 1% crystalline silica, which includes quartz and cristobalite (2010 personal communication from Pest Management Regulatory Agency, Health Canada, to Risk Management Bureau, Health Canada; unreferenced).

The use of quartz as an abrasive in household cleaners appears to be declining as several products have been reformulated to either eliminate or reduce quartz content (HPD 2010).

In Canada, quartz is currently listed in the Therapeutic Products Directorate's internal Non-Medicinal Ingredients Database as present in one disinfectant cream cleaning product; cristobalite was not identified in the Database (2010 personal communication from Therapeutic Products Directorate, Health Canada, to Risk Management Bureau, Health Canada; unreferenced). Neither quartz nor cristobalite are listed in the Drugs Product Database as a medicinal ingredient in pharmaceutical drugs (DPD 2010).

Quartz is listed as a permitted topical non-medicinal abrasive ingredient in the Natural Health Products Ingredients Database (NHPID) and is present in eight face makeup products currently listed in the Licensed Natural Health Products Database (LNHPD) (LNHPD 2010; NHPID 2011). Quartz was identified in 60 personal care products currently listed in the Consumer Product Safety Directorate's Canadian Cosmetic Notification System (CNS) (CNS 2009). Products in the CNS reported to contain quartz include anti-wrinkle preparations, eye and face makeup, lipstick, hair dyes, shampoos and grooming products, as well as skin cleansers, moisturizers and tanning preparations. These products are formulated as either loose or pressed powders, aerosols, gels, creams, liquids and lotions. Quartz, cristobalite, and crystalline silica are not listed on the Canadian Cosmetics Ingredients Hotlist either as prohibited substances or substances approved up to set limits (Health Canada 2010). Cristobalite is not currently listed as being present in any of the notified products in the LNHPD or the CNS (CNS 2009; LNHPD 2010).

Quartz and cristobalite have been identified in the formulations of incidental additives (quartz less than 1%, and cristobalite less than 1.5% in polymeric materials and inks) and as components in food packaging materials (less than 6% in paperboard) (2010 emails from Food Directorate, Health Canada to Risk Management Bureau, Health Canada, unreferenced). However considering their physico-chemical properties (insolubility, negligible vapour pressure), inhalation exposure for the general population of Canada to either quartz or cristobalite from these applications is considered to be extremely low.

Releases to the Environment

Estimation of Quartz Content in Airborne Particulate Matter

The National Pollutant Release Inventory (NPRI) comprises information reported by facilities, emission summaries and trends for key air pollutants, based on facility reported data and emission estimates for other sources such as motor vehicles, residential heating, forest fires and agriculture (Environment Canada 2010). While the NPRI does not document quartz releases to the environment, releases of respirable particulate matter (PM) to the environment are documented. Combining information on PM releases

contained in the NPRI with measurements of silicon in PM conducted under the National Air Pollution Surveillance Program of Canada (NAPS), the quantities of quartz released in respirable PM in 2007 (completed by some estimates obtained for 2008) were calculated. Releases of cristobalite are not accounted for in most calculations because it is assumed to be of low natural occurrence in Canada (see previous section describing sources) and is used in amounts markedly less than quartz by industry (see previous section describing uses).

Quartz is a component of airborne particulate matter (Environment Canada and Health Canada 2000). Releases of PM matter with aerodynamic diameters less than 2.5 μm and less than 10 μm ($PM_{2.5}$ and PM_{10}, respectively) are extensively reported in the NPRI. In 2009, NAPS measured concentrations (in $\mu g/m^3$) of $PM_{2.5}$, PM_{10}, and silicon in the ambient air of 24 urban locations (NAPS 2010). A dichotomous sampler was used, which divided the PM into two size classes: the class of particles with aerodynamic diameters 2.5 to 10 μm and the class less than 2.5 μm. The two fractions were combined together to obtain the total PM_{10}, which refers to the quantity of particles with aerodynamic diameters less than 10 μm. A median percent SiO_2 content was derived from the 24 ratios of Si to PM, and a molar ratio of 2.14 was used to convert Si levels to SiO_2 levels. The median $\%SiO_2$ of PM_{10} amounted to 5.22% and that for $PM_{2.5}$ was 2.52%. These ratios were applied to the corresponding PM_{10} and $PM_{2.5}$ NPRI data emissions of dust from paved and unpaved roads, construction activities, agricultural activities, and other less important anthropogenic sources. The resulting SiO_2 quantities released include all forms of silica (crystalline and non-crystalline) as well as other silicate minerals; therefore they represent the upper bound for quartz emissions into the atmosphere in Canada. The emissions of particulate matter in air reported by the NPRI and the estimated amounts of quartz are listed in Table 4.

The SiO_2 percentages derived from NAPS data can be compared with the measured quartz contents in the aerosols of 22 urban regions in the United States, which were reported in a study conducted in 1980 by Davis et al. (1984). The aerosols were collected on dichotomous filters that divided the PM into two size classes: less than 2.5 μm and from 2.5 to 15 μm. The PM_{15} fraction refers to the two fractions combined together. Quartz was determined in the fractions using X-ray diffractometry. The median quartz percentage of PM_{15} was 5.58% and that of $PM_{2.5}$ was 0.35%. As noted above, the median percentage of SiO_2 in PM_{10} (5.22%) derived from the NAPS data has been used in this assessment to estimate anthropogenic emissions. This approach is conservative because quartz comprises only a fraction of all of the forms of SiO_2 expected to be present (range in PM_{15} reported to be 2 to 70% (Davis et al 1984)). Comparing the quartz concentration in $PM_{2.5}$ (0.35%) reported by Davis et al. (1984) with the percentage of SiO_2 in $PM_{2.5}$ (2.52%) estimated with the NAPS data suggests the NAPS-based value overestimates the contribution of quartz to that fraction. Despite this difference of nearly an order of magnitude, the % SiO_2 of 2.52% for $PM_{2.5}$ was used in this assessment to obtain a conservative estimate of anthropogenic emissions in this particulate fraction.

Table 4. **Anthropogenic emissions of fine particulate matter in air reported by the NPRI in 2007 (Environment Canada 2010), together with quantities of quartz estimated to be released by these sources.**

Source	PM_{10} (kg)	$PM_{2.5}$ (kg)	% SiO_2 (conservative estimate of quartz / cristobalite)			Estimated release of quartz (kg)	
			PM_{10}	$PM_{2.5}$	Reference	PM_{10}	$PM_{2.5}$ [a]
Dust from unpaved road	2.71×10^{9}	4.02×10^{8}	5.22	2.52	NAPS 2010	1.41×10^{8}	1.01×10^{7}
Dust from paved road	6.35×10^{8}	1.52×10^{8}	5.22	2.52		3.31×10^{7}	3.83×10^{6}
Construction operations	1.10×10^{9}	2.18×10^{8}	5.22	2.52		5.74×10^{7}	5.50×10^{6}
Agriculture tilling	8.95×10^{8}	2.50×10^{7}	5.22	2.52		4.67×10^{7}	6.30×10^{5}
Agriculture (animals)	1.95×10^{8}	3.05×10^{7}	5.22	2.52		1.02×10^{7}	7.70×10^{5}
Quarries and sand pits [b]	1.10×10^{6}	2.08×10^{5}	10 to 95		IARC 1997; Dumont 2006	1.10×10^{5} - 1.04×10^{6}	2.08×10^{4} - 1.98×10^{5}
Coal mining [b]	2.46×10^{7}	2.46×10^{6}	1.7 to 73		Bragg 2009	4.18×10^{5} - 1.80×10^{7}	4.18×10^{4} - 1.80×10^{6}
Coal-fired power plants [b,c]	1.16×10^{7}	6.24×10^{6}	4 to 14.5		Meij et al. 2000	4.65×10^{5} - 1.69×10^{6}	2.50×10^{5} - 9.05×10^{5}
Other sources [d]	3.91×10^{8}	3.00×10^{8}	5.22	2.52	NAPS 2010	2.04×10^{7}	7.56×10^{6}
Total – anthropogenic emissions	**5.95×10^{9}**	**1.13×10^{9}**	--	--	--	**3.30×10^{8}**	**3.10×10^{7}**

[a] Estimates may also be calculated using the percentage of quartz of 0.35% in $PM_{2.5}$ obtained from the study of Davis et al. (1984) – see text for explanations.

[b] Emissions provided by the NPRI for 2008.

[c] Cristobalite may also be present: see text for explanations.

[d] This category includes abrasives manufacture, aluminum industry, asbestos industry, asphalt paving industry, cement and concrete industry, chemicals industry, mineral products industry, foundries, grain industries, iron and steel industries, iron ore mining industry, non-ferrous smelting and refining industry, pulp and paper industry, wood industry, upstream petroleum industry, downstream petroleum industry, other industries, petroleum product transportation and distribution, commercial and residential fuel combustion, mobile sources (air, marine, vehicles), incineration, miscellaneous, and the open sources wastes, mine tailings and prescribed burning.

Emissions from Anthropogenic Sources

Roads, Construction and Agriculture

Major sources of open anthropogenic emissions of fine PM include agricultural tilling and associated wind erosion, animal activities (agriculture), construction operations, dust from paved roads, and dust from unpaved roads. In 2007, reported emissions by the NPRI for open sources of fine PM totalled 5.5 billion kg and 828 million kg for PM_{10} and $PM_{2.5}$, respectively (Environment Canada 2010). The combined releases of the five major sources were estimated to make up 88% and 67% of the quartz releases in the PM_{10} and $PM_{2.5}$ fractions, respectively (Table 4).

Quarries and Sand Pits

Releases to air from quartz deposits occur by wind erosion, sand handling and extraction. Sand and gravel mining, and quarrying activities release PM into air (Table 4). Dumont (2006) mentions that silica sand has high silica content (95% SiO_2 or more). Granite rock contains 10-30% of quartz, while quartz content in shale is up to 30% (IARC 1997). Not surprisingly, the purity of quartz in silica sand deposits and sand pits varies from one site to another. Therefore, a range of quartz content in the mineral deposits exploited was considered for the estimation of the quartz releases in the atmospheric fine particulate matter. Maximum upper and lower limits for quartz content were set to 10% (if quarries were to extract exclusively granite) and 95% (if all the production was represented exclusively by silica sand). In 2008, the quantity of quartz released in PM_{10} was thus estimated to be between 1.10×10^5 kg and 1.04×10^6 kg and that in $PM_{2.5}$ was estimated to range between 2.08×10^4 kg and 1.98×10^5 kg (Table 4). These estimates indicate that activities at quarries and sand pits would contribute less than 1% of the quartz emissions of human origin as fine PM in Canada.

Coal Mining and Power Generation

Coal mining activities release dust that may have substantial quartz content. Quartz is present in coal, and combustion of coal generates particulate matter in residual ash. Depending on the origin and types of coal, silicon content may vary in coal and in released fly ash (Vassilev et al. 2007). Both cristobalite and quartz may be formed by coal combustion (Vassilev et al. 2003).

Power generation is the largest coal consumer in Canada. A survey of six Canadian coal mines located beside coal-fired power plants showed that SiO_2 is the inorganic oxide most commonly reported in coal samples (Goodarzi 2002). Bituminous and sub-bituminous coals are the most mined coals in Canada with 97% of total sales (Natural Resources Canada 2009). Between 1.7 and 73% of SiO_2 is reported in bituminous and sub-bituminous coal (Bragg 2009). The percentages of SiO_2 reported in these coals represent maximum possible quartz contents since not all of their silicon (reported as SiO_2) will be in the form of quartz. Quartz releases by these mining activities within particulate matter are conservatively estimated in Table 4.

In the Netherlands, coal type ratios similar to the estimates used for Canada (above) are used for power generation (Borm 1997). Meij et al. (2000) found between 4 and 14.5% of

quartz in coal fly ash from Dutch coal-fired power plants. Quartz releases in air were estimated for the year 2008 using these ratios and are presented in Table 4. Cristobalite may be a minor constituent of coal fly ash in a proportion varying between 0.5 and 1% (Vassilev et al. 2003). However, cristobalite was not included in the above calculations.

Overall, these estimates indicate that activities in the coal mining and power generation sectors would contribute less than 8% of the quartz (and cristobalite) emissions of anthropogenic origin as fine PM in Canada.

Uncertainties in the Estimated Atmospheric Releases

There are significant uncertainties in estimating anthropogenic emissions of elements and minerals (Pacyna and Pacyna 2001). To reduce this uncertainty, more precise information on the crystalline SiO_2 fraction of fine particulates released from of each source category would be required. Emissions from industrial activities included in the category 'other sources' (e.g., vehicles, grain industries, etc.) are likely overestimated but their overall contribution to total emissions of fine PM remains modest (Table 4).

Environmental Fate

Typical fugacity modelling is not applicable to quartz and cristobalite because, as is the case for other essentially non-volatile chemicals, these substances exert zero partial pressure and fugacity in air (Diamond et al. 1992). However, there is ample evidence that quartz is found in the form of fine particulate matter in the atmosphere.

Being refractory to weathering, quartz can be carried for long distances by eolian transport (pertains to the activity of the winds). For example, one study noted that Asian dust can be transported within five days from the Gobi Desert in China to the mountain ranges between British Columbia and California, a distance greater than 8000 km (Husar et al. 1998). The mean diameter of this material was between 2 and 3 μm and was dominated by the single minerals quartz, K-feldspar and plagioclase (Husar et al. 1998; Jeong and Chun 2007). A significant dust fall on northern Scandinavia originated from western North Africa, and hence particles were transported for at least 7000 km before reaching their final destination. Mineralogically, these particles were dominated by small round quartz grains with a mean diameter of 2.7 μm (Franzén et al. 1994). Finally, microscopic analyses of particulate matter collected during six long-range transport events led researchers to conclude that large quartz grains (> 62.5 μm) can be transported over great distances, up to 10000 km, to oceanic and terrestrial locations (Middleton et al. 2001).

Quartz and cristobalite are characterized by low water solubilities (ranging from insoluble to 8.7 mg/L), negligible vapour pressures (~0 Pa), negligible Henry's Law constants, and negligible affinities for organic carbon (Table 2). These crystalline minerals exhibit a low geochemical mobility in aqueous environments whatever the ambient conditions are: oxidizing or reducing, acid or alkaline (Garrett 2004).

Despite low solubilities, quartz and cristobalite may slightly dissolve and dissociate upon introduction into water according to the reaction:

$$SiO_2\,(s) + 2\,H_2O \rightarrow H_4SiO_4\,(aq) \qquad [1]$$

where **s** and **aq** stand for 'solid' and 'aqueous' species, respectively. The reaction product is the weak ortho-silicic acid with an acid dissociation constant (pK_a) of 13.2 determined at 25°C and for an ionic strength of 0 M (Smith and Martell 2004). Under conditions commonly found in oxic fresh waters (i.e., pH between 5 and 9; redox potential [E_h] between 0.5 and 1 V), the undissociated acid will be the dominant species in solution (Brookins 1988) and complexation with dissolved cations will be minimal.

Silicic acid occurs naturally in North American fresh waters at concentrations up to 20 mg/L SiO_2 (Wetzel 2001). This dissolved silica may not be in chemical equilibrium with quartz and originates probably from amorphous silica contained in bottom sediments or in watershed soils. Amorphous silica is estimated to have solubility in water varying between 15 and 150 mg/L in the temperature range of 20 to 25°C (OECD 2004; Waddell 2006). In fact, most surface waters are greatly under-saturated with respect to silica. This is attributed to the slowness with which silicates dissolve, to processes of surface adsorption of silicic acid by Al and Fe oxyhydroxides, and to the activity of organisms that use silica, particularly diatoms (Krauskoff 1956; Wilding et al. 1977; Wetzel 2001; Hiemstra et al. 2007). It can be concluded that the natural presence of silica in surface waters has to be considered when determining background levels of SiO_2 in the environment.

Persistence and Bioaccumulation Potential

Environmental Persistence

QSAR models, while usually used by Environment Canada to estimate persistence as environmental degradation half-lives, cannot be used for quartz and cristobalite. Therefore, a qualitative approach has been undertaken. Quartz is one of the minerals least susceptible to chemical dissolution and physical alteration (Moore 1999). Although cristobalite is not thermodynamically stable at ambient temperature, it is metastable because its conversion to quartz occurs very slowly, being in the order of geological time (Moore 1999). Despite their resistance to degradation, these substances release small amounts of silicates into solution when in contact with water. Once in solution these silicates take the form of ortho-silicic acid which is stable (does not degrade) in this medium (i.e., in surface waters, groundwater, and pore waters of soil and sediments).

Empirical evidence strongly suggests that the persistence of solid-phase quartz and cristobalite in natural ecosystems is very long. It is therefore concluded that quartz and cristobalite do meet the persistence criteria in air, water, soil or sediment (half-life in air $\geq$ 2 days, half-lives in soil and water $\geq$ 182 days and half-life in sediment $\geq$ 365 days), as set out in the *Persistence and Bioaccumulation Regulations* (Canada 2000).

Potential for Bioaccumulation

Evaluation of bioaccumulation potential based on log K_{OW} values (often estimated using QSARs) is not applicable to the present substances. Bioaccumulation potential in aquatic exposures is typically quantified by determining either a bioconcentration factor (BCF) or a bioaccumulation factor (BAF). As stable crystalline solids, quartz and cristobalite are expected to have very limited potential for uptake through the gill or gut of aquatic organisms. The physical accumulation of solid quartz and cristobalite particles in lungs of terrestrial animals is discussed in the section on ecological effects.

Despite their resistance to degradation, these substances do release small amounts of silicon (as silicic acid) into solution when in contact with water. However, BCF and BAF ratios are inappropriate when applied to some elements because they are considered of little usefulness in predicting their hazards (Schlekat et al. 2007). For example, some elements naturally may be highly accumulated from the surrounding medium because of their nutritional essentiality. For diatoms (aquatic micro-algae), dissolved silicic acid is a macro-nutrient required for the formation of their frustules (Marchetti et al. 2010). Furthermore, the importance of dissolved silicon in the development, physiology and skeletal structure of algae, plants and animals is acknowledged (Markert 1994, European Commission 2000a, Martin 2007).

Based on the available published information, quartz and cristobalite do not meet the bioaccumulation criterion (BAF or BCF ≥ 5000) as set out in the *Persistence and Bioaccumulation Regulations* (Canada 2000).

Potential to Cause Ecological Harm

Ecological Effects Assessment

A – Toxicity in the Aquatic Compartment

No data were found with regards to the toxicity of quartz and cristobalite to aquatic organisms. However, there are empirical toxicity data available for suspensions of synthetic amorphous silica (CAS RN 7631-86-9), which is a reasonably close analogue of the crystal forms being assessed by virtue of their chemical formula, SiO_2, and their low solubility in water determined to be less than 150 mg/L (OECD 2006; Waddell 2006). Toxicity data for dissolved forms of soluble silicate salts were also examined in order to understand how the aquatic toxicity of dissolved silicon alone (no suspended particles) is expressed. Results of these studies are presented in Tables 5a and 5b; they were critically reviewed using Robust Study Summaries and found to be of satisfactory confidence for this risk assessment.

Evaluation of the short-term toxicity of synthetic amorphous silica was undertaken by the company Degussa AG following the Organization of Economic Cooperation and Development (OECD) guidelines for testing of sparingly soluble chemicals, and was reported in an OECD Screening Information Data Set (SIDS) assessment report (OECD 2004). Test solutions were prepared by stirring an excess concentration (1000 or 10000 mg/L loading) for 20 hours and the resulting suspensions were tested (OECD 2004). Toxicity values were based on nominal treatment (loading) levels because aqueous

concentrations of silica were not measured. Results including organisms used and endpoints monitored are presented in Table 5a.

Table 5a. Empirical data for the short-term toxicity of synthetic amorphous silica

Test organism	Type of test	Endpoint	Nominal concentration (mg SiO_2/L)	Reference
Danio rerio (zebrafish)	Acute (96 hours)	LL_0[a]	10,000	Degussa 1992a,b
Daphnia magna	Acute (24 hours)	LL_{50}[b]	> 10,000	Degussa 1992c,d

[a] LL_0 - The estimated loading of the substance that corresponds to the survival of all the test organisms relative to controls.

[b] LL_{50} - The loading of the substance that is estimated to immobilize 50% of the test organisms. This is interpreted as a lethal endpoint by the OECD.

Information regarding the toxicity of soluble silicate salts for aquatic organisms was found in 18 papers ranging in date of publication from 1953 to 2001. Organisms used included species of bacteria, micro-algae, crustaceans, molluscs, marine polychaete worms and fish (ECOTOX 2006; OECD 2007b). Many of these studies provided insufficient experimental details, had significant methodological deficiencies or did not respect the natural ecology of the tested species. Six studies provided reliable data (Table 5b) and all used sodium silicates at concentrations expected to be below the water solubilities of the test compounds which are greater than 200,000 mg/L (OECD 2007b). The toxicity of these salts can be primarily attributed to the silicate ions released into solution upon dissolution, as the aquatic toxicity of the sodium (Na) ion is very low with acute LC_{50} values much greater than 1000 mg Na/L (Mount et al. 1997).

The lower aquatic toxicity of synthetic amorphous silica compared with that of the sodium silicate salt is shown by the toxic responses of the fish *Danio rerio* exposed to these compounds in water. After 96-hours exposure to sodium silicate at a concentration of about 500 mg SiO_2/L, 50% of the test population were killed (i.e., LC_{50}, see Table 5b). Exposure to amorphous silica at a loading of 10,000 mg SiO_2/L caused no mortality (Table 5a). Both tests employed young fish in similar test waters (Degussa 1992a, 1992b; OECD 2007b), and organisms were exposed to both particulate and dissolved silica in the test with amorphous silica. These results are consistent with the idea that the low solubility and slow kinetics of dissolution of synthetic amorphous silica limit the release of SiO_2 ions in water, hence limit the expression of the toxicity of these ions for aquatic organisms exposed to this substance.

The previous empirical evidence, including the results for the closer analogue, synthetic amorphous silica, indicates that quartz and cristobalite are not highly hazardous to aquatic organisms.

Table 5b. Empirical data for the toxicity of soluble silicates[a]

Test organism	Type of test	Endpoint	Value (mg SiO_2/L)	Reference
Micro-algae *Scenedesmus subspicatus*	Unknown [b] (72 hours)	EC_{50} (biomass)	89	OECD 2007b
Crustacea *Ceriodaphnia dubia*	Acute (48 hours)	LC_{50} [c]	33.5	Warne and Schifko 1999
Daphnia magna	Acute (48 hours)	LC_{50}	731	OECD 2007b
	Unknown [d] (100 hours)	LC_{50}	106	Freeman and Fowler 1953
Fish *Danio rerio*	Acute (96 hours)	LC_{50}	508	OECD 2007b
Fish *Gambusia affinis*	Acute (96 hours)	LC_{50}	1,142	Wallen et al. 1957

[a] The higher concentrations are expected to be below the solubilities of the compounds tested – see text for explanations.

[b] There is no consensus among regulatory regimes as to whether tests with micro-algae lasting 72 hours should be considered short-term. In addition, biomass is not the preferred endpoint for such studies (ECHA 2008; CCME 2009).

[c] LC_{50} The concentration of a substance that is estimated to be lethal to 50% of the test organisms.

[d] One hundred hours is not a standard duration for toxicity tests.

B – Toxicity caused by Inhalation in Terrestrial Organisms

Pulmonary diseases caused by silica dust have been known since antiquity, and numerous clinical descriptions of various pathologies have been made (Harley and Vallyathan 1996). A brief summary of the current knowledge on these illnesses (primarily fibrosis and silicosis) is presented below based on descriptions provided, notably by Allison (1975), Bowden and Adamson (1984), Cantin et al. (1988), Berry et al. (1991), Green and Vallyathan (1996) and Fubini (1998).

Development of fibrosis and silicosis in terrestrial organisms is mainly dependent on the quantity of particulate exposure and size of the silicon dioxide crystals. Particles less than 5 μm in diameter have a greater chance of being deposited in the alveoli and not in the primary airways. Furthermore, the potential of the inhaled material to catalyze Reactive Oxygen Species (ROS) release (as discussed on pages 45-47) and persistently activate inflammatory cells would determine the cytotoxicity of a given dust. This type of dust is generated notably by grinding macroscopic crystals of quartz, because the surface produced by mechanical cleavage of a chemical bond is usually very reactive. Fresh ground dusts are more hazardous than aged ones. The presence of contaminants such as carbon and inorganic ions decreases the toxicity of crystalline silica. Silica surfaces rendered hydrophobic (as in coal ashes) presents decreasing hazard potential. Finally, the fibrogenic activities of silicates decrease in order from cristobalite, followed by quartz and lastly amorphous silica.

Empirical and Experimental Data on Terrestrial Organisms

Eight studies have been found on the effects of respirable crystalline silica on terrestrial mammals and birds (Table 6a). They address chronic exposures of animals in their ambient environment. Detection and/or quantification of particles in lung tissues were made with the help of X-ray diffraction techniques and analyses of birefringence (double refraction) with polarized light. There are also known cases of occupation-related pneumoconiosis in horses and mules used in mines and quarries in the past (Smith and Jones 1961).

Table 6a. Empirical data for inhalation toxicity of quartz and cristobalite to terrestrial animals[a]

Animal species	Exposure		Number of organisms and age	Size of particles in lung tissues	Effects	Reference
	Type	Level				
Horse (*Equus ferus caballus*)	Chronic *in situ* (cristo-balite)	High (soil)	9 with ages varying from 2½ to 20 years-old	Sub-micron	Granulomatous pneumonia with associated pulmonary fibrosis	Schwartz et al. 1981
	Chronic *in situ* (cristo-balite & quartz)	Not mentioned	20 with ages varying from 2 months- to 20 years-old	Intracytoplas-mic inclusions of SiO_2 within macrophages in all horses, size not mentioned	Silicosis leading to death (euthanasia) for 9 horses	Berry et al. 1991
Water buffalo (*Bubalis bubalis*)	Chronic *in situ* (quartz)	High (near a quartz quarry)	2	Silicate particles observed in tissues, size not mentioned	Severe silicosis leading to death (sacrificed) for both animals	Roperto et al. 1995
Camel (*Camelus sp.*)	Chronic *in situ* (quartz)	8.25×10^3-22×10^3 µg/m^3 in PM_{10} of which 15 to 26% is free silica	2 4-years old & 20-years old	Free silica particles observed in lung tissue, size not mentioned	Silicosis, alveolar collapse and interstitial emphysema for the old camel No pathologies in the young camel	Xu et al. 1993
Camel (*Camelus dromeda-rius*)	Chronic *in situ* (quartz)	High Arid areas of Somalia	134 unknown ages, and both sexes represented	Main dust constituent in lungs and bronchial lymph nodes was silica, size not mentioned	Dust-laden macrophages found in lungs of 94 animals; 22 of them developed fibrosis	Hansen et al. 1989
Badger (*Meles meles*)	Chronic *in situ* (quartz)	Not mentioned	3	3.6±0.5 µm	Macroscopic lesions and silicosis	Higgins et al. 1985
Ring-necked pheasant	Chronic *in situ* (quartz)	High (pens with	5 females	Particles less than 1 µm in	Pulmonary silicosis, hepatomegaly,	Evans et al. 1988

(*Phasianus colchicus torquatus*)		sandy soil)		diameter	cardiomegaly, and egg-yolk peritonitis	
Kiwi (*Apterix sp.*)	Chronic *in situ* (quartz)	High (enclosures with sandy soil)	38 of which 24 were in captivity; 7 were free-living Adults and juveniles	Mixed dust made mainly of crystalline silica in captive birds; size not mentioned Levels higher in adults than in juveniles	Pneumoconiosis but absence of fibrosis in captive adult birds Normal lungs in immature captive birds. Normal lungs in all free-living ones	Smith et al. 1973

[a] **Definitions**: pneumoconiosis: general term to designate a lung disease resulting from inhalation of dust; silicosis: lung disease caused by inhalation of crystalline silica dust, and resulting in inflammation and scarring in forms of nodular lesions in the upper lobes of the lungs; fibrosis: excessive development of fibrous connective tissue in an organ or tissue as a reparative or reactive process; hepatomegaly: condition of having an enlarged liver; cardiomegaly: condition of having an enlarged hearth.

In the studies mentioned above, exposure was ill-defined or, at best, defined in a qualitative way. However, quartz and cristobalite have been tested on laboratory animals such as rats, guinea pigs and sheep, for which exposure was quantitatively defined. Table 6b includes seven of these studies that provided detailed descriptions of experimental protocols, presented adequate survival in controls at the end of exposures (e.g., > 80%), and for which exposure was via inhalation. The study on intratracheal exposure of sheep (Bégin et al. 1989) provided information on dose-response relationships and is discussed below.

The endpoint reported in Table 6b is pulmonary fibrosis. The lowest reliable effect value is a clear example of pulmonary fibrosis in a sensitive species of animal in the laboratory that was reported in a study by Porter et al. (2001). The effect concentration of 15.3 mg SiO_2/m^3 found in this study to produce a severe fibrosis in the lungs of rats exposed to respirable quartz, was selected as the Critical Toxicity Value (CTV) for terrestrial organisms exposed to aerosols rich in quartz and/or cristobalite. Porter et al. (2001) exposed Fischer 344 rats to a quartz aerosol of a particle size ≤ 2 µm for 116 days. Control rats were exposed to air filtered through particle filters and a charcoal bed. Temperature (22°C to 26°C), humidity (40 to 70%), and ammonia (≤ 5 ppm) were monitored continuously. The concentration of silica aerosol was measured every day by gravimetry. The degree of lung fibrosis, monitored throughout the study, was determined with the help of a scoring system based on histological examinations of lungs. A score of 0 corresponded to no damage and a score of 9 to severe and widespread damage. After 116 days of exposure to a mean concentration of 15.3 mg SiO_2/m^3, a severe fibrosis was observed in the rats exposed to quartz. The mean fibrosis score of these five rats, 5.2 ± 1.2, was statistically different ($P<0.05$) from that of the five control rats, 0.0 ± 0.0; additional information on this study is provided in Table 6b.

Table 6b. Experimental data for inhalation toxicity of quartz and cristobalite to mammals in laboratory.

Test organism	Substance	MMAD [a] (µm)	Type of test	Number of animals per replicate	Mean concentration in air (mg SiO_2/m^3)	Lung burden (mg particle)	Endpoint (semi-quantitative estimate)	Reference
Albino rat	Quartz	NA [b]	Short-term 2 weeks and 4 weeks	6 to 8 ♂	200	ND [b]	Fibrosis (degree not mentioned)	Prasad et al. 2000
SPF-bred Wistar rat	Quartz	8 (mean)	Subchronic (91 days) followed by 52 weeks post-exposure	10 ♂and 10 ♀	58.5	4.6 ♂ 2.9 ♀	Interstitial fibrosis in ~ 100% of specimens at 52 weeks (degree not mentioned)	Reuzel et al. 1991
Fischer-344 rat (CDF)	Quartz	≤ 2	Subchronic (116 days)	5	15.3	6.5	Severe fibrosis at 116 days [c,d]	Porter et al. 2001
Fischer-344 rat	Cristo-balite	1.3	Subchronic (91 days) followed by a 8 month post-exposure	4	3.0	1.64	Fibrosis at 8 months (degree not mentioned)	Johnston et al. 2000
Fischer-344 rat	Quartz	< 2.5	Subchronic (6 months)	8	2.0, 10.2, and 19.3	ND	10.2 and 19.3: slight to moderate fibrosis in all rats, 6 months [c]	Kutzman 1984
Sheep	Quartz	< 5	Subchronic (12 months)	36	100 mg injected in trachea resulting in an internal exposure of 8.25×10^7 µg/m^3 lung [e]	Average: 1.94±0.33 µg/mL broncho-alveolar lavage	Early fibrosis 12 months after initial injection [c]	Bégin et al. 1989
Syrian	Quartz	1.2	Long-term	15 to 19	3.1 of which	3.3	Slight interstitial	Muhle et al.

golden hamster			18 months		76.1% was respirable		fibrosis in 100% of animals at 18 months [c]	1998

[a] MMAD: Mass Median Aerodynamic Diameter**;**.
[b] NA: not available; ND: not determined
[c] Degree of fibrosis determined with the help of a scoring system based on histological examinations.
[d] The mean fibrosis score of silica-exposed rats is significantly different from that for controls ($P<0.05$).
[e] Lung volume is directly related to body size. The relationship for mammals is $LV = 6.3\times10^{-5}M_b^{1.02}$ where M_b is the body mass in kilograms and LV is lung volume in cubic meters (Schmidt-Nielson 1997). Body weights of animals were given in the paper.

Accumulation in the Lungs of Terrestrial Organisms

The question of the accumulation of quartz and cristobalite via inhalation is substantiated by the following observations made from the empirical and experimental studies presented above.

Accumulation of particles in lung tissues. The eight *in situ* studies in Table 6a reported the accumulation of fine particles of crystalline silica, quartz, or of cristobalite, in macrophages, walls of the alveoli and/or draining lymph nodes following continuous exposures to these particles in the ambient air. Three of these studies indicated that the internalized particles were less than 5 µm in size. The same can be inferred for the five other studies because, according to Allison (1975), nearly all inorganic particles that remain in air for long periods and penetrate into the terminal air spaces are less than 5 µm in diameter.

Effect of age on accumulation. In the study with kiwis (Table 6a), ash contents of lungs tend to indicate that adult captive kiwis had higher levels of silicates than juvenile captive kiwis. The study with the camels (Table 6a) reported an absence of pathology in the young camel which indicates that, for a similar exposure, it had accumulated fewer silica particles in its lungs than the 20-year old camel.

Increase in accumulation and effects with exposure. In the study with the kiwi, ash contents of lungs of captive individuals tended to be higher than those of free-living individuals. In addition, none of the free-living birds developed lesions to their lungs whereas 50% of the captive ones had pneumoconiosis. Schwartz et al. (1981) demonstrated the presence of crystalline silica in the lungs of a horse with silicosis and the absence of crystals in a control horse without silicosis (whose origin was not mentioned).

Dose–response relationships. None of the *in situ* studies of Table 6a could quantitatively relate exposure to effects, because exposures were defined only qualitatively or because too few quantitative treatments were used. In the experimental study with the sheep (Table 6b), an internal exposure gradient with quartz particles developed over time because the degree of quartz retention in lungs varied from one animal to another. Twelve months after the initial injection, total lung capacities and vital capacities (both in litres), were inversely related to quartz contents of lungs, with Spearman *r* coefficients of -0.541 and -0.548, respectively ($P<0.001$).

Links to effects at higher levels of biological organization. The ecological relevance of the above study results is indicated by the observation that pulmonary silicosis can eventually translate into effects at levels higher than those at the organ level (Table 6a). Horses experiencing heavy silicosis caused by cristobalite were euthanized because they were expected to die from respiratory distress. A similar end was observed for buffalo chronically exposed to quartz in ambient air. In the study with pheasants, all the birds examined came from a pheasant farm affected by high mortalities and poor egg production. However, it cannot be excluded that a factor other than aerial exposure to quartz is co-responsible for these effects.

Natural background exposure. The study with the camels (Table 6a) indicates that natural occurrence of crystalline silica in fine atmospheric PM may lead to its accumulation in lungs of terrestrial animals, and eventually to silicosis depending on the level of natural exposure. The importance of this natural burden also depends on behavioural habits which may bring animals in close contact with soil dust, as for example the preference of the badger to dig its den in sandy soil (Higgins et al. 1985).

The above results support the idea that quartz and cristobalite in the fine (respirable) fraction of aerosols have the characteristics of physically accumulating substances: (1) they are infinitely persistent; (2) they are accumulated via inhalation in the lung tissues and not just deposited in the airways of organisms; (3) they may not be easily excreted resulting in an accumulation in organisms over time and in long biological half-lives; (4) tissue concentrations increase with increasing exposure in air; and (5) higher levels in tissues lead eventually to toxic effects in a dose-dependent manner.

C – Toxicity in Other Environmental Compartments

No suitable ecological effects studies were found for quartz and cristobalite in media other than water and air.

Ecological Exposure Assessment

Data concerning concentrations of silica in the Canadian environment have been identified (Table 7). No data specific to quartz or cristobalite were found.

With regards to dissolved silica concentrations, no significant differences were observed between regions (Table 7) even if the geological nature varied among the locations reported. For that matter, silica content of soil and sediment is expected to be different from one region to another. However, it is likely that silica levels are controlled by processes of surface adsorption by Al and Fe oxyhydroxides, and the activity of organisms that use silica, and these processes would tend to dampen the effects of differences in natural source strength between regions. No quantitative exposure scenarios were developed for releases of dissolved forms of silicon from quartz and cristobalite into water because it is expected that dissolved forms of silicon will present very low risks of ecotoxicity in this compartment. Explanations are given in the section on characterization of ecological risks.

In air, quartz releases are associated with particulate matter (Environment Canada and Health Canada 2000). For NAPS data (Table 7), when raw data were not available for individual sites, statistical analyses were performed for the purpose of this assessment on the annual highest reported value for each site. Four sites were chosen to represent remote sites not suspected to be heavily influenced by human activities. Farmlands were not used to estimate background or remote values. Samples collected in remote locations contained lower concentrations of silica in PM_{10} fractions than those obtained in urban sites. This is consistent with the idea that human activities may have a significant impact on quartz presence in air.

Concentrations of quartz in the air of agricultural areas reported in Table 7 (Green et al. 1990) are not directly comparable with those of remote or urban sites because the former were measured based on total particulate matter. Zobeck and Van Pelt (2006) studied aerial emissions of dust by wind from a bare agricultural field (100 m radius) in western Texas. Concentrations of PM_{10} at 100 m downwind from the margin of the field, and at a height of 2 m, ranged from nearly 0 to 2000 µg/m^3, with most of the values being less than 40 µg/m^3. Data were collected every second for a period of 5 hours in the middle of the day. Quartz concentrations in these samples would vary from 0 to ~104 µg SiO_2/m^3 with a central tendency towards 2 µg SiO_2/m^3, using the estimated percentage of quartz in PM_{10} (5.22%) given in Table 4.

Table 7. Measured and modelled concentrations of silica in water and air in Canada[a]

Location	Year of sampling	Concentration range (minimum–maximum)	Percentiles			N[b]	Reference
			5th	Median	90th		
Dissolved silica in surface waters (mg SiO_2/L)							
Alberta lake	2000-2006	1.05-16.2	2.50	7.20	12.4	40	Alberta Environment 2010
Yukon rivers	2002-2008	0.170-42.8	2.70	7.87	13.0	216	Environment Canada (Pacific and Yukon regional) 2004
Atlantic provinces	1989-2002	0.02-82	0.4	6	17	13929	Environment Canada (Atlantic) 2002
Measured concentrations of quartz in air (µg SiO_2/m^3)							
2 agricultural areas in Alberta [c]	1990 (in TSP) [c]	0.4-27.2	N/A[d]	7	N/A	N/A	Green et al. 1990
	2009 (in $PM_{2.5}$)	--	--	--	0.63 0.76[e]	--	Alberta Environment 2010
Site downwind from a coal power plant in Alberta	2008 (in PM_{10})	--	--	3.2 3.3 [f] (mean data from 2 days)	--	2	Government of Alberta 2010
Site impacted by dust from unpaved road in Alberta	2008 (in PM_{10})	--	--	11.6 6.3 1.5 [g] (mean data from 3 days)	--	3	Government of Alberta 2010
4 remote /	1996	0.01-6.68	0.05	0.41	2.39	320	NAPS 2010

rural sites in Canada [h]	1999 2006 (in PM_{10})						
24 urban sites in Canada [i]	2009 (in PM_{10})	0.73-8.77	0.92	3.73	6.48	1549	NAPS 2010
Modelled concentrations of quartz in air (µg SiO_2/m^3)							
Sandstone quarry in BC	2008 (in PM_{10})	4.8-104.9 [j]	--	38.5	--	44	SCREEN3 1995
Granite quarry in BC		1.37-5.84 [k]	--	3.09	--	44	
Sand and gravel pit in Ontario		2.82-4.90 [l]	--	2.82	--	44	
Modelled concentrations of cristobalite in air (µg SiO_2/m^3)							
Industrial operation in Canada	2008 (in PM_{10})	3×10^{-3} – 2.14 [m]	--	0.98	--	44	SCREEN3 1995

[a] A molar ratio of 2.14 was used to convert Si levels, obtained in publications, to SiO_2 levels given in this table.
[b] Number of samples
[c] The same areas were sampled in 1990 and 2009 (Red Deer and Medicine Hat). TSP is Total Suspended Particulates.
[d] N/A is not available
[e] Concentrations estimated from the 99th percentiles of $PM_{2.5}$ concentrations measured in 2009, and the estimated percentage of quartz in $PM_{2.5}$ (2.52%) given in Table 3.
[f] Concentrations estimated from the one-hour average concentrations measured in 2008, and the upper range of the estimated percentage of quartz in PM_{10} produced by power plants (14.5%), given in Table 3.
[g] Concentrations estimated from the one-hour average concentrations measured during 3 consecutive days in 2008, and the estimated percentage of quartz in PM_{10} (5.22%) given in Table 3.
[h] The four remote sites sampled were Egbert (Ontario), Golden (British Columbia), Kejimkujik (Nova Scotia) and Elk Island (Manitoba).
[i] The 24 urban sites sampled were Halifax (Nova Scotia), Saint John (New Brunswick), Montreal (3 sites), Quebec city (Quebec), Ottawa, Windsor, Toronto (2 sites), Hamilton, Wallaceburg, Simcoe and Pt Petre (Ontario), Winnipeg and Flin Flon (Manitoba), Saskatoon (Saskatchewan), Edmonton and Calgary, (Alberta) (2 sites), Vancouver (2 sites), Victoria, Abbotsford and Quesnel (British Columbia), Yellowknife (North West Territories).
[j] Range of modelled maximum 1-hour concentrations from 100 to 10000 m of the site area. A percentage of 95% (Dumont 2006) was used to convert modelled PM_{10} concentrations to quartz concentrations.
[k] Range of modelled maximum 1-hour concentrations from 100 to 10000 m of the site area. A percentage of 30% (IARC 1997) was used to convert modelled PM_{10} concentrations to quartz concentrations.
[l] Range of modelled maximum 1-hour concentrations from 100 to 10000 m of the site area. A percentage of 33% (Shiraki and Holmén 2002) was used to convert modelled PM_{10} concentrations to quartz concentrations.
[m] Range of modelled maximum 1-hour concentrations from 100 to 10000 m of the site area. A percentage of 1% (Vassilev et al. 2003) was used to convert modelled PM_{10} concentrations to cristobalite concentrations.

Concentrations of fine particulate matter emitted from unpaved roads are variable because of the many factors influencing the amount of dust generated by traffic. These factors can be specific to the road, to the geographic area and/or related to the characteristics of the vehicles (Edvardsson and Magnusson 2009). Edvardsson and

Magnusson (2009) studied the downwind horizontal diffusion of PM_{10} produced by an automobile passing every minute on a gravel road at a speed of 55 to 60 km/h. Measured concentrations of PM_{10}, at 1.3 m above the ground, were 566 µg/m^3 and 200 µg/m^3 at 5 m and 30 m from the road, respectively. These values convert to 29.5 µg SiO_2/m^3 and 10.4 µg SiO_2/m^3 taking the estimated percentage of quartz in PM_{10} (5.22%) presented in Table 3. The quartz concentrations reported in Table 7 for a dusty mine haul road in Alberta have been calculated with the same method. These values, obtained for 3 consecutive days, were 1.5, 6.3 and 11.6 µg SiO_2/m^3 (Government of Alberta 2010).

No monitoring data were found for quarries and sand and gravel pits in Canada. The computer program SCREEN3 (SCREEN3 1995) was used to estimate maximum 1-hour quartz concentrations, at 1 meter above the ground, emitted by these sources. Input parameters included emission rates, dimensions of source areas, and characteristics of winds. The values for these parameters were determined for the locations in question using NPRI emission data (Environment Canada, 2010), annual average data for winds (Environment Canada 2003) and dimensions of source areas with maps available on the Internet. The facilities reporting the largest quantities of PM_{10} to the NPRI in 2008 were selected in developing conservative scenarios for exposure (Environment Canada 2010). Data for a sandstone quarry (41000 kg of PM_{10} for the whole year), a granite quarry (65300 kg of PM_{10} for the whole year), and a sand and gravel pit (46000 kg of PM_{10} for the whole year) were selected. Maximum percentages of quartz for these materials, provided in the literature, were used: 95% for sandstone (Dumont 2006), 30% for granite (IARC 1997), and 33% for sand and gravel (Shiraki and Holmén 2002). The highest concentration of quartz provided by these worst-case scenarios (104.9 µg SiO_2/m3) was obtained at a distance of 884 m from a sandstone quarry. A 1-hour maximum concentration of 5.84 µg SiO_2/m^3 was estimated for a granite quarry, and 4.90 µg SiO_2/m^3 for a sand and gravel pit (Table 7).

The modelled quartz concentrations obtained for the sand and gravel pit are somewhat similar to the quartz concentrations in the PM_{10} measured downwind from a sand and gravel operation in California (Shiraki and Holmén 2002). Mean concentrations for the dry season were 32.6 and 9.4 µg quartz/m^3 at 259 and 750 m from the facility respectively. Corresponding values for the operation in Canada are respectively 3.4 µg SiO_2/m^3 and 4.6 µg SiO_2/m^3 at 300 and 800 m, respectively, from the area source.

An industrial operation reported, under section 71 of CEPA 1999, releasing more than 10000000 kg of cristobalite to land in 2006 (Environment Canada 2009). This industrial operation also reported to the NPRI the release of fine particulate matter (PM_{10}) to the atmosphere (Environment Canada 2010). To this effect, a very conservative exposure scenario for the air was designed using SCREEN 3 (SCREEN3 1995). Input values included the quantity of PM_{10} released in 2008 (6.43×10^5 kg for the whole year), the actual height of the plant stack (121 m), and the default values for meteorological and other parameters required to run the model (SCREEN3 1995). A content of cristobalite of 1% (Vassilev et al. 2003) was used as a default value for the less than 10-µm-sized particulate matter emitted by the stack. The highest concentration of cristobalite, 2.14 µg SiO_2/m^3**,** was obtained at a distance of 509 m from the stack (Table 7).

No soil and sediment exposure concentration data were reported because crystalline silica is not expected to have harmful effects by contact in these media.

No site-specific exposure scenarios were developed for the environmental releases of quartz and cristobalite (with the exception of the above-mentioned facility) reported by the respondents of the section 71 survey for 2006. Most reported releases were to land, or were treated as wastes transferred to waste treatment and disposal facilities for which no releases to the environment are expected (Environment Canada 2009).

No exposure scenarios were developed for quartz and cristobalite in pest control products. These products are already regulated by the Pest Management Regulatory Agency (PMRA) under the *Pest Control Products Act*.

Characterization of Ecological Risk

The approach taken in this ecological screening assessment was to examine relevant scientific and technical information and develop conclusions based on a weight-of-evidence approach and applying precaution as required under CEPA 1999. Lines of evidence considered include results from conservative risk quotient calculations, as well as information on persistence, bioaccumulation, toxicity, sources and fate of the substance.

Water (Dissolved and Particulate Phases)

Quartz and cristobalite have been demonstrated to have a low potential for acute toxicity to aquatic organisms. No acute effects in receiving waters are expected because the acute toxicity of suspensions of the analogue synthetic amorphous silica is very low (Table 5a). In addition the water solubilities of quartz and cristobalite, determined to be 6.4 mg SiO_2/L and ~ 18 mg SiO_2/L, respectively, are less than the lowest acute value obtained with soluble silicates, a LC_{50} of 33.5 mg/L (Table 5b).

Given their environmental persistence, the potential for chronic effects of quartz and cristobalite is of particular interest because in principle these substances would occur at concentrations lower than acute ones. Nevertheless, chronic ecotoxicity caused by exposure to solid forms of these substances is not expected because of their very low acute toxicity (Table 5a). In addition dissolved forms of the substances are unlikely to cause chronic effects because of their low solubilities, their slow dissolution, and the fact that dissolved concentrations are expected to be greatly under-saturated with respect to the solid phases (see explanations in the section on environmental fate). In addition, natural background concentrations of silica in water may approach or exceed the solubilities of quartz and cristobalite (Table 7) because of dissolution of various amorphous forms of silica. It is understood that no ecotoxic effects should be observed in the typical background range of a substance in the medium of interest under natural

conditions. Cristobalite is expected to be of lower natural occurrence than quartz in Canada (Wilding et al. 1977).

Air (Inhalation of Particles)

Quartz may be released from a variety of anthropogenic sources rendering terrestrial fauna susceptible to exposure to respirable quartz in the ambient environment. Notably, the activities related to agriculture and construction, use of unpaved roads, and exploitation of quarries and sand and gravel pits all contribute to atmospheric emissions of PM_{10} containing quartz. Quartz and cristobalite are persistent and under continuous exposure conditions may physically accumulate in the lung tissues of terrestrial organisms. These crystalline phases can cause fibrosis and silicosis and eventually lead to death depending on the severity and duration of exposure.

A risk quotient analysis, integrating conservative to very conservative estimates of exposure with toxicity information, was performed for the air compartment to determine whether there is potential for ecological harm in Canada. The Predicted Environmental Concentrations (PEC) used for this analysis were based on the maximum possible estimated quartz and cristobalite contents of suspended particulate matter released from each of the anthropogenic sources mentioned in Table 7; these values are reported in Table 8. The Predicted No Effect Concentration (PNEC) was derived from the CTV of 15.3 mg SiO_2/m^3 obtained with rats exposed to respirable quartz in the laboratory (Table 6b). An assessment factor of 10 was applied to the CTV to account for uncertainties associated with extrapolation from a laboratory to field study and for inter-species and intra-species variability. A larger assessment factor was not considered necessary since the CTV was not short term but of moderate length (116 days), the study was performed on a sensitive species and the effect (fibrosis) is not a typical acute ecological endpoint such as mortality. This calculation resulted in a PNEC of 1530 µg SiO_2/m^3 applied to both quartz and cristobalite. The resulting Risk Quotients (RQ) shown in Table 8 range from 0.001 to 0.069. It should be noted that even if a larger assessment factor of 100 was applied, none of the resulting RQs would be above 1. Consistent with these findings, Dungworth (1982) observed that pneumoconioses caused by inorganic dusts are uncommon in animals because they are not occupationally exposed to these dusts. These results suggest that exposure to respirable quartz and cristobalite released into the air from anthropogenic sources in Canada is unlikely to cause harm to terrestrial fauna.

Table 8. Risk quotients (RQs) calculated for the anthropogenic sources of quartz and cristobalite to the air considered in this assessment; see text for explanations [a]

Source/facility	Location	PEC (µg SiO_2/m^3)	PNEC (µg SiO_2/m^3)	RQs
Quartz				
Agricultural areas	Alberta	27.2	1530	0.018
Urban areas	Many cities around Canada	8.77		0.006

Downwind from a coal fired power plant	Alberta	3.3		0.002
Emissions from an unpaved road	Alberta	11.6		0.008
Sand and gravel pit	Ontario	4.90		0.003
Granite quarry	British Columbia	5.84		0.006
Sandstone quarry	British Columbia	105		0.069
Cristobalite				
Industrial operation	Canada	2.14	1530	0.001

[a] Biogeochemical background concentrations were not considered in the derivation of PECs and PNECs.

Uncertainties in Evaluation of Ecological Risk

Large variability is expected in individual responses of animals to long-term inhalation of crystalline silica (Mauderly 1996). Rat strains used in toxicological studies with quartz and cristobalite are more genetically uniform than animals in nature, hence their intra-population responses are likely less variable than those of wildlife populations. Furthermore, important differences in physiology, detoxification mechanisms, and rates of clearance of particles in the lung will contribute to accentuate differences in chemical sensitivities among species (Mauderly 1996). The assessment factor of 10 that was applied to the CTV is intended to account (in part) for uncertainties associated with such inter-species and intra-species variations in sensitivity.

Severe silicosis may not be the most sensitive endpoint for ecotoxicity. For example, growth and reproduction are usually sensitive endpoints but these were not evaluated in the inhalation studies with laboratory animals reported in this assessment. The assessment factor of 10 applied to the CTV is also intended to account for this uncertainty.

Another important source of uncertainty is the paucity of measured concentrations of quartz or cristobalite in aerosols of anthropogenic origin in Canada, such as those from the exploitation of mineral deposits (e.g., bentonite, granite, sand and gravel aggregates, sandstone), construction activities and agricultural practices, and open sources such as unpaved roads. Quartz or cristobalite contents in these aerosols are often not known with certainty. Nevertheless, the worst-case scenarios developed for this assessment indicate that such releases likely will not cause ecological concerns in Canada.

Potential to Cause Harm to Human Health

Exposure Assessment

Environmental Media and Foods

The exposure assessment is focussed on respirable quartz and cristobalite, which in ambient air comprises a component of total particulate matter (PM). In Canada, data on

the concentrations of silicon in PM was available and used as a surrogate for quartz and cristobalite. This approach is conservative because the measured silicon includes all silicon-containing substances and therefore represents the upper limit for quartz and cristobalite in ambient air. A study in the United States (Davis et al. 1984) reported quartz represents between 2 and 70 % of the silicon substances in PM_{15}. Based on these data, silicon-containing substances are calculated to comprise approximately 5 % of PM and quartz and cristobalite may comprise from 0.1 to 3.5% of PM in Canada.

Ambient air concentrations of $PM_{2.5}$, PM_{10} and silicon are measured and reported as part of the National Air Pollution Surveillance (NAPS) program. There are several methods for collecting and analyzing PM. One distinction is continuous versus filter-based samplers. Continuous monitors allow for automated data collection and analysis, enabling PM data to be used in the calculation of the Air Quality Health Index (AQHI 2010), while filter-based samples allow for the speciation of the collected PM. A second distinction is $PM_{2.5}$ and PM_{10} versus $PM_{2.5}$(dichot) and PM_{10}(dichot); the suffix (dichot) indicates that a dichotomous sampler was used, which divides the PM into two fractions. PM_{10}(dichot) refers to the fraction of particles with aerodynamic diameters from 2.5 to 10 µm and $PM_{2.5}$(dichot) is the fraction less than 2.5 µm. Therefore, PM_{10}(dichot) must be added to $PM_{2.5}$(dichot) in order to obtain the total PM_{10}, which refers to the quantity of particles with aerodynamic diameters less than 10µm.

In 2009, over 2700 days of filter-based $PM_{2.5}$(dichot) samples and 1900 days of filter-based PM_{10}(dichot) samples were analyzed. From these samples, silicon concentrations were determined on over 1600 samples of $PM_{2.5}$(dichot) and over 1500 samples of PM_{10}(dichot) (NAPS 2010).

Table 9. Concentrations of PM and SiO_2 in Canada in 2009 from filter based PM_{10} measurements

	50^{th} Percentile (µg/m^3)		Maximum (µg/m^3)	
	Range	Average	Range	Average
Total PM_{10}	8.4 – 22.3 Yellowknife, Northwest Territories / Montreal, Québec	16.6	26.5 – 97.7 Yellowknife, Northwest Territories / Edmonton, Alberta	66.7
Total SiO_2 in PM_{10}	0.1 – 2.1 Pt. Petre, Ontario / Calgary, Alberta	0.7	0.7 – 8.8 Halifax, Nova Scotia / Edmonton, Alberta	3.7

An estimate of exposure to quartz and cristobalite can be obtained by assuming that all the silicon in the PM is represented stoichiometrically as SiO_2 and multiplying the reported concentration of silicon by 2.14 to obtain a value for silica as represented by silicon dioxide (see formula below).

$$SiO_2 \text{ concentration} = \text{Si concentration} \times \frac{60.08\ gSiO_2/mol}{28.09\ gSi/mol} = \text{Si concentration} \times 2.14$$

The SiO_2 concentration includes all forms of silica (crystalline and non-crystalline), as well as silicate minerals; therefore, it represents an upper bound for respirable quartz and cristobalite in ambient air. The range and average of 50th percentiles and the range and average of maximum concentrations of PM_{10} and SiO_2 measured in Canada in 2009 are presented in Table 9 (NAPS 2010). The 50th percentile data provides information on the central tendency and the maximum concentrations define the upper bound.

One study was found to estimate the quartz content and elemental composition, including silicon, of PM_{15} (particles with aerodynamic diameter less than 15 µm in several American urban areas sampled in 1980 (Davis et al., 1984). Using the data reported by Davis et al. (1984), the amount of quartz as a percentage of the total SiO_2 was determined to range from 2 to 70% with an average of 31%. The average (31%) reported by Davis et al. (1984) is consistent with the concentration of quartz in the upper continental crust reported by Reimann and de Caritat (1998), which ranges from 30.3 to 30.8%, suggesting that the quartz and cristobalite present in PM_{10} is derived from the Earth's crust.

Studies of respirable quartz and cristobalite in indoor air were not identified. One Canadian study was identified that reported filter-based PM_{10} concentrations in 48 personal and indoor samples collected in Windsor, Ontario, during 2005 (Niu et al. 2010). The personal exposure monitoring of PM_{10} resulted in a range of 8.0 to 48.3 µg/m^3, and the indoor levels of PM_{10} were reported to range from 2.2 to 40.7 µg/m^3 (Niu et al. 2010). The NAPS data for 2009 identified ambient air levels of PM_{10} in Windsor were in the range of 3.9 to 65.7 µg/m^3.

The intake of respirable quartz and cristobalite by the general population of Canada is estimated by means of a range that covered the lowest 50th percentile SiO_2 concentration ($PM_{2.5}$(dichot) plus PM_{10}(dichot)), measured in Pt. Petre, Ontario, (0.12 µg/m^3) to the highest maximum concentration measured in Edmonton, Alberta (8.77 µg/m^3), Appendix I. The outdoor data were used to represent the indoor levels, because information on indoor silicon concentrations was not available, and the range of PM_{10} measured indoors is generally lower than the outdoor range (Niu *et al.* 2010). Thus, this approach conservatively overestimates exposure within homes.

The highest exposure group based on these calculations is children ages 0.5 to 4 years with an estimated daily intake ranging from 0.07 to 5.26 µg/kg-body weight (bw) per day; the estimated daily intake decreases with age due to changes in the ratio of inhalation rates to body weights; the daily intake of adults, 20-59 years old, is estimated to range from 0.03 to 2.00 µg/kg-bw per day.

Concentrations of quartz and cristobalite in drinking water were not identified. Measurements of quartz concentrations are not commonly reported in the literature owing to the difficulty in separating the silica contributions of quartz from other sources and the

slow rate of quartz dissolution; for example a quartz particle 0.23 mm in radius would be reduced to 0.22 mm after 100 000 years (Schulz and White 1999).

Due to its widespread occurrence quartz is a component of most soils. One study describing the mineralogy of house dust (80 to 300µm particle size) in Canada was identified. In this study, 120 samples of house dust were collected from six Ontario communities (Barrie, Burlington, Cambridge, Hamilton, Sudbury and Thunder Bay) (Woldemichael et al. 2009). The mineral content of the samples was determined to be approximately 60% of the total mass of house dust; the remainder was comprosed of organic material (dander, insect fragments etc.). Quartz was the most abundant mineral observed, comprising approximately 30% of the total mineral content or 20% of the total mass of house dust.

Information on the levels of quartz and cristobalite in foods was not identified. Note that amorphous silica only, not quartz or cristobalite, is commonly used as an anti-caking agent in milled foods.

The exposure estimate from ambient air was based on measurements of silicon in over 1600 samples of $PM_{2.5}$(dichot) and over 1500 samples of PM_{10}(dichot) obtained from locations in 6 provinces (British Columbia, Alberta, Saskatchewan, Manitoba, Ontario, Québec and Newfoundland and Labrador) and 1 territory (Northwest Territories). Therefore, confidence is high that the general population exposure is well represented. Confidence is high that the estimate is conservative (i.e., it overestimated general population exposure) because (1) the upper end of the calculated range is based on the highest measured silicon concentration (converted to SiO_2) (2) the highest 50^{th} percentile (2.1µg/m^3) is more than half the average of the maximum values (3.7 µg/m^3) and (3) quartz and cristobalite comprise only a portion of the total SiO_2, which includes other silicate minerals as well as non-crystalline forms.

Consumer Products

Quartz is listed as an ingredient in 60 cosmetic products in Canada. The types of products include anti-wrinkle preparation, eye and face makeup, lipstick, hair dyes, shampoos, and grooming products, as well as skin cleansers, moisturizers and tanning preparations. These products are formulated as loose and pressed powders, aerosol foams, gels, creams, liquids, and lotions (CNS 2009). Exposure to respirable quartz from the use of these products was considered low because they are not formulated for spray application, the loose powders were reported to contain less than 0.1% quartz, and in these products the substance is not expected to be free but associated with other components of the formulation.

The general population of Canada may also be exposed to respirable quartz and cristobalite through the use of powdered household cleaning products containing quartz and cristobalite which function as abrasives. One product identified on the Household Products Database (HPD) was reported to contain up to 80% quartz (HPD 2010). This value was used to derive an upper-bounding exposure estimate of 0.02 µg/kg-bw per

event from the use of cleaning products using the ConsExpo model (ConsExpo 2006). Details are presented in Appendix II, with the caveat that this product may no longer be in the marketplace.

An assessment of the household use of cat litter was carried out by the California Environmental Protection Agency in response to an application for a safe use determination for products containing crystalline silica (SUD 1999). Usage data compiled by manufacturers of cat litter indicate the average amount of cat litter poured per replacement activity is 3.3kg. The 3-minute time-weighted average breathing zone concentrations of respirable particulate matter were measured and reported to range from 8.6 to 141 μg/m^3 per kg of cat litter associated with pouring 4.54 kg (10.0 lb) of conventional and "scoopable" cat litter. Exposure to quartz from the use of cat litters was estimated to be 0.033 μg/kg-bw per event, based on the maximum concentration of particulate matter reported and the average amount of litter poured per exchange; details are shown in Appendix II.

One experimental study was identified in which empirical data was obtained to quantify the amount of dust generated when amateurs sanded drywall compound with a block sander, pole sander, wet sponge sander, or ventilated sander (Young-Corbett and Nussbaum 2009). In this study, the highest mean concentration of particulate collected with a median cut-point of 10μm located in the breathing zone of the test subject was reported to be 6.31 mg/m^3, which was used to derive an exposure estimate from this activity (Young-Corbett and Nussbaum 2009). The experimental exposure duration was considered to fall within the range of 30 minutes to 3 hours, resulting in an upper-bound exposure estimate ranging from 2 to10 μg/kg-bw per event.

Quartz is an ingredient in a large number of paints and coatings. To estimate inhalation exposure to quartz from these products, the scenario of spray painting of wall paints with an airless spray gun was considered because it would generate respirable particles and the surface area and duration of painting are likely to be maximal. While acknowledging that the use of spray guns by consumers is not expected to be common, these tools are available to rent or purchase at do-it-yourself (DIY) stores, and there is some use by consumers. Exposure to respirable paint particles was estimated by means of measurements from controlled studies in which the entire walls of poorly ventilated test rooms were painted with interior flat latex paints by professional painters using an airless sprayer (NPC 2004). The maximum concentration of 13% quartz in paint in Canada (email from Risk Management Bureau, Health Canada to Existing Substances Risk Assessment Bureau, Health Canada, unreferenced) was used to estimate exposure. The exposure estimates also assumed that the consumer would use recommended personal protective equipment. The specific inputs and assumptions used in deriving the estimate are presented in Appendix II.

Based on the maximum concentration of respirable paint particles measured in these controlled studies, and the maximum concentration of quartz identified, the upper-bound estimate of exposure to quartz from spray painting of walls is 0.95 μg/kg-bw per event (see Appendix II).

Once paints have dried, the quartz is contained within the cured paint. Decorating and renovating activities such as sanding are known to generate respirable particles (Koponen et al. 2009). Based on the maximum breathing zone concentration of respirable dust generated by professionals sanding in controlled studies (NPC 2004), and the maximum reported concentration of quartz in paint, an upper-bound estimate of exposure to quartz contained within the cured paint from sanding of walls is estimated to be 0.9 μg/kg-bw per event during sanding (see Appendix II).

Mixing and loading powdered cement products, which have been reported to contain up to 65% quartz or cristobalite (HPD 2010), may result in exposure to respirable dusts by the general population. An upper-bound exposure estimate of 1×10^{-4} μg/kg-bw per event from the mixing and loading of cement products was derived using the ConsExpo model (ConsExpo 2006). Details are presented in Appendix II.

Confidence in the estimate of exposure from the use of powdered cleaning products is low because no information was available on the particle size distribution of the powders, nor was information available describing the concentration of PM_{10} generated during cleaning activities. Confidence is moderate that the estimate represents an upper bound because the maximum concentration in a product no longer on the market was used to estimate exposure; multiple products have been reformulated with the current formulation not containing either quartz or cristobalite (HPD 2010). Additionally, cleaning products seeking certification under the EcoLogo program in Canada cannot be formulated with any component considered by IARC to be a Group I, known carcinogen (EcoLogo 2008).

Confidence in the exposure estimate for pouring cat litter is moderate to high. The usage data were provided as average values and the respirable particulate matter levels were upper bounds normalized to the amount of product handled.

Confidence in the exposure estimate of drywall sanding is high because measurements of respirable PM in the breathing zone of amateurs were identified. Confidence is high that this estimate is conservative because a broad range of exposure durations were covered, the highest mean concentration was used in the exposure estimation, and the median particle size cut-off was 10 μm, which therefore included a wide particle size distribution, spanning respirable to nonrespirable fractions.

Confidence in the estimate of exposure to quartz and cristobalite from spray painting is high because the respirable air concentration fraction is based on empirical data. Confidence that the estimate of exposure is conservative is also high because the maximum reported concentration of quartz in paint was used. Additionally, the measurements and assumptions are considered as a worst-case scenario with respect to such factors as ventilation and use patterns. It is also emphasized that because homeowners typically use rollers to apply interior paints, on an occasional basis, chronic or subchronic airborne exposure to respirable quartz from applying wall paints from either spray or roller application method would be negligible for consumers. Painting with a roller does not produce large amounts of spray, and most of the droplets would be too large to be respirable; as a result no personal protective equipment is recommended.

Confidence in the estimate of exposure to quartz and cristobalite from sanding paint is high, because the respirable air concentrations are based on empirical data. Confidence that the estimate of exposure is conservative is also high because the maximum concentration of quartz reported in paint was used. Furthermore, the controlled wall sanding studies were designed to provide a worst-case estimate of potential exposures in that they involved professional painters sanding walls in a poorly ventilated room for a several hours. In addition to the inadequate ventilation, the maximum measured concentration of respirable dust was used to calculate these estimates, and it did not incorporate the use of personal protective equipment. Finally, most of the quartz in dried paint would be expected to remain bound within the paint matrix of the particles.

Health Effects Assessment

Basis for Categorization

The International Agency for Research on Cancer (IARC) has classified respirable quartz and cristobalite from occupational exposure as Group 1 carcinogens (*carcinogenic to humans*). This classification is based on sufficient evidence in humans and in experimental animals (IARC 1997). The U.S. National Toxicology Program classified crystalline silica of respirable size as known to be a human carcinogen. The basis for their classification is sufficient evidence from human studies indicating a causal relationship between exposure to respirable crystalline silica and increased lung cancer rates in workers (NTP 2004). No classification has been identified relating to the genotoxicity of quartz or cristobalite.

Epidemiological data-Cancer

There is an extensive dataset of human studies investigating the link between crystalline silica exposure and cancer. IARC (1997) identified over 50 epidemiological studies based on occupational exposure to dust containing respirable crystalline silica. Main industry sectors from which the human data are derived include gold mines, foundries, granite/stone industry, pottery workers and refractory brick workers. From the least confounded studies, it was noted that lung cancer tended to increase with the following parameters: cumulative exposure (Checkoway et al. 1993, 1996); duration of exposure (Costello and Graham, 1988; Merlo et al. 1991; Partanen et al. 1994; Costello et al. 1995; Dong et al. 1995); peak intensity of exposure (Burgess et al. 1997; Cherry et al. 1997; McDonald et al. 1997); presence of radiographically defined silicosis (Amandus et al. 1992; Dong et al. 1995); and length of follow-up time from date of silicosis diagnostic (Partanen et al. 1994). See Appendix III .

By definition, clinically or pathologically diagnosed silicosis implies prior exposure to silica (Silicotics). It does not follow that a history of exposure to silica necessarily results in silicosis (Nonsilicotics). It may be that the presence of silicosis is simply an indication of an exposure to silica sufficiently high to potentially induce lung cancer (Rees and Murray 2009) The typical “Silicotic” lung nodule is shown in Figure 1.

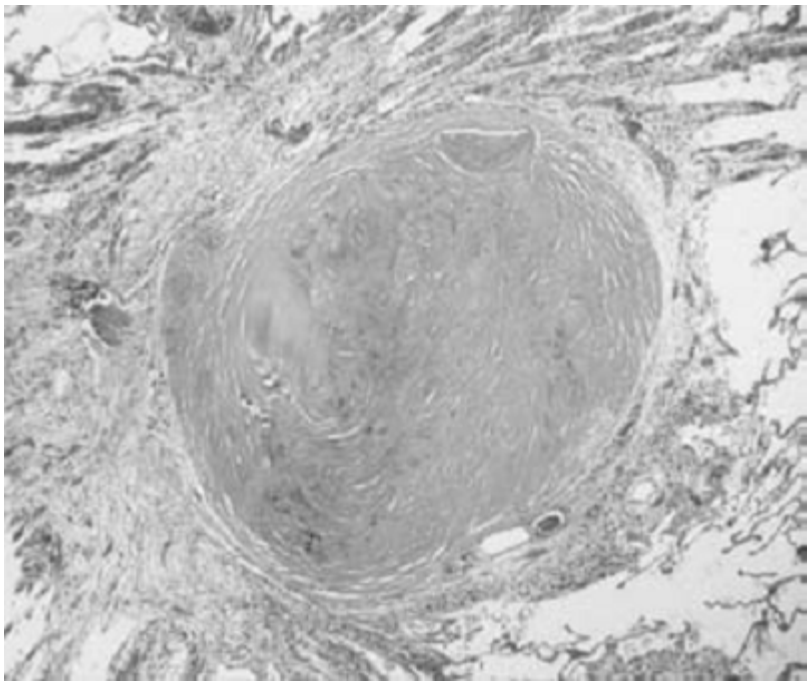


Figure 1. Silicotic nodule characterised by a central zone of hyalinised collagen with a whorled appearance and peripheral dust-containing macrophages (Rees and Murray 2007)

Since the IARC (1997) report, a large number of epidemiological studies have been published. Those more recent studies are generally updates from supplementary follow-up, results from nested case-control studies of previously assessed cohorts, or new results based on refined exposure assessments or adjustment for confounders. Refer to Appendix III for a list of studies and descriptions of key post-IARC studies.

Considering the important published body of epidemiological studies available, meta-analyses of these data have been subsequently conducted. Below is a description of the most relevant meta-analyses.

Steenland et al. (2001) pooled the data from 10 cohort studies containing quantitative exposure estimates for crystalline silica in order to analyze the risk related to lung cancer. Further follow-up was conducted for five studies and new quantitative exposure estimates were developed or modified for seven studies. Studies in coal mines and foundries were excluded. The pooled cohort standardized mortality ratio (SMR, against national rates) was 1.2 (CI 1.1-1.3). Through a case-control analysis, odds ratios (ORs) by quintile of cumulative exposure were 1.0, 1.0 (CI, 0.85–1.3), 1.3 (CI, 1.1–1.7), 1.5 (CI, 1.2–1.9), 1.6 (CI, 1.3–2.1). ORs by quintile of average concentration were 1.0, 1.4 (CI, 1.1–1.7), 1.6 (CI, 1.3–2.0), 1.6 (CI, 1.2–2.0), 1.7 (CI, 1.2–2.3). The results from the case-control analysis show a statistically significant trend with duration of exposure and thus provide support to the importance of the lung burden of the occurrence of cancer. In addition, the observation that the ORs are not statistically significant in the lower quintiles also provides evidence against a non-threshold mechanism. Overall, the authors concluded that the results support carcinogenicity conclusion presented by IARC (1997).

To investigate the link between crystalline silica, silicosis and lung cancer, Kurihara et al. (2004) gathered epidemiological data published between 1966 and 2001. Quality of study, adjustment for confounding factors, co-exposure to other carcinogens and availability of a more recent analysis of a same cohort were taken into consideration in the final selection of the studies. Over 50 studies were selected and pooled according to type of study and the parameter being linked to lung cancer (i.e. silica exposure, presence of silicosis in subjects). Analysis of the relationship between exposure to silica and lung cancer included 17 cohort and 13 case-control studies. For the analysis of lung cancer versus silicosis, 11 cohort and 5 case-control studies were selected. Results presented here will focus on the analysis of the 17 cohort and 13 case-control studies. The third analysis included six cohort and two case-control studies to evaluate the risk of lung cancer in non-silicotics. A random effect model was used to conduct each meta-analysis. Pooled risk ratios (RRs) were 1.32 (CI, 1.23–1.41) for crystalline silica exposure, 2.37 (CI, 1.98–2.84) for individuals determined to have silicosis (Figure 1, silicotics) and 0.96 (CI, 0.81–1.15) for individuals with no evidence of silicosis (non-silicotics) with exposure to silica. These results highlight the fact that silicosis has a stronger temporal relationship with crystalline silica exposure and support the hypothesis that this could be a preliminary stage in the development of cancer.

The meta-analysis from Pelucchi et al. (2006) included 28 cohort, 15 case-control and two proportionate mortality ratio studies from a variety of occupational settings conducted between 1996 and 2005. Risk ratios (RRs) were calculated based on type of study and silicosis status by means of fixed and random effect models (results presented here are from the random model). The RRs for all cohort studies was 1.34 (CI, 1.25–1.45), and were 1.69 (CI, 1.32–2.16) for silicotics (Figure 1), 1.25 (CI, 1.18–1.33) for those with undefined silicosis status and 1.19 (CI 0.87–1.57) for non-silicotics. The RR for non-silicotics was based on only one study. In the case-control studies, the general RR was 1.41 (CI, 1.18–1.67), and the same sub-groups as mentioned above resulted in RRs of 3.27 (CI, 1.32–8.2), 1.41 (CI, 1.18–1.70) and 0.97 (CI, 0.68–1.38). The silicotic and non-silicotic sub-groups contained only one study each. The proportionate mortality ratio (PMR) for the last two studies was 1.24 (CI, 1.05–1.47). Pelucchi et al. (2006) noted that the association between lung cancer and exposure to crystalline silica was more consistent for silicotics, i.e., those diagnosed with silicosis (Figure 1) and RR values split into type of occupational settings in which participants worked.

A number of occupational epidemiological studies have also identified tumours outside of the lungs in persons with high silica exposure. However, these results are sparse and often inconsistent and have not been unequivocally linked to exposure to either quartz or cristobalite. Some of the reported locations are: oesophagus (Yu et al. 2005; Wernli et al., 2006; Pan et al. 1999), stomach (Finkelstein et al. 1987; Koskela et al. 1987; Cocco et al. 1996; Parent et al. 1998), liver (Kauppinen et al. 1992; Une et al. 1995), skin (Partanen et al. 1994; Rafnsson and Gunnarsdottir 1997) and bone (Steenland and Beaumont 1986; Forastiere et al. 1989). However, sufficient epidemiological or toxicological data do not currently exist for quantitative assessment of the exposure-response relationship for these health effects (IPCS, 2000).

Animal Data – Cancer

The positive results from human data are supported by experimental studies conducted in rats where clear and consistent increases in lung tumours have been noted after chronic inhalation exposure. Study details are presented on appendix III. In the nine rat studies identified, five were inhalation studies (Dagle et al. 1986; Muhle et al. 1989; Spiethoff et al. 1992; Holland et al. 1996) and four were intratracheal instillation studies (Holland et al. 1983; Groth et al. 1986; Saffiotti 1990, 1992). All studies except one inhalation study showed increased incidence of lung tumours. For the inhalation studies, with treatment related tumours concentrations ranged from 1 to 50 mg/m^3 and duration of exposure ranged from 29 days to 2 years. In the inhalation study with no treatment-related tumours, exposure was 60 mg/m^3 for 13 weeks. For the intratracheal instillation studies, doses ranged from 4 to 57 mg/kg-bw. Exposure regimes were diverse and included single instillation with observation for up to 2 years, to weekly instillation for 10 weeks. It is noteworthy that the single intratracheal administration of 95% pure quartz particles (<5 μm) resulted in an increased incidence of silicotic granulomas after 3 weeks and lung tumours after 11 months. The most common tumours reported across the long term rat studies were adenocarcinomas[3], however other tumors such as squamous-cell carcinoma[4], alveolar carcinoma and bronchiole-alveolar adenoma were also reported, and all animals that developed tumours also showed some degree of fibrosis.

Of particular interest is the study conducted by Saffiotti et al. (1992) in which rats received a single intratracheal instillation of various crystalline silica dusts or ferric oxide, allowing direct administration into the bronchial tree. The doses were 12 or 20 mg of Min-U-Sil 5 quartz (MQZ), 12 mg of hydrofluoric-acid-etched Min-U-Sil 5 quartz (HFMQZ), 12 mg of cristobalite, 12 mg of tridymite, and 12 mg of ferric oxide suspended in saline. All groups were observed until 6 months post exposure, except for both MQZ groups, the HFMQZ group, and the ferric oxide group which were observed up until 17 months post-exposure. Interim sacrifices were conducted at 6, 11, and 17 months. The rat lungs showed a clear progression of effects. The sequence of pathological events were, an initial inflammatory response leading to a marked hyperplasia and hypertrophy of alveolar cells after one month, and at six months hyperplasia was evident but no lung tumours were observed. In this study, lung tumours were observed starting at the 11 month sacrifice with a 17% and 42% incidence in males and females, respectively, and at 17 months incidences were 32% and 59%. No lung tumours were found in ferric oxide treated rats. Similar studies have also been conducted in hamsters and mice. Although treated mice and hamsters showed treatment related signs (inflammation or fibrosis), no tumours were observed in hamsters. No increase in the incidence of lung tumours was seen in mice treated with quartz, however silicotic granulomas and lymphoid cuffing around airways but no fibrosis were seen in the lungs of quartz-treated mice (IARC 1997).

[3] Adenocarcinomas are of epithelial origin

[4] Squamous cells are found in the tissue that forms the surface of the skin, the lining of hollow organs of the body, and the passages of the respiratory and digestive tracts.

Genotoxicity

Potential genotoxicity has been assessed in multiple *in vitro* and *in vivo* assays. A brief summary of the positive results observed in each type of assay is presented in Table 10. Refer to Appendix IV for information on the species, cell types and other summarized information.

Table 10. Summary of positive results over total number of results for each assay and each category

Assay	Animal data		Human data		Positives/Total	
	In vitro	In vivo	In vitro	In vivo[d]	In vitro	In vivo
Rec Assay	0/1				0/1	
DNA strand break	1/1	2/2	5/5[b]	1/1	6/6	3/3
Sister chromatid exchange	0/1		0/1[c]	1/1	0/2	1/1
Micronucleus	2/3	0/1	2/2[b]	1/1	4/5	1/2
Chromosome aberration	0/1			1/1	0/1	1/1
Aneuploidy/polyploidy	0/3				0/3	
Cell transformation	4/4				4/4	
Hprt mutation	1/2	2/2[a]	1/1[b]		2/3	2/2
Oxidative DNA damage		4/5	2/2		2/2	4/5
DNA binding		1/1				1/1
p53 activation		0/1				0/1

a. one assay conducted with crystalline silica: cristobalite
b. one assay conducted with "ultrafine crystalline silicon dioxide"
c. crystalline silica: tridymite
d. crystalline silica dust (subtypes not provided)

All of the *in vivo* human genotoxicity studies are based on three independent studies that used blood samples from workers from diverse occupational settings with confirmed exposures to crystalline silica dust; however, quantification of exposure was not provided. No direct adjustment for smoking was done in any of the studies. After stratification by smoking status, sister chromatid exchange remained statistically significant in both smokers and non-smokers although the frequency was higher in smokers (Sobti and Bhardwaj, 1991). For the chromosome aberration assay conducted as part of the same study, the increased frequency was no longer significant after stratification. In the DNA damage study by Basaran et al. (2003), the authors concluded that smoking contributed to the increased DNA damage observed since results were

greater in smokers versus non-smokers. For the micronucleus assay, the frequency of micronuclei in nasal epithelial cells was higher in smokers ($p = 0.002$) but did not differ statistically when using peripheral blood lymphocytes (Demircigil et al. 2010).

The role of *in situ* generation of reactive oxygen species (ROS) and reactive nitrogen species (RNS) has been well established in the following types of DNA damage: small scale insertions, DNA base pair deletion, base modification, chromosomal change/loss, microsatellite instability, DNA strand break, 8-hydroxydeoxyguanosine (8-OHdG) mutation and point mutations (Azad et al. 2008). ROS and RNS generation is postulated to be a part of the DNA damage mechanism by crystalline silica. Studies below are given to support this hypothesis.

Saffiotti et al. (1992) exposed DNA *in vitro* to various crystalline silica dusts, to hydrogen peroxide (H_2O_2), or to both. Results show that DNA damage was limited when dust or H_2O_2 were administered alone but increased with the co-exposure. When the reactive oxygen scavenger, dimethylsulfoxide, was added to the test system, DNA strand break was inhibited, data supporting the viewpoint that it is the presence of radicals generated in response to quartz and cristobalite that causes the DNA damage and not quartz or cristobalite themselves.

Further supporting the potential implication of a secondary mechanism (i.e., inflammation) in the DNA damage observed in studies of silica exposure, it should be noted that increases in micronucleus and DNA strand breaks have been observed by Liu et al. (1996) and Zhong et al. (1997) after *in vitro* exposure to amorphous silica. However, exposure to amorphous silica does not result in lung tumours and, thus, amorphous silica is not considered to be a carcinogenic form of silica.

In the studies conducted by Driscoll et al. (1995, 1997), *hprt* mutation assays both *in vitro* and *in vivo* were positive in response to quartz. The positive results *in vivo* were seen only in the presence of significant inflammatory responses in the treated animals (Driscoll et al. 1997). Also, in a parallel *in vitro* experiment, Driscoll et al. (1997) incubated rat alveolar epithelial cells with the bronchoalveolar lavage fluid from the rats exposed to quartz. Both macrophage and neutrophil enriched lavage cells induced mutation in the exposed alveolar epithelial cells. Addition of catalase (an enzyme which inactivates H_2O_2) before incubation inhibited the increase in *hprt* mutation.

Johnston et al. (2000) exposed rats to either crystalline or amorphous silica in a manner to induce the same level of inflammation in the lungs. The inflammatory response was assessed by measuring the proportion of neutrophils in the bronchiolar lavage fluid. The actual concentrations were 3 and 50 mg/m^3 for crystalline and amorphous silica, respectively. The rats were exposed for 13 weeks. *Hprt* mutation frequency was measured in the alveolar epithelial cells at the end of the exposure period. Mutation frequency was greatly increased only in the crystalline silica treated rats, no treatment related increase was found in the rats treated with the amorphous form.

In the 8-OHdG assay conducted by Seiler et al. (2001c) to monitor DNA damage by reactive oxygen species, female rats were exposed to 0, 0.3, 1.5, and 7.5 mg/animal of quartz via intratracheal instillation. Effects were observed 90 days post-exposure. A clear dose-response relationship was identified between quartz exposure and various inflammation markers (differential cell count, protein, lung surfactant lipids and tumour necrosis factor alpha). Inflammation was present starting at the lowest dose. However, 8-OHdG showed a statistically significant increase starting at 1.5mg only. Similarly, Schins (2002) noted that in their laboratory 8-OHdG and DNA strand breaks were observed at concentrations at or above 10 ug/m^3 in rat lung epithelial cells.

With the aim of investigating the role of ROS in lung carcinogenesis, Knaapen et al. (1999) incubated rat lung epithelial cells with polymorphonuclear (PMN) leukocytes (involved in the inflammatory process and responsible for the release of certain ROS) or H_2O_2. Statistically significant increases in 8-OHdG were observed in the presence of PMN or H_2O_2 in a dose-response manner.

In a series of experiments, Cassel et al (2008) demonstrated that that the chronic fibrosis seen in a murine model of silicosis *in vivo* is dependent on the presence of adaptor molecule ASC and Nalp3 inflammazome. These data support a potential mode of action whereby silica triggers cellular responses that, in turn, activate alveolar macrophages, and through that process result in an inflammatory response and silicosis (Brown et al. 2007). In mice deficient in Nalp3 inflammazome, the development of inflammation and collagen deposition was significantly reduced compared with normal mice 3 months after the initial intranasal instillation of silica (Cassel et al. 2008).

Non-neoplastic Effects

Chronic non-cancer effects have been identified in both experimental animals and also in individuals exposed to respirable crystalline silica in occupational settings. The most readily diagnosed and also the most prevalent effect identified from long term exposures in these occupational settings is silicosis, a diffused nodular pulmonary fibrosis.

In humans, the lowest observed adverse effect concentration (LOAEC) was identified in a U.S. cohort study from Steenland and Brown (1995a). The study was conducted on 3330 gold miners (all white males), who had an average of 9 years underground exposure during the period from 1940 to 1965. The cohort was followed up through 1990. Silicosis was identified through death certificates or chest X-rays. A job-exposure matrix together with work history was used to estimate individual exposure. The total silica content in the respirable dust in the mine was estimated at 13% and the median crystalline silica exposure was 0.05 mg/m^3. In this sub-population of miners, 170 cases of silicosis were identified. The best predictor for risk of silicosis was cumulative exposure, which varied from less than 1% for a 0.5 mg/m^3 per year exposure to 68–84% when exposed to more than 4 mg/m^3 per year (based on the average daily dust exposure during the workday each year and summed over time for each miner). The main limitations identified by the authors include the limited number of radiographic surveys, the potential bias from death certificates (relying on death certificates instead of relying on repeated x-rays, which

were lacking for each miner, may have underestimated the number of cases) and the fact that the conversion of dust counts to gravimetric measurements may not be accurate based on the estimation of 13% silica content in the respirable dust. Although a relatively large number of samples (n = 82) were collected in two different surveys, there was a broad range of silica content in these samples (1% to 48%, SD = 9). The percentage of respirable quartz may have differed in earlier years, but data were lacking for these years.

Two other human studies have identified similar LOAECs based on the critical endpoint of radiographic confirmed silicosis. A LOAEC of 0.053 mg/m^3 was identified in a cross sectional study of South African black gold miners (Churchyard et al. 2004) and a LOAEC of 0.064 mg/m^3 was derived in a mining community population-based random sample survey in Colorado (Kreiss and Zhen 1996). See Appendix V for study details.

In a rat inhalation study, the LOAEC identified was 0.74 mg/m^3 based on lipoproteinosis, multifocal inflammatory cell infiltrate, and alveolar hyperplasia (Muhle et al. 1989, 1991). Rats were exposed to 0 or 1 mg/m^3 of quartz (containing 74% of respirable quartz) for 6 hours/day, 5 days/week for 24 months.

Drew and Kutzman (1984) and Muhle et al. (1998) identified LOAECs of 2 and 3 mg/m^3, respectively, after exposing rats or hamsters to quartz via inhalation for at least 6 months. All the effects observed were related to inflammation and fibrosis of the lung tissue.

Data for shorter exposure durations were only available in experimental animals.

Johnston et al. (2000) exposed male rats (4 animals per dose) to 0 or 3 mg/m^3 of cristobalite via inhalation for 6 hours/day, 5 days/week during 13 weeks. Pulmonary inflammation and fibrosis were observed in the exposed group at the end of treatment. When mice were similarly exposed to 5 mg/m^3 of quartz for 6 hours/day, 5 days/week for 15 or 27 weeks, the authors observed increased spleen weight and formation of plaque in the spleen (Burns et al. 1980).

In a 4-week inhalation study, Henderson et al. (1995) exposed female rats to 0, 0.1, 1 or 10 mg/m^3 of quartz for 6 hours/day, 5 days/week. Bronchoalveolar lavage fluid was evaluated at 1, 8, and 24 weeks after exposure. Elevated levels of granulocytes and significant elevation of markers of cytotoxicity (lactate dehydrogenase [LDH] and β-glucuronidase [β-glu]) were observed at concentrations of 1 mg/m^3 and higher. The increased levels of LDH and β-glu were only significant at 24 weeks after exposure. A LOAEC of 1 mg/m^3 was identified at 24 weeks.

Warheit et al. (1995) exposed rats to 0, 10 or 100 mg/m^3 of cristobalite via inhalation for 6 hours/day for 3 days. Animals were observed 3 months after exposure. Elevated levels of granulocytes and elevated markers of cytotoxicity from the lung lavage fluid were noted in all exposed groups. Another study of similar duration (9 days) conducted in mice also identified a LOAEC of 10 mg/m^3. Effects observed included minimal interstitial thickening, accumulations of mononuclear cells and slight lymphoid tissue hypertrophy in the lungs (Davis et al. 1988).

The acute studies identified for quartz or cristobalite were all conducted using intratracheal instillation exposure. Two studies observed effects in the lungs after instillation of a 0.75 mg/kg-bw dose of quartz in rats (Clouter et al. 2001; Seiler et al. 2001a). Effects reported were increased fibrogenic structural changes (microscopic) in lung tissues and a change in surfactant phospholipid ratio in bronchoalveolar lavage fluid 90 days post-exposure in one study (Seiler et al. 2001a). Inflammatory response in the lungs was observed 3 and 14 days after exposure in the other study (Clouter et al. 2001).

Although silicosis has been identified as the main non-cancer effect of silica exposure, available epidemiologic data as well as animal data provide some evidence for several other effects associated with silica exposure. This data is presented below.

Autoimmune and chronic renal effects have been identified in workers exposed to crystalline silica and other substances concurrently. The most frequently reported autoimmune diseases in crystalline silica exposed workers are scleroderma, rheumatoid arthritis, polyarthritis, mixed connective tissue disease, systemic lupus erythematosus, autoimmune haemolytic anaemia, and dermatopolymyositis. Several epidemiologic studies conducted on silica-exposed workers reported a statistically significant increase in death or cases of autoimmune diseases compared to general population. Sluis-Cremer et al. (1985), and Steenland and Brown (1995b) reported deaths or cases from systemic sclerosis (a process in which soft organs or tissue hardens). Other case control studies by Sluis-Cremer et al. (1986) and Klockars et al. (1987) reported excess deaths or cases related to rheumatoid arthritis among miners exposed to crystalline silica. Although an association of silica exposure and autoimmune diseases have been documented, the exact cellular mechanism is not fully understood (Otsuki et al. 1998).

Significant increase in chronic renal disease and subclinical renal changes in workers exposed to crystalline silica (Ng et al. 1992a, 1993; Steenland et al. 1992; Steenland and Brown 1995b; Calvert et al. 1997) are also believed to be due to adverse effects on the immune system as a result of exposure to crystalline silica.

Occupational exposure to crystalline silica is also closely associated with chronic obstructive pulmonary disease (COPD), which includes chronic bronchitis, abnormalities in pulmonary function tests (which measures lung volume, airflow, expiratory volume in 1 second, blood gas exchange and other aspects of lung function) and emphysema. According to a review of available epidemiologic studies, the risk of COPD is greater among gold miners, particularly those who have a history of tobacco smoking (Oxman et al. 1993).

Cor pulmonale (i.e., enlargement of the right ventricle of the heart because of the structural or functional abnormalities of lungs that causes pulmonary hypertension) is another complication associated with silicosis and silica exposure (Murray et al. 1993).

No developmental or reproductive toxicity studies were identified. However, considering the substances are insoluble, have negligible vapour pressure, and are particulates, it is

unlikely that they would be bioavailable to cause generalised systemic effects or specific effects at the reproductive and developmental level.

No adequate studies via the oral or dermal route have been identified. Likewise, based on the physico-chemical properties of these substances and because dermal or oral effects were not observed in workers who were incidentally exposed through those routes, there are no reasons to believe that effects other than the ones identified would occur.

The confidence in the health effects database for quartz and cristobalite is considered to be high. A large human-based dataset was identified for carcinogenicity, genotoxicity, and chronic exposure. As well, data in experimental animals were identified for carcinogenicity, genotoxicity and chronic to acute exposure. However, the studies available are all essentially via the inhalation or intratracheal route.

Characterization of Risk to Human Health

Based principally on the assessment of the International Agency for Research on Cancer, a critical effect for characterization of risk to human health for respirable quartz and cristobalite is carcinogenicity. Quartz, cristobalite and crystalline silica have not been classified for genotoxicity by other governments or organizations. Numerous epidemiological studies have identified a positive correlation between workplace exposure to crystalline silica and increased risks of lung cancer. Furthermore, when studies were pooled into different meta-analyses, relative risks were consistently positive and within the same range. In contrast, unlike some other minerals, there is little evidence that low-level exposure to silica causes adverse health effects in man, but this does not mean that significant non-occupational exposures could not occur in specific geographic areas of the environment (Rees and Murray 2007). In Sweden, it has been reported that aggressive engineering controls, to reduce silica dust in the workplace, has eliminated silicosis in Sweden (Gerhardsson 2002), and by corollary indicating that existing exposures outside of Swedish workplace do not poses a risk for silicosis to the general population.

Experimental data from rat studies are similar to the effects reported in humans in industrial settings. On balance, the experimental data from rat studies demonstrating the sequence of events that result in carcinogenesis is consistent with the reported findings from the human industrial workplace epidemiology studies.

In 1995, Klein and Christopher, on behalf of the Office of Scientific Affairs within the California Department of Toxic Substances Control, reviewed the evidence on the carcinogenicity of crystalline silica and concluded that the weight of evidence for both rats and humans indicates that fibrotic and silicotic lesions in the lung result from inhalation exposure to crystalline silica and that lung cancer is secondary to those lesions in the lung (Klein and Christopher 1995). Although the mechanism of induction for the lung tumours has not been fully elucidated, there is sufficient supportive mode of action evidence from the data presented to demonstrate that a threshold approach to risk

assessment is appropriate based on an understanding of the key events in the pathogenesis of crystalline silica induced lung tumours.

The lines of evidence include the following:

- In experimental studies, all rats that developed tumours also showed fibrosis.
- Adenocarcinomas, the most common type of tumour identified in rats, are commonly associated with fibrosis and deeply scarred lung tissue.
- Experimental rat studies showed a clear progression of the effects from initially mild inflammation, followed by fibrosis over-time, leading eventually to lung tumours.
- Tumours are not present in all treated species dosed in the same way.
- The tumours, both in rats and humans, are concentrated in the lungs only, although other organs are indirectly exposed.
- In human studies, cancer risk is often more significant in workers exposed over a 20-year period or to higher cumulative exposure levels; however a consistent finding is that the onset of silicosis, requires a smaller lag period than that for the appearance of tumours.
- Similarly, cancer risk is often more significantly associated at higher quintiles of exposure compared to the lower quintiles.
- Lung cancer rates are higher in workers confirmed to have silicosis versus similarly exposed workers that do not have silicosis.
- The vast majority of the positive genotoxicity assay results can be explained by the generation of reactive oxygen species, as demonstrated experimentally, where ROS scavenging prevents the genotoxicity.
- In vivo, macrophage deficient mice (macrophages produce ROS in response to crystalline silica) do not develop silicosis nor do they develop tumors and the Nalp3 inflammazome, a key factor in the macrophage initiated inflammatory response, is required for the development of pulmonary fibrosis after inhalation of silica.
- Though inhalation exposure to crystalline silica in multiple occupational settings is clear, the increase in risk, based on the several recent meta-analyses of the multiple human epidemiological studies, remains low.

Therefore, a threshold approach is used to characterize risk to human health from the inhalation route of exposure.

Because SiO_2 makes up only approximately 5% of PM_{10} in Canada, the measured silicon concentrations (converted to SiO_2) are considered the most relevant data for the estimation of exposure to quartz and cristobalite by the general population of Canada. The PM_{10} silicon content in 24 urban Canadian centres provided the information needed to calculate an upper limit for the concentration of quartz and cristobalite in ambient air. Chronic exposure to SiO_2 which includes quartz and cristobalite via inhalation of ambient air is estimated based on the 50^{th} percentile (0.1 – 2.1 $\mu g/m^3$) SiO_2 range measured in PM_{10} in Canada in 2009; the upper end of this range (2.1$\mu g/m^3$) is quite close to the average of the maximum values reported at each site (3.7$\mu g/m^3$). Comparison of the above mentioned range of total SiO_2 exposure (i.e. not corrected for actual quartz or

cristobalite content) to the 50 µg/m^3 quartz concentration associated with silicosis in humans, gives a margin of exposure (MOE) ranging from 23 to 500. It should be noted that these MOEs are based on the conservative and protective assumption that all SiO_2 measured in air is present as quartz and cristobalite.

Supporting the view that the actual MOEs are larger than those determined in this assessment are the data showing that in the United States the quartz content ranged from 2 to 70% (median 31%) of the total SiO_2 measured (Davis 1984) in PM_{15}. If the assumption is made that quartz comprises a similar percentage of the SiO_2 fraction of PM_{10} in Canada, MOEs ranging from 30 to 25 000 are derived for the range of 2 to 70% quartz and 74 to 1600 for the median (31%) quartz content.

Considering that the MOEs are based on a human epidemiological workplace LOAC they are considered protective of an event preceding and associated with the development of tumours in the occupational exposure setting. This scenario represents a worst case for the general population, because exposures from ambient air are lower than the LOAC estimated for underground mine workers. Additional support of the view that the MOEs are protective of the general population is obtained by comparing with the current Canadian Provincial Human Occupational Exposure Limits for respirable silica which ranges from 25 (crystalline) to 2000 (amorphous) µg/m^3 and the Canada Labour Code with an Occupational Exposure Limit of 25 µg/m^3 for the respirable fraction in air (Carex Canada 2010). These occupational exposure limits are greater than the conservatively estimated non-occupational general population exposure to silica. Weighing these considerations the MOEs for the general population exposed to ambient air are considered adequate to address uncertainties in the health effects and exposure databases MOEs for consumer activities for infrequent (sanding drywall or paint, spray painting) or very short duration (use of hard surface cleaners or cat litter) consumer activities were not derived as these are infrequent and the critical health effects are associated with long-term, non-acute exposures.

Uncertainties in the Evaluation of Risk to Human Health

There exist a number of differences between rat and human lung, which may lead to different forms of pulmonary toxicity and lung cancer. They include cell types, tissue histology, airway geometry and ventilation, clearance rates, and damage or repair mechanisms (ILSI 2000; Levy 1996).

While there is sufficient evidence to support key events in a threshold mode of action approach for lung tumours, the molecular mechanism is still not fully elucidated. Also, despite the fact that the effects seen in rats parallel the effects observed in human studies, additional mechanistic studies could further clarify why lung tumours are not seen in all experimental animals.

The use of human studies in establishing critical effect levels does introduce some uncertainties due to the presence of confounding factors (such as coexposure and lifestyle effects) and some additional variability in exposure quantification, but prevents the

introduction of uncertainties if interspecies differences in sensitivities, respiratory tree architecture, and dose extrapolation had to be adjusted for.

At this time, within the epidemiology literature there is debate on whether human workplace exposure to silica which does not cause silicosis can be associated with lung cancer. In a meta-analysis designed to examine this question, Erren et al. (2009) reported that even after applying sophisticated statistical tools on apparently relevant epidemiological studies conducted to-date, they were not able to determine whether workplace exposure to silica which does not cause silicosis can be associated with lung cancer. Thus, the question of whether silica exposure, in the absence of silicotic response, results in lung tumours remains unanswered.

There is some uncertainty in the concentrations of quartz and cristobalite in ambient air because they were estimated based on the total silicon content of PM_{10}. As described in the Sources Section of the assessment, quartz and cristobalite are both naturally occurring. Quartz is found abundantly in many types of rock formations while cristobalite can be produced at extreme temperatures in the ashes of volcanic eruptions. Unlike quartz, the natural occurrence of cristobalite is limited to specific geographic regions and mineral types, such as the bentonites of Princeton, British Columbia. It is therefore anticipated that cristobalite levels in Canadian ambient air are very small.

Confidence is very high that the upper end of the range based on the highest concentration of silicon measured in Canada in 2009 is conservative (i.e. overestimated). This is because in a comprehensive analysis of PM_{10} samples, quartz and cristobalite only account for a portion of the total SiO_2 present in samples collected. The exposure estimate from ambient air was based on measurements of silicon in over 1600 samples of $PM_{2.5}$(dichot) and over 1500 samples of PM_{10}(dichot) obtained from locations in 6 provinces (British Columbia, Alberta, Saskatchewan, Manitoba, Ontario, Québec and Newfoundland and Labrador) and 1 territory (Northwest Territories). Therefore, confidence is high that the general population exposure is well represented. Confidence is high that the estimate is conservative (i.e. it overestimated general population exposure) because (1) the upper end of the calculated range is based on the highest measured silicon concentration (converted to SiO_2) (2) the highest 50^{th} percentile (2.1µg/m^3) is more than half the average of the maximum values (3.7 µg/m^3) and (3) quartz and cristobalite comprise only a portion of the total SiO_2, which includes other silicate minerals as well as non-crystalline forms.

Conclusion

Based on the information presented in this final screening assessment, it is concluded that quartz and cristobalite do not meet the criteria in paragraphs 64*(a)* and *(b)* of CEPA 1999, as they are not entering the environment in a quantity or concentration or under

conditions that have or may have an immediate or long-term harmful effect on the environment or its biological diversity or that constitute or may constitute a danger to the environment on which life depends. Additionally, quartz and cristobalite meet the criteria for persistence, but do not meet the criteria for bioaccumulation potential, as set out in the *Persistence and Bioaccumulation Regulations* (Canada 2000).

On the basis of the adequacy of the margins between estimated exposures to quartz and cristobalite and critical effect levels in humans, it is concluded that quartz and cristobalite do not meet the criteria in paragraph 64*(c)* of CEPA 1999, as they are not entering the environment in a quantity or concentrations or under conditions that, for the general population in Canada, constitute or may constitute a danger to human life or health.

It is therefore concluded that quartz and cristobalite do not meet any of the criteria under section 64 of CEPA 1999.

These substances will be considered for inclusion in the Domestic Substances List inventory update initiative. In addition and where relevant, research and monitoring will support verification of assumptions used during the screening assessment.

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Appendix I: Upper-bounding estimates of daily intake of quartz and cristobalite by the general population in Canada

Route of exposure	Estimated intake (µg/kg-bw per day) of respirable quartz and cristobalite by various age groups					
	0–6 months[a]	0.5–4 years[c]	5–11 years[c]	12–19 years[d]	20–59 years[e]	60+ years[f]
Air[g]	0.03 – 2.46	0.07 – 5.26	0.06 – 4.10	0.03 – 2.33	0.03 – 2.00	0.02 – 1.74
Total intake	0.03 – 2.46	0.07 – 5.26	0.06 – 4.10	0.03 – 2.33	0.03 – 2.00	0.02 – 1.74

[a] Assumed to weigh 7.5 kg, to breathe 2.1 m^3 of air per day, to drink 0.8 L of water per day (formula fed) or 0.3 L/day (not formula fed) and to ingest 30 mg of soil per day (Health Canada 1998).

[b] Assumed to weigh 15.5 kg, to breathe 9.3 m^3 of air per day (Health Canada 1998).

[c] Assumed to weigh 31.0 kg, to breathe 14.5 m^3 of air per day (Health Canada 1998).

[d] Assumed to weigh 59.4 kg, to breathe 15.8 m^3 of air per day (Health Canada 1998).

[e] Assumed to weigh 70.9 kg, to breathe 16.2 m^3 of air per day (Health Canada 1998).

[f] Assumed to weigh 72.0 kg, to breathe 14.3 m^3 of air per day (Health Canada 1998).

[g] The estimated intake of quartz and cristobalite from air is based on a concentration range of 0.12 to 8.77µg SiO_2/m^3, which represents the lowest 50^{th} percentile to the maximum concentration of silicon measured in silicon in over 1600 samples of PM2.5(dichot) and over 1500 samples of PM10(dichot) covering sampling locations in 6 provinces (British Columbia, Alberta, Saskatchewan, Manitoba, Ontario, Québec and Newfoundland and Labrador) and 1 territory (Northwest Territories). Outdoor air measurements are used to represent the indoor environment.

Appendix II: Estimated upper bounding intake from the use of consumer products.

Product scenario	Assumptions	Estimated exposure
Powdered cleaning product	Concentration: 80% (HPD 2010)[a] **General assumptions** - Exposure frequency: 2/week (RIVM 2006) - Body weight: 70.9 kg (Health Canada 1998) **Inhalation route** - ConsExpo Model: exposure to spray (RIVM 2006) - Inhalation rate: 0.675m^3/hour (Health Canada 1998) - Spray duration: 1minute (RIVM 2006) - Exposure duration: 60minutes (RIVM 2006) - Room volume: 15m^3 (RIVM 2006) - Room height: 2.5m (RIVM 2006) - Ventilation rate: 2.5 /hour (RIVM 2006) - Mass generation rate: 0.62g/s (RIVM 2006) -Density non-volatile 3g/cm^3 (RIVM 2006) -Weight fraction non volatile: 1 (RIVM 2006) - Airborne fraction: 0.2 (RIVM 2006) - Particle size distribution: 75µm (coefficient of variance 0.6) (RIVM 2006), maximal diameter: 300 µm - Inhalation cut-off diameter: 10 µm - Uptake fraction: 1	**Event concentration** =1.4 µg/m^3 **Inhalation** Acute dose = 0.02 µg/kg-bw per event
Pouring cat litter	Concentration: 15% (HPD 2010) **Assumptions** -Average annual usage: 148 kg (SUD 1999) -Average time between changes: 8.2 days (SUD 1999) -Average amount per change: 3.3 kg (SUD 1999) -Exposure duration: 0.05 hours (180 seconds) (SUD 1999) -Respiration rate: 0.675 m^3/hour (Health Canada 1998) - Body weight: 70.9 kg (Health Canada 1998) -Upper-bound respirable dust: 141 µg/m^3-kg litter (SUD 1999) Exposure = (respiration rate × exposure duration × respirable dust concentration × amount per change × quartz concentration) ÷ body weight Exposure = (0.675 m^3/hour × 0.05 hour × 141µg/m^3-kg × 3.3 kg × 15%) ÷ 70.9 kg = 0.033 µg/kg-bw per event	**Event concentration** =7.0 µg/m^3 **Inhalation** Acute dose = 0.033 µg/kg-bw per event

Product scenario	**Assumptions**	**Estimated exposure**
Drywall sanding	Concentration: 5% (MSDS 2010) **General assumptions** - Exposure frequency[b]: 1/year (RIVM 2006) - Body weight: 70.9 kg (Health Canada 1998) **Inhalation Route** - Inhalation Rate: 0.675m^3/hour (Health Canada 1998) - Breathing zone concentration: 6.31mg/m^3 (Young-Corbett and Nussbaum 2009)[c] - Exposure duration: 0.5-3 hours (expert judgement) Acute exposure = inhalation rate × breathing zone concentration × quartz concentration × exposure duration ÷ body weight Acute exposure = 0.675m^3/hour × 6.31mg/m^3 × 5% × 3 hours) ÷ 70.9kg = 10 µg/kg-bw per event	**Event concentration** =316 µg/m^3 **Inhalation** Acute dose = 2-10 µg/kg-bw per event

Product scenario	**Assumptions**	**Estimated exposure**
Painting walls using an airless sprayer	Maximum concentration: 13% (email from Risk Management Bureau to Existing Substances Risk Assessment Bureau, unreferenced) **General assumptions** - Exposure frequency: 1/year (RIVM 2006) - Body weight: 70.9 kg (Health Canada 1998) **Inhalation Route** - Inhalation rate: 0.675m^3/hour (Health Canada 1998) - Breathing zone concentration: 5.14 mg/m^3 (NPC 2004)[e] - Exposure duration: 3 hours[d,f] (NPC 2004) - Recommended respirator is used, removes 95% of respirable paint aerosol (3M Occupational Health and Safety Division 2010). The use of suitable respiratory protection is recommended both in the manuals for airless sprayers and at DIY shops that sell and rent these sprayers, as well as for any spray application of paint. The assumed respiratory protection is for a recommended respirator. Such units are modestly priced and readily available at DIY stores. Other types of readily available protection, such as N95 masks, afford a similar degree of protection to that assumed in the assessment. Acute Exposure = Inhalation rate × breathing zone concentration × quartz concentration x respiraable fraction (PPI) × exposure duration ÷ body weight Acute exposure $= \frac{0.675 m^3/hour \times 5.14 mg/m^3 \times 13\% \times 5\% \times 3 hour}{70.9 kg}$	**Event concentration, adjusted for use of respirator** =33 µg/m^3 **Inhalation** Acute dose = 0.954 µg/kg-bw per event

Product scenario	Assumptions	Estimated exposure
Sanding paint	Maximum concentration: 26% (quartz); 10% (cristobalite) **General assumptions** - Exposure frequency: 1/year (RIVM 2006) - Body weight: 70.9 kg (Health Canada 1998) **Inhalation Route** - Inhalation rate: 0.675m^3/hour (Health Canada 1998) - Breathing zone concentration: 0.15 mg/m^3 (NPC 2004)[g] - Exposure duration: 2.4 hours (NPC 2004) Acute Exposure = Inhalation rate × breathing zone concentration × quartz concentration × exposure duration ÷ body weight Acute exposure = (0.675m^3/hour × 0.15mg/m^3 × 26% × 2.4hour) ÷ 70.9kg	**Event concentration** =4 µg/m^3 **Inhalation** Acute dose = 0.9 µg/kg-bw per event
Loading cement	Concentration: 65% (HPD 2010) **General assumptions** - Exposure frequency: 1/year (RIVM 2007) - Body weight: 70.9 kg (Health Canada 1998) **Inhalation Route** - ConsExpo Model: exposure to spray (RIVM 2007) - Inhalation rate: 0.675m^3/hour (Health Canada 1998) - Spray duration: 1.33minutes (RIVM 2007) - Exposure duration: 1.33minutes (RIVM 2007) - Room volume: 1m^3 (RIVM 2007) - Room height: 1m (RIVM 2007) - Ventilation rate: 0.6 per hour (RIVM 2007) - Mass generation rate: 2.5µg/minute (RIVM 2007) -Density non-volatile 1.8g/cm^3 (RIVM 2007) -Weight fraction non volatile: 1 (RIVM 2007) Airborne fraction: 1 (RIVM 2007) Particle size distribution: Portland cement, 14µm (coefficient of variance 0.5) (RIVM 2007) - Inhalation cut off diameter: 10µm - Uptake fraction: 1	**Event concentration** =0.7 µg/m^3 **Inhalation** Acute dose = 1×10^{-4} µg/kg-bw per event

[a] Product is no longer on the marketplace
[b] It is assumed that drywall sanding will occur at the same frequency as painting.
[c] Median cut point 10µm: 6.31±3.20mg/m^3; median cut point 4µm: 4.65±2.32mg/m^3.
[d] The typical amount of time spent spray painting in 1 day was reported to be 3 hours.
[e] The maximum breathing zone concentration of total respirable aerosol was selected although this value did not correspond to the highest content of crystalline silica. The flow properties of paint with higher silica content seem to be such that respirable fractions are reduced. Also, it is

less likely that a paint with a high crystalline silica content would be applied by spraying since the silica can erode spray nozzles.

[f] Spray painting would not be the method of choice for homeowners/consumers to paint large areas due to the expense of the equipment and the potential for contaminating non-target surfaces.

[g] The maximum breathing zone concentration of total respirable dust from professional painters was selected to represent an upper bound for DIY projects by homeowners.

Appendix III Cancer studies

Endpoint	Lowest effect level/Results
Laboratory animals and *in vitro*	
Carcinogenicity	**Positive inhalation studies:** Male and female F344 rats (total of 72) were exposed 6 hours/day, 5 days/weeks for up to 24 months to 50 mg/m3 of Min-U-sil 5 quartz through whole body inhalation. At 4, 8, 12 and 16 months, groups of 5 rats/sex were removed to study the time course of lesion development. No lung tumours were observed in controls. The overall tumour incidence was 12 % (10 of 53 in females, 1 of 47 in males) and the tumours were of the epidermoid type. Survival time showed a dose-response relationship with length of time exposed (Dagle et al., 1986). Female F344 rats (total of 62) were exposed 6 hours/day, 4 days/week for 83 weeks to filtered air or 12 mg/m^3 of Min-U-sil 5 quartz through nose-only inhalation. The same number of controls was exposed to filtered air and an additional 15 rats were used as unmanipulated controls. Lung tumour incidence in exposed rats was 30%: 18 of 60 animals developed tumours including 3 epidermoid carcinomas and 11 adenocarcinomas (Holland et al., 1986). Groups of 50 rats/sex (strain not specified) were exposed 6 hr/day, 5 days/week for 24 months to filtered air or 1 mg/m^3 of DQ-12 quartz through whole-body inhalation. An additional 50 rats/sex were exposed to 5 mg/m^3 of titanium dioxide (TiO_2) as positive controls. In the exposed group, 18 animals developed tumours (12 females, 6 males), as opposed to 3 animals (males and females) and 2 animals (males and females) for the control and positive control groups respectively. The majority of the tumours observed were adenocarcinomas. The mean mass of particle at the end of the exposure period was 0.91 mg/lung (Muhle et al., 1989). Female Wistar rats (total of 540) were exposed 6 hr/day, 5 days/week for 29 days to 0, 6 or 30 mg/m^3 of DQ-12 quartz through nose-only inhalation. Half of the animals in each group were injected intravenously with a single dose of TiO_2. Results for the rats injected with TiO_2 are not presented here.

Endpoint	Lowest effect level/Results
	Rats were examined at various intervals and up to 24 months post exposure. Lung tumour incidence was 0% (0/85), 45% (37/82) and 52% (43/82) for the control, low-dose and high-dose groups respectively. Squamous-cell carcinoma was the most abundant tumour type, followed by bronchiole-alveolar carcinoma and bronchiole-alveolar adenoma (Spiethoff et al., 1992). **Other inhalation/intratracheal studies:** Wagner et al. 1980; Holland et al. 1983; Pratt et al. 1983; Renne et al. 1985; Groth et al. 1986; Wilson et al., 1986; Rosenbruch et al. 1990; Saffiotti 1990, 1992; Reuzel et al. 1991; .
Humans	
Carcinogenicity	<u>Checkoway et al. (1996)</u> A cohort mortality study was conducted on 2266 diatomite workers employed in the U.S. between 1942 and 1987 for whom quantitative exposure to asbestos could be evaluated. Lung cancer mortality rates were compared with those in the general male population. Cumulative crystalline silica exposure was estimated for each worker by means of a semi-quantitative matrix based on duration of exposure and intensity of exposure from different jobs. Overall lung cancer SMR was 1.41 (CI 1.05-1.85), unadjusted. SMRs based on crystalline silica index ranged from 1.00 to 1.79 after adjustment for asbestos exposure but did not reach statistical significance. This is a follow up study from one of the key positive studies identified in IARC (Checkoway et al., 1993). <u>Merlo et al. (1991)</u> Mortality of a cohort of Italian male refractory brick workers (1022 individuals) employed for more than 6 months between 1954 and 1977 was compared with that in the Italian male population. Workers were exposed to mean dust concentrations of between 200 and 500 µg/m^3 with silica content between 30 and 65%. Lung cancer SMR was 1.51 (CI, 1.00–2.18). Mortality was also stratified for length of employment and tenure. Workers employed before 1957 or with at least 19 years of employment and at least 19 years of latency showed the highest ratios, 1.77 (CI, 1.03–2.84) and 2.01 (CI, 1.07–3.44) respectively. Smoking habits were compared with those in the general population and did not show significant differences. Key IARC study. <u>Partanen et al. (1994)</u>

Endpoint	Lowest effect level/Results
	Lung cancer incidence was analysed in 811 male silicotic Finish patients diagnosed between 1936 and 1977. Cases came mostly from the foundries, mining and quarrying, the stone industry and the glass and ceramic industry. Incidence was calculated against rates from males of the general population based on age groups and time period. Lung cancer SIR was 2.89 (CI, 2.35–3.48). When broken down by histological type, squamous cell carcinoma showed the highest rate, 3.25 (CI, 2.25–4.54). Smoking data was collected on a subgroup of the cohort. After indirect analysis, author concluded that tobacco did not explain the lung cancer increment. Key IARC study. Costello et al. (1995) Cohort mortality study was conducted on 1022 workers from 20 U.S. stone operations employed for 1 or more years between 1940 and 1980. Cristalline silica (α-quartz) content in respirable dust was 37, 11, and 15% for granite, limestone and traprock operations. Mean of personal respirable exposure to cristalline silica was 0.06 mg/m^3 for granite and 0.04 mg/m^3 for limestone and traprock. Mineral fibers were present in several operations but only one contained asbestos. Overall SMRs for lung cancer were slightly elevated but not statistically significant (1.29; CI, 0.96–1.70). The only time SMR was statistically significant was for workers with latency over 20 years (1.48; CI, 1.02–2.09). When segragated by type of rock, SMR for granite workers with > 20 latency was 3.35 (CI, 1.34–6.90). All death occurred among those with at least 10 years tenure. Key IARC study. Dong et al. (1995) Standardized risk ratios (SSR) were calculated from a cohort mortality study of silica and clay brick workers from 11 refractory plants in China. The cohort included 6266 workers, observed from 1963–85 and the mortality ratios were compared with those in 11 470 male steel workers. The overall SSR for lung cancer 1.49 ($p < 0.01$). When broken down by silicosis status, SSRs were 2.10 (CI, 1.46–2.92) and 1.10 (CI, 0.75–1.58) for silicotics versus non-silicotics. When considering smoking status, SSRs for smokers were 2.34 (CI, 1.45–3.58) in silicotics and 1.20 (CI, 0.74–1.83) in non-silicotics; and 2.13 (CI, 1.10–3.72) and 0.85 (CI, 0.34–1.75) for silicotics versus non-silicotics non-smokers. Authors noted that lung cancer rates increased with latency and severity of

Endpoint	Lowest effect level/Results
	silicosis. Key IARC study. Steenland and Sanderson (2001) Lung cancer mortality was examined in industrial sand workers through a cohort of 4626 employed between the 1950s and 1988. The mortality follow-up began in 1960. Individual quantitative exposure for respirable silica was estimated through a job-exposure matrix by means of personal samples for respirable silica collected from 1974 through 1988. The matrix considered plant production levels (4), time periods (3) and job categories (10). Standard life-table analysis were calculated against US population rates (SMRs) or using the lowest quartile of the exposed as the referent (SRRs). Within this study, a nested case-control analysis was also conducted. Each case was matched to 100 controls for sex, race and date of birth. For this analysis, lifetime excess risk was calculated against age-specific male lung cancer mortality rates taken from surveillance data. Smoking data from a subset of the cohort suggested that 10-20% of the lung cancer excess might be related to smoking. Cohort SMR for lung cancer was 1.60 (CI, 1.31–1.93). When divided into quartiles of cumulative exposure, SMRs and SRRs did not show a statistically significant trend although some increase in values could be noted. In the nested case-control, trends were statistically significant for quartile of cumulative exposure (no lag) and average exposure, but only the OR for average exposure to >0.065 mg/m3 was significant (2.26; CI, 1.17–4.38). McDonald et al. (2005) In a follow-up study, a cohort of 2455 sand-producing plant workers from North America was studied to further investigate the risks of lung cancer related to the exposure to silica while allowing adjustment for smoking. The cohort was composed of 2455 workers employed for at least 3 years between 1940 and 1979. The exposure estimates were based on company records of respirable silica exposure and protective equipment (respirator) use. Mean exposure level was calculated for each job and each year. SMR for lung cancer was 147 (no confidence interval specified) when compared with U.S. population rates. A nested case-control analysis was also conducted from that cohort where 108 cases were matched on date of birth, and date of hire to two controls from the same plant who survived the case. ORs for lung cancer were statistically significant for average silica

Endpoint	Lowest effect level/Results
	concentration >260 µg/m3 (2.36; CI 1.00–5.59), but not for cumulative exposure or years employed. However, there were significant trends across exposure categories for cumulative and average concentration of silica. Adjustment for smoking was applied. Graham et al. (2004) The relationship between lung cancer and quartz exposure was assessed in a cohort mortality study of Vermont granite workers. The cohort consisted of 5408 men employed in the manufacturing plants or quarries at some time between 1950 and 1982. Follow-up was carried out until 1996. General SMR for all workers and time period was 1.18 (CI, 1.03–1.35). When data were segregated between types of workers a clearer relationship between silica exposure and lung cancer was observed in shed workers (1.31; CI, 1.13–1.51) while the SMR for quarry workers did not reach statistical significance. Workers with 30 and more years of tenure and 40 or more years of latency consistently showed the highest SMRs. As a means of evaluating quality effect, the cohort was also analyzed based on workers who were employed before 1940 when control measures where implemented versus only employed post-1940. However, SMRs fell within the same range between the two groups. No adjustment was made for smoking. Attfield and Costello (2004) Excess lung cancer was assessed in a cohort mortality study of the Vermont granite industry workers. Subjects included males employed in the industry between 1950 and 1982 who were X-rayed at least once in the surveillance program with an extended follow-up from 1982 to 1994. Cumulative exposure was calculated based on a job-time exposure matrix using exposure data collected between 1924 and 1977. Three significant time periods were considered (before 1940, 1940–1950 and after1950) to account for significant changes in exposure following dust control measures. Subjects were divided into 8 groups based on cumulative exposure (0, 0.25, 0.5, 1.0, 1.5, 2.0, 3.0, 6.0 mg-year/m^3). Results of the person–year analysis show an almost consistent rise with exposure levels with SMR for the 2.0 and 3.0 mg-year/m^3 (respectively 1.47 and 1.70) being statistically significant. The decreased SMR for the highest exposure group (SMR = 1.16) could not be explained. SRR calculations showed similar trends. No adjustment for smoking was made. However authors mention

Endpoint	Lowest effect level/Results
	that the use of quantitative exposure assessment and the presence of marked gradients of exposure make it unlikely that smoking would greatly confound results. No other major occupational confounding exposures were present. Lifetime excess risk was also estimated but will not be discussed here. Results (or treatment of data) do not necessarily agree with Graham and Costello, (2004) who used the same cohort. See letter to editor. Cherry et al. (1998) A cohort mortality study was conducted on 5115 male workers from the pottery, refractory, and sandstone industries in the region of Stoke-on-Trent, UK born between 1916 and 1945. Data were gathered from a registry of workers exposed to dust and subject to periodic medical surveillance employed between 1929 and 1992. Work history, smoking habit, chest radiograph readings and previous exposure to other hazardous dust were recorded. Men previously exposed to asbestos or employed in foundries, coal mines and other trades involving exposure to dust were excluded. Exposure calculation was based on respirable dust samples collected since the 1950s. SMR were calculated against national and Stoke-on-Trent rates and were respectively 1.91 (CI, 1.48–2.42) and 1.28 (CI, 0.99–1.62) for lung cancer. A nested case-control study was also conducted on 52 lung cancer cases matches to three to four referents for age and date of first exposure (total number of referents 195). For this study, individual cumulative and lifetime exposure to crystalline silica were calculated by means of an exposure matrix. Odds ratios (ORs) were calculated for cumulative exposure, duration and average concentration. Only average concentration was statistically significant with ORs for average concentration and are 1.67 (CI, 1.13–2.47), 1.66 (CI, 1.14–2.41) and 1.60 (CI, 1.11–2.31) for no lag, 10-year and 20-year lag respectively, after adjustment for smoking. Cassidy et al. (2007) The role of crystalline silica dust in lung cancer was assessed in a community based analysis. The study included 2852 lung cancer cases recruited between 1998 and 2002, and 3104 controls. An exposure matrix was constructed based on the probability, intensity and duration of silica exposure. The general OR for lung cancer was 1.37 (CI, 1.14–1.65). Statistically significant trends (p =< 0.0001) were observed for duration of exposure in years (ORs 1.25–1.73), duration of

Endpoint	Lowest effect level/Results
	exposure in hours (ORs 1.16–1.88) and cumulative exposure (ORs 1.07–2.08), and were based on a 20-year lag. ORs were adjusted for age, sex, region, smoking, education, insulation dust, and wood dust. Vida et al. (2010) A pooled analysis of two case-control studies was conducted in Montreal workers exposed to respirable crystalline silica. The first study included 857 lung cancer cases and 1410 controls controls recruited between 1979 and 1986. The second study was conducted between 1996 and 2001 and included 738 cases and 899 controls. General OR for lung cancer from crystalline silica exposure was 1.31 (CI, 1.08–1.59) and increased to 1.67 (CI, 1.21–2.31) for the "substantial exposure" category. No quantitative estimates of exposure were provided. ORs were adjusted for smoking and for other occupational exposure such as asbestos, benzo(a)pyrene, chromium IV, and diesel emissions but not for arsenic, nickel, and PAHs which were not considered to contribute meaningfully to the model. Other key IARC (1997) studies: Costello and Graham 1988 (see Graham et al. 2004 and Attfield and Costello 2004); Checkoway et al. 1993 (see Checkoway et al. 1996); Burgess et al. 1997 (see Cherry et al. 1998); Cherry et al. 1997 (see Cherry et al. 1998); McDonald et al. 1997 (see Cherry et al. 1998). Other post-IARC (1997) studies: deKlerk and Musk 1998; Filmore et al. 1999; Ulm et al. 1999; Chan et al. 2000; Carta et al. 2001; Cocco et al. 2001; McDonald et al. 2001; Chen and Chen 2002; Kjarheim et al. 2002; Tsuda et al. 2002; Watkins et al. 2002; Brown and Rushton 2003; Cogglia et al. 2003; Kauppinen et al. 2003; Menvielle et al. 2003; Ogawa et al. 2003; Westberg and Bellander 2003; Merlo et al. 2004; Pinkerton et al. 2004; Brown and Rushton 2005; McDonald et al. 2005; Chen et al. 2006; Marinaccio et al. 2006; Chen et al. 2007; Yu et al. 2007; Birk et al. 2009; Burgdahl et al. 2010; Vacek et al. 2010.

Appendix IV. Genotoxicity data

Endpoint	Lowest effect level/results
Laboratory animal data	

Endpoint	Lowest effect level/results
Genotoxicity *in vitro*	**Rec-assay** **Negative**: *Bacillus subtilis*, type of silica not specified (Kada et al. 1980; Kanematsu et al. 1980) **DNA strand breaks** **Positive**: using λHindIII-digested, herring sperm genomic or PM2 supercoiled DNA (Saffiotti et al. 1992; Daniel et al. 1993, 1995) **Sister chromatid exchange** **Negative**: Chinese hamster V79-4 cells (Price-Jones et al. 1980) **Micronucleus** **Negative**: Syrian hamster embryo cells (Oshimura et al. 1984) **Positive**: Syrian hamster embryo cells (Hesterberg et al. 1986) **Positve**: Chinese hamster lung fibroblasts V79 (Nagalakshmi et al. 1995) **Chromosomal aberrations** **Negative**: Chinese hamster lung fibroblasts V79 (Oshimura et al. 1984) **Aneuploidy** **Negative**: Chinese hamster lung cells V79-4 (Price-Jones et al. 1980) **Negative**: Syrian hamster embryo cells (Oshimura et al. 1984) **Polyploidy** **Negative**: Syrian hamster embryo cells (Hesterberg et al. 1986) **Cell transformation** **Positive**: BALB/3T3/31-1-1 mouse cells (Saffiotti and Ahmed 1995; Keshava et al. 1999) **Positive**: Syrian hamster embryo cells (Hesterberg and Barrett 1984) **Positive**: fœtal rat lung epithelial cells (Williams et al. 1996) **Mutation** **Negative**: hprt locus in rat RLE-6TN alveolar epithelial cells (Driscoll et al. 1995) **Positive**: hprt locus in rat RLE-6TN alveolar epithelial cells (Driscoll et al. 1997)

Endpoint	Lowest effect level/results
Genotoxicity *in vivo*	**Oxidative DNA damage** **Positive**: 8-hydroxy 2´deoxyguanosine DNA extract from rat lung (Yamano et al. 1995; Seiler et al. 2001c; Schins et al. 2002; Seiler et al. 2004) **Negative**: 8-hydroxy 2´deoxyguanosine DNA extract from Wistar rat peripheral blood leukocytes (Yamano et al. 1995) **Mutagenecity** **Positive**: hprt locus in rat alveolar epithelial cells (Driscoll et al. 1997; Johnston et al. 2000) **Negative**: p53 in mice lung tissue (Ishihara et al. 2002) **Micronucleus** **Negative**: in albino mice (Vanchugova et al. 1985) **DNA binding** **Positive**: calf thymus (Mao et al. 1994) **DNA strand break** **Positive**: using rat epithelial lung cells (Knaapen et al. 2002; Schins et al. 2002)
Human data	
Genotoxicity *in vitro*	**Micronucleus** **Positive**: human embryonic lung Hel 299 cells (Nagalakshmi et al. 1995) **Positive**: using human lymphoblast cells (Wang 2007) **Sister chromatid exchange** **Negative**: human lymphocytes (Pairon et al. 1990) **Oxidative DNA damage** **Positive**: 8-hydroxy 2'deoxyguanosine DNA extract from human lung epithelial cells (Schins et al. 2002) **Positive**: comet assay using human lung epithelial cells (Fanizza et al. 2007) **DNA strand break** **Positive**: comet assay using human lung epithelial cells (Schins et al. 2002; Fanizza et al. 2007) **Positive**: comet assay using human lung epithelial cells, presence of cytotoxicity (Cakmak et al. 2004) **Positive**: comet assay using human lymphoblast cells (Wang 2007) **Positive**: comet assay using rat alveolar macrophages, presence of cytotoxicity (Zhang et al. 2000)

Endpoint	Lowest effect level/results
	Mutagenecity **Positive**: hprt locus in human lymphoblast cells (Wang 2007)
Genotoxicity *in vivo*	**Sister chromatid exchange** **Positive**: Blood samples were collected from 50 workers in the stone crusher industry exposed to stone dust. The dust contained 50-60% silica. Individuals not exposed to such dust were used as controls. Smoking habits, alcohol consumptions and age were recorded. The frequency of sister chromatid exchange was statistically higher ($p < 0.001$) in the exposed workers (7.51). When separated by smoking status, the difference remained significant in smokers (7.80 in exposed versus 5.45 in controls) as well as in non-smokers (6.92 versus 4.92).(Sobti and Bhardwaj 1991) **Chromosomal aberration** **Positive**: See details of the study protocol above. The incidence of chromosomal aberrations in the exposed group was 2.72% and 1.28% in the control group ($p < 0.01$). When separated by smoking status, the difference was statistically significant in smokers (2.88 in exposed versus 1.27 in controls) but not in non-smokers (2.37 versus 1.28). (Sobti and Bhardwaj, 1991) **DNA damage** **Positive**: Exposure-control study of foundry and pottery workers. Each case was matched to one control of comparable age, smoking habit and socio-economic status. The controls consisted of healthy workers with no history of occupational silica or chemical exposure. DNA damage was assessed in peripheral blood lymphocytes using the Comet assay. The DNA damage was significantly higher in the exposed workers. Smoking also contributed to the DNA damage observed since when comparing smokers versus non-smokers exposed workers occurrence was higher in smokers. No direct correction for smoking was performed. Potential exposure to other carcinogens were not quantified but were noted (Basaran et al. 2003). **Micronucleus** **Positive**: The presence of micronucleus was evaluated in the peripheral blood lymphocytes and nasal epithelial cells of workers involved in grinding, missing, bagging and sandblasting jobs exposed to crystalline silica dust. 50 cases were matched for age, gender and smoking status to 29

Endpoint	Lowest effect level/results
	controls. The frequency of micronucleus was three-fold higher in the nasal epithelial cells of the exposed group and two-fold higher in peripheral blood lymphocytes as compared with controls. No direct correction for smoking was made. Potential exposure to other carcinogens not quantified. (Demircigil et al. 2010)

Appendix V Non-neopastic effects

Endpoint	Lowest effect level/Results
Laboratory animals and *in vitro*	
Acute toxicity	**Lowest intratracheal LOAEL** = 0.75 mg/kg-bw based on increased fibrogenic structural changes (microscopic) in lung tissues and change in surfactant phospholipid ratio in bronchoalveolar lavage fluid ($p<0.01$) in female Wistar rats (10 per dose) after single intratracheal instillation of 0, 0.15, 0.3, 0.6, 1.2 or 2.4 mg/rat (0, 0.75, 1.5, 3, 6, or 12 mg/kg-bw) of DQ12 quartz in saline. Fibrosis was observed 90 days after exposure (Seiler et al. 2001a). Other LOAEL = 0.25 mg/rat (0.75 mg/kg-bw) based on inflammatory response in lungs of male Sprague Dawley rats observed in 3 and 14 days after single intratracheal instillation of 0, 0.25, or 1 mg/rat DQ12 quartz in saline (Clouter et al. 2001) Other LOAEL = 3 mg/kg-bw based on increased pulmonary response (reflecting inflammation, toxicity and cell proliferation) in rats and hamsters after single intratracheal instillation of 3 or 12 mg/kg-bw of quartz. A significantly higher response was seen in rats than hamsters (Seiler et al. 2001b). Other LOAEL = 12 mg/rat (40 mg/kg-bw) based on silicotic nodules (granulomas) and fibrosis in F344/NCr male and female rats obseved at 21–30 days after single intratracheal instillation of 0 or 12 mg "Min-U-Sil" per rat in saline (Saffiotti et al. 1996).
Short-term repeated-dose toxicity	**Lowest inhalation LOAEC** = 1 mg/m^3 based on elevated levels of granulocytes (approximately 2.5%, mainly neutrophils) and significant elevation of markers of cytotoxicity (Lactate dehudrogenase [LDH] and β-glucuronidase [β-glu]) in bronchoalveolar lavage fluid in

Endpoint	Lowest effect level/Results
	female F344/N rats exposed to 0, 0.1, 1, or 10 mg/m^3 of quartz (Min-U-Sil); 6 hours/day, 5 days/week for 4 weeks. Bronchoalveolar lavage fluid was evaluated at 1, 8, and 24 weeks after exposure. Effects were significant ($P \leq 0.05$) at 24 weeks after exposure. Authors concluded that NOAEC = 0.1 mg/m^3 (Henderson et al. 1995). Other inhalation LOAEC =10 mg/m^3 based on elevated levels of granulocytes (approx 34%, mainly neutrophils) and elevated markers of cytotoxicity in lung lavage fluid in CD rats (24 per dose, sex not reported) exposed to 0, 10, or 100 mg/m^3 of cristobalite; 6 hours/day for 3 days. Effects were observed 3 months after exposure (Warheit et al. 1995). Other inhalation LOAEC = 10 mg/m^3 based on a minimal degree of interstitial thickening, accumulations of mononuclear cells and slight lymphoid tissue hypertrophy in C3HHeN mice exposed to 10 mg/m^3 of cristobalite for 8 days and 43 mg/m^3 for 9 days (Davis et al. 1998). Other inhalation LOAEC = 70 mg/m^3 based on adverse lung pathology in New Zealand Black, C3H/HeN, BALB/c and MRL/Mpj mice exposed to 0 or 70 mg/m^3 of cristobalite for 5 hours/day for 12 days. A substantial variation in response (both in type and intensity of reaction) was evident between strains. New Zealand Black mice were the most susceptible with extensive alveolar proteinaceous deposits, pulmonary inflammation and fibrosis (Davis et al. 1998). Inhalation NOAEC = 5 mg/m^3 based on no treatment related effects in female Balb/c mice exposed to roughly 5 mg/m^3 of "Min-U-Sil 5" for 6 hours/day, 5 days/week, for 3 and 9 weeks (Burns et al. 1980).

Endpoint	Lowest effect level/Results
Subchronic toxicity	**Lowest inhalation LOAEC** = 3 mg/m^3 based on pulmonary inflammation and fibrosis at 13 weeks, which persisted throughout the recovery period in male F344 rats (4 animals per dose) exposed to 0 or 3 mg/m^3 of cristobalite; 6 hours/day; 5 days/week, for 13 weeks, and then up to 8 months untreated (Johnston et al. 2000). Other inhalation LOAEC = 5 mg/m^3 based on an increased spleen weight and an increased response to *E. coli* (i.e. formation of plaque forming cells in the spleen) in female Balb/c mice exposed to roughly 5 mg/m^3 of "Min-U-Sil 5" for 6 hours/day, 5 days/week for 15 and 27 weeks (Burns et al. 1980).
	Lowest intratracheal LOAEL = 5 µg/rat per week [about 15 µg/kg-bw per week] based on pulmonary inflammation (increased polymorphonuclear leukocytes and alveolar macrophage activation) at both dose levels with both types of quartz in male Sprague Dawley rats (10 per dose) exposed to weekly doses of 5 or 20 µg/rat of freshly fractured or aged alpha-quartz for 12 weeks (Porter et al. 2002).
Chronic toxicity	**Lowest inhalation LOAEC** = 0.74 mg/m^3 based on lipoproteinosis, multifocal fibrosis (moderate fibrosis in 92% of silica-exposed rats at 24 months), inflammatory cell infiltrate and alveolar hyperplasia in F344 rats (50 males and females per dose) exposed to 0 and 1 mg/m^3 of DQ 12 quartz (74% respirable α quartz) for 6 hours/day, 5 days/week for 24 months. Survival reached 40% in the control group and ranged between 35 and 49% in the exposed groups. There was no statistical difference in survival between the control and exposed groups and the deaths were not related to exposure according to authors (Muhle et al. 1989, 1991). Other inhalation LOAEC = 2 mg/m^3 based on increased collagen and elastin content of lungs; type II cell hyperplasia in male and female F344 rats exposed to 0, 2, 10 and 20 mg/m^3 of "Min-U-Sil 5"; 6 hours/day, 5 days/week for 6 months (Drew and Kutzman, 1984b). Other inhalation LOAEC = 3 mg/m^3 based on Increased relative lung weight, chronic pulmonary inflammation and slight interstitial fibrosis, as well as changes in the lung associated lymph nodes in Syrian golden hamster; Han:AURA; (132 males and females per dose) exposed to ; 0

Endpoint	Lowest effect level/Results
	or 3 mg/m^3 of DQ12 quartz; 6 hours/ day, 5 days/week for up to 78 weeks (Muhle et al. 1998).
Developmental toxicity	No data
Reproductive toxicity	No data
Behavioural toxicity/ neurotoxicity	No data
Humans	
Chronic toxicity	A cohort study was conducted on 3330 U.S. gold miners (all are white males), who had an average of 9 years underground exposure during the period 1940 to 1965. The cohorts were followed up through 1990. Silicosis was identified through death certificates or chest X-rays taken during two cross sectional surveys in 1960 and 1976. The cohorts were categorized to 5 major job groups to create a job–exposure matrix. The job–exposure matrix together with work history was used to estimate individual exposure. The silica content in the respirable dust in the mine was estimated at 13%. The median crystalline silica exposure was 0.05 mg/m^3. 170 cases of silicosis were identified. The authors have identified several limitations of the study: (1) by limiting the detection of silicosis cases to two radiographic surveys and death certificates may have caused a bias effect and (2) conversion of dust counts to gravimetric measurements (in this study, 10 mpccf* = 0.1 mg/ m^3), may not be accurate based on the estimation of 13% silica content in the respirable dust. LOAC (based on silicosis) = 0.05 mg/m^3 (Steenland and

Endpoint	Lowest effect level/Results
	Brown 1995a, 1995b) A cross sectional study on 520 black gold miners (age >37 years) from a South African gold mine was conducted to measure the prevalence of silicosis and also to investigate exposure-response relationship with silica dust. The miners were recruited for the study and chest radiographs were taken during their annual medical surveillance examination between November 2000 and March 2001. Silicosis was defined as International Organization Classification radiological profusion of 1/1 or greater. Twenty two occupational groupings were considered when calculating cumulative dust and silica exposure. The mean length of employment was 21.8 years (range from 6.3 to 34.5 years). The mean intensity of respirable dust exposure was 0.37 mg/m^3 (range 0-0.7 mg/m^3) and quartz 0.053 mg/m^3 (range 0-0.095 mg/m^3). Historical dust data were not available. To get the cumulative exposure, assumptions were made that current dust concentrations and quartz fractions were reasonably closer to the average concentrations for last two to three decade (supported by other available data). The prevalence of silicosis among in-service black miners was 18.3 to 19.9% depending on the radiograph reader. Silicosis prevalence increased significantly with increasing length of service, from 1.6% among miners with less than 15 years of service to 47% among miners with over 30 years of service ($p<0.001$) and also with increasing cumulative quartz exposure ($p<0.001$). LOAC (based on silicosis) = 0.053 mg/m^3 (Churchyard et al. 2004). A community population-based random sample survey was conducted to investigate the exposure-response relationship for silicosis among 134 men over age 40 who live in a mining town in Colorado. The study group included previous mining workers (100) and people who never worked in mining (34, used as an internal control group to assess potential over diagnosis of radiologic silicosis). Postero-anterior chest radiographs were taken. Silicosis was defined as subjects with a median radiologic profusion of small opacities of ≥1/0 using the 1980 International Labour Organization classification. Exposure was calculated using 3 exposure indices: (1) occupational history (2) gravimetric dust exposure data (3) gravimetric silica exposure data. Average silica exposure was 0.064 mg/m^3 (range 0.026–0.195 mg/m^3) The length of

Endpoint	Lowest effect level/Results
	exposed time range from <20 years to >30 years. The prevalence of silicosis was 32%, which was observed at an average of 36.1 years after fist silica exposure. Silicosis prevalence rate has a strong positive correlation with cumulative silica exposure, mean silica exposure, duration of exposure and the time since last silica exposure. LOAC (based on silicosis) = 0.064 mg/m^3 (Kreiss and Zhen 1996). **Some of other epidemiological studies that provided dose-response relationship for silicosis:** Davis et al. 1983; Muir et al. 1991; Graham et al. 1991; Hnizdo and Sluis-Cremer 1993; Ng and Chan 1994; Rosenman et al. 1996; Cherry et al. 1998; Hughes et al. 1998.