



WORLD HEALTH ORGANIZATION
INTERNATIONAL AGENCY FOR RESEARCH ON CANCER

IARC Monographs on the Evaluation of Carcinogenic Risks to Humans

Volume 68 Silica

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SILICA

Crystalline silica - inhaled in the form of quartz or cristobalite from occupational sources (Group 1)

Amorphous silica (Group 3)

For definition of Groups, see [Preamble Evaluation](#).

Vol.: 68 (1997) (p. 41)

Crystalline silica:

CAS No.: **14464-46-1**

Chem. Abstr. Name: **Cristobalite**

CAS No.: **14808-60-7**

Chem. Abstr. Name: **Quartz**

CAS No.: **1317-95-9**

Chem. Abstr. Name: **Tripoli**

CAS No.: **15468-32-3**

Chem. Abstr. Name: **Tridymite**

Amorphous silica:

CAS No.: **112945-52-5**

Chem. Abstr. Name: **Pyrogenic (fumed) amorphous silica**

CAS No.: **112926-00-8**

Chem. Abstr. Name: **Precipitated silica; silica gel**

CAS No.: **61790-53-2**

Chem. Abstr. Name: **Diatomaceous earth (uncalcined)**

CAS No.: **60676-86-0**

Chem. Abstr. Name: **Vitreous silica**

CAS No.: **68855-54-9**

Chem. Abstr. Name: **Flux-calcined diatomaceous earth**

5. Summary of Data Reported and Evaluation

5.1 Exposure data

Silica (silicon dioxide) occurs in crystalline and amorphous forms. Of the several crystalline polymorphs of silica found in nature, quartz is by far the most common, being abundant in most rock types, notably granites, sandstones, quartzites and in sands and soils. Cristobalite and tridymite are found in volcanic rocks. Because of the wide usage of quartz-containing materials, workers may be exposed to quartz in a large variety of industries and occupations. Respirable quartz levels exceeding 0.1 mg/m³ are most frequently found in metal, non-metal and coal mines and mills; in granite quarrying and processing, crushed stone and related industries; in foundries; in the ceramics industry; in construction and in sandblasting operations. Cristobalite is formed

from quartz or any other form of silica at high temperatures (> 1400 °C) and from some amorphous silicas (e.g. diatomaceous earth) at somewhat lower temperatures (800 °C). Cristobalite exposure is notably associated with the use and calcination of diatomaceous earth as well as refractory material installation and repair operations. Few data exist on non-occupational exposures to crystalline silica. It has been estimated that respirable crystalline silica levels in the low $\mu\text{g}/\text{m}^3$ range are common in ambient air. Exposure may also occur during the use of a variety of consumer or hobby products.

Amorphous silica is found in nature as biogenic silica and as silica glass of volcanic origin. One form of biogenic silica, diatomaceous earth, originates from the skeletons of diatoms deposited on sea floors and contains small amounts of cristobalite and quartz. After calcination (which significantly increases the cristobalite content), diatomaceous earth is used as a filtration agent, carrier for pesticides, filler in paints and paper and as a refractory or abrasive product in a variety of industries. Occupational exposure to both amorphous and crystalline silica may occur during the production and use of diatomaceous earth. Fibres of amorphous silica are produced by a variety of plants, such as sugar cane and rice, and may be inhaled when released into the air during farming operations.

Large quantities of synthetic amorphous silica are produced as pyrogenic (fumed) silicas and wet process silicas (precipitated silicas and silica gels) which are used, notably, for reinforcing elastomers, for thickening resins, paints and toothpaste, and as free-flow additives. Exposure to synthetic amorphous silica may occur during its production and use. Synthetic amorphous silica may also be ingested as a minor constituent (< 2%) of a variety of food products where it serves as an anti-caking agent, and as an excipient in some pharmaceutical preparations. Silica fume is a form of amorphous silica (with small amounts of crystalline silica) unintentionally released into the air from certain metallurgical processes.

The mechanical, thermal and chemical history of a silica particle determines its surface properties and presence and abundance of various surface functionalities. Surface reactivity varies among silica samples from different sources. Heating converts hydrophilic surfaces into hydrophobic ones. In particular, freshly fractured surfaces are more reactive than aged ones.

5.2 Human carcinogenicity data

The evaluations for both crystalline and amorphous silica pertain to inhalation resulting from workplace exposures. Lung cancer was the primary focus. The Working Group's evaluation of the epidemiological evidence for potential causal relations between silica and cancer risk was focused principally on findings from studies that were least likely to have been distorted by confounding and selection biases. Among these studies, those that addressed exposure-response associations were especially influential in the Working Group's deliberations.

Crystalline silica

Possible differences in carcinogenic potential among polymorphs of crystalline silica were considered. Some studies were of populations exposed principally to quartz. In only one study (that of United States diatomaceous earth workers) was the exposure predominantly cristobalite. Studies of mixed environments (i.e. ceramics, pottery, refractory brick) could not delineate exposures specifically to quartz or cristobalite. Although there were some indications that cancer risks varied by type of industry and process in a manner suggestive of polymorph-specific hazards, the Working Group could only reach a single evaluation for quartz and cristobalite. Nonetheless, the Working Group did note a reasonable degree of consistency across studies of workers exposed to one or both polymorphs.

Ore mining

Seventeen cohort and five case-control studies were reported on ore miners potentially exposed to silica dust. The majority of these studies reported an elevated mortality for lung cancer among silica-exposed workers. However, in only a few ore mining studies were confounders such as other known occupational respiratory carcinogens taken into account. In such studies consistent evidence for a silica-lung cancer relationship was

not found. Noteworthy instances where a relationship between lung cancer and crystalline silica was not detected include two independent studies of gold miners in South Dakota, United States, a study of miners in one lead and one zinc mine in Sardinia, Italy, and a study of tungsten miners in China. The results of most of the other studies could not be interpreted as an independent effect of silica - workers were concomitantly exposed to either radon, arsenic, or both, and in some cases other known or suspected occupational respiratory carcinogens were present in the work environment (e.g. diesel exhaust, polycyclic aromatic hydrocarbons, cadmium). In a few studies, no information was provided on exposure to radon or arsenic, in spite of the likelihood of these exposures.

Quarries and granite works

Six cohort studies were available for review. These studies provide important information on cancer risks because the workplace environments were generally free of reported exposures to potentially confounding agents (e.g., radon). All studies revealed lung cancer excesses. Direct quantification of silica dust exposure concentrations in relation to lung cancer risk was not conducted in any of these studies, mainly due to sparse occupational hygiene measurement data. However, some studies provided indications of exposure-response associations when surrogate dose data, such as duration of employment and category of exposure, were used. For example, findings for lung cancer include a nearly twofold mortality elevation among long-term granite shed workers in Vermont, United States, an eightfold elevation among sandstone workers in Copenhagen, Denmark, and a relative risk of roughly 3.5 among crushed granite stone workers in the United States with long duration of exposure and time since exposure onset. One study of German slate quarry workers indicated a more prominent relationship between employment duration and lung cancer among workers with silicosis than among workers without silicosis. The Working Group regarded radiographic evidence of silicosis as a marker of high exposure to silica.

Ceramics, pottery, refractory brick and diatomaceous earth industries

In refractory brick and diatomaceous earth plants, the raw materials (amorphous or crystalline silica) are processed at temperatures around 1000 °C with varying degrees of conversion to cristobalite. The results of two cohort studies of refractory brick workers from China and Italy and of one cohort study of diatomaceous earth workers from the USA provided consistent evidence of increased lung cancer with overall relative risks of about 1.5. In the study of refractory brick workers from China, a modest increasing trend of lung cancer was found with radiographic profusion category. A nearly twofold elevated lung cancer risk was found among long-term workers in the Italian study. In the study of United States diatomaceous earth workers, increasing exposure-response gradients were detected for both non-malignant respiratory disease and lung cancer mortality.

In ceramic and pottery manufacturing plants, exposures are mainly to quartz, but where high temperatures are used in ovens, potential exposures to cristobalite may occur. In a cohort study of British pottery workers, lung cancer mortality was slightly elevated; a nested case-control analysis of lung cancer did not show an association with duration of exposure, but indicated a relationship between lung cancer mortality and average and peak exposures in firing and post-firing operations, with relative risks of approximately 2.0. In an Italian case-control study, apart from a fourfold increase in lung cancer in registered silicotics, there was a small increase in lung cancer for subjects without silicosis. In a case-control study from the Netherlands, there was little relationship overall between work in ceramics and lung cancer risk, but there was some suggestion that lung cancer risk was related to cumulative exposure.

Foundry workers

There were only three large cohort studies of foundry workers where silica dust or silicosis were considered as risk factors for cancer. One study from Denmark found a slightly elevated risk of lung cancer in silicotics compared with non-silicotics. Two studies, one from the United States and one from China, yielded conflicting results for lung cancer. The Chinese study suggested positive associations of silica with both lung cancer and stomach cancer, although there remained a potential for confounding by exposures to polycyclic aromatic hydrocarbons. The United States study did not demonstrate an association of lung cancer with cumulative silica exposure.

Silicotics

The vast majority of studies on registered silicotics reported excess lung cancer risks, with relative risks ranging from 1.5 to 6.0. Excesses were seen across countries, industries and time periods. A number of studies reported exposure-response gradients, using varying indicators of exposure. Some studies, in particular one from North Carolina (USA) and one from Finland, provide reasonable evidence for an unconfounded association between silicosis and lung cancer risk.

Summary of findings for crystalline silica (quartz and cristobalite)

For the evaluation of crystalline silica, the following studies provided the least confounded examinations of an association between silica exposure and cancer risk: (1) South Dakota, United States, gold miners; (2) Danish stone industry workers; (3) Vermont, United States, granite shed and quarry workers; (4) United States crushed stone industry workers; (5) United States diatomaceous earth industry workers; (6) Chinese refractory brick workers; (7) Italian refractory brick workers; (8) United Kingdom pottery workers; (9) Chinese pottery workers; (10) cohorts of registered silicotics from North Carolina, United States and Finland. Not all of these studies demonstrated excess cancer risks. However, in view of the relatively large number of epidemiological studies that have been undertaken and, given the wide range of populations and exposure circumstances studied, some non-uniformity of results would be expected. In some studies, increasing risk gradients have been observed in relation to dose surrogates - cumulative exposure, duration of exposure or the presence of radiographically defined silicosis - and, in one instance, to peak intensity exposure. For these reasons, the Working Group therefore concluded that overall the epidemiological findings support increased lung cancer risks from inhaled crystalline silica (quartz and cristobalite) resulting from occupational exposure. The observed associations could not be explained by confounding or other biases.

Amorphous silica

Very little epidemiological evidence was available to the Working Group. No association was detected for mesothelioma with biogenic amorphous silica fibres in the three community-based case-control studies. Separate analyses were not performed for cancer risks among a subset of diatomaceous earth industry workers exposed predominantly to amorphous silica.

5.3 Animal carcinogenicity data

Various forms and preparations of crystalline silica were tested for carcinogenicity by different routes of exposure.

Different specimens of quartz with particle sizes in the respirable range were tested in four experiments in rats by inhalation and in four experiments in rats by intratracheal instillation. In these eight experiments, there were significant increases in the incidence of adenocarcinomas and squamous-cell carcinomas of the lung; marked, dense pulmonary fibrosis was an important part of the biological response.

Pulmonary granulomatous inflammation and slight to moderate fibrosis of the alveolar septa but no pulmonary tumours were observed in hamsters in three experiments using repeated intratracheal instillation of quartz dusts.

No increase in the incidence of lung tumours was seen with one sample of quartz in the strain A mouse lung adenoma assay and with another quartz sample in a limited inhalation study in mice. Silicotic granulomas and lymphoid cuffing around airways but no fibrosis were seen in the lungs of quartz-treated mice.

In several studies in rats using single intrapleural or intraperitoneal injection of suspensions of several types of quartz, thoracic and abdominal malignant lymphomas, primarily of the histiocytic type (MLHT) were found. In rats, intrapleural injection of cristobalite and tridymite with particles in the respirable range resulted in

malignant lymphomas, primarily MLHT.

A pronounced positive interactive effect of one sample of quartz and Thorotrast (an α -radiation emitting material) on pulmonary carcinogenesis was observed in one inhalation study in rats. Enhancement of benzo[a]pyrene-induced respiratory tract carcinogenesis by two different samples of quartz was seen in one intratracheal instillation study in hamsters.

In two studies in hamsters given mixtures of quartz and ferric oxide (1 : 1) by intratracheal instillation, no pulmonary tumours were observed.

Diatomaceous earth was tested by oral administration in rats and by subcutaneous and intraperitoneal injection in mice. No increase in the incidence of tumours was found after oral and subcutaneous administration; after intraperitoneal injection, a slightly increased incidence of intra-abdominal lymphosarcomas was reported.

In one test by intrapleural injection of biogenic silica fibres to rats, the silica fibres were not found to influence the tumour response to crocidolite but a small number of pleural mesotheliomas was reported in animals injected with 15,16-dihydro-11-methylcyclopenta[a]phenanthren-17-one followed by administration of the biogenic silica fibres.

A food-grade micronized synthetic amorphous silica was tested by oral administration to mice and rats. No increased incidence of tumours was seen. In one study in rats using intrapleural implantation of two different preparations of synthetic amorphous silica, no increased incidence of tumours was observed.

5.4 Other relevant data

Crystalline silica

Crystalline silica deposited in the lungs causes epithelial and macrophage injury and activation. Crystalline silica translocates to the interstitium and the regional lymph nodes. Crystalline silica results in inflammatory cell recruitment in a dose-dependent manner. Neutrophil recruitment is florid in rats exposed to high concentrations of quartz; marked, persistent inflammation occurs accompanied by proliferative responses of the epithelium and interstitial cells. In humans, a large fraction of crystalline silica persists in the lungs, culminating in the development of chronic silicosis, emphysema, obstructive airways disease and lymph node fibrosis in some studies. In-vitro studies have shown that crystalline silica can stimulate release of cytokines and growth factors from macrophages and epithelial cells; evidence exists that these events occur *in vivo* and contribute to disease. Crystalline silica stimulates release of reactive oxygen and nitrogen intermediates from a variety of cell types *in vitro*. Oxidative stress is detectable in the lungs of rats following exposure to quartz.

Much less is known about the acute lung responses to inhaled crystalline silica in humans. Subjects with silicosis show an inflammatory response characterized by increased macrophages and lymphocytes but minimal increases in neutrophil numbers.

Only one human study was available on subjects exposed to dust containing crystalline silica, with no indication of the level of exposure; it showed an increase in the levels of sister chromatid exchange and chromosomal aberrations in peripheral blood lymphocytes.

Most cellular genotoxicity assays with crystalline silica have been performed with quartz samples. Some studies gave positive results, but most were negative. Some quartz samples induced micronuclei in Syrian hamster embryo cells, Chinese hamster lung V79 cells and human embryonic lung Hel 299 cells, but not chromosomal aberrations in the same cell types. Two quartz samples induced morphological transformation in Syrian hamster embryo cells *in vitro* and 5 quartz samples induced transformation in BALB/c-3T3 cells. While quartz did not induce micronuclei in mice *in vivo*, epithelial cells from the lungs of rats intratracheally exposed to quartz showed *hprt* gene mutations. Inflammatory cells from the quartz-exposed rat lungs caused mutations

in epithelial cells *in vitro*. Direct treatment of epithelial cells *in vitro* with quartz did not cause *hprt* mutation.

Tridymite was tested in only one study, where it induced sister chromatid exchange in co-cultures of human lymphocytes and monocytes.

Increasing in-vitro and in-vivo evidence suggests that the rat lung tumour response to crystalline silica exposure is a result of marked and persistent inflammation and epithelial proliferation. Other pathways such as a role for crystalline silica surface-generated oxidants or a direct genotoxic effect are not ruled out; however, at present, there is no convincing evidence for these alternative pathways.

Amorphous silica

Amorphous silicas have been studied less than crystalline silicas. They are generally less toxic than crystalline silica and are cleared more rapidly from the lung.

Biogenic silica fibres induced ornithine decarboxylase activity of epidermal cells in mice following topical application. No data were available to the Working Group on the genotoxicity of other amorphous silica particles.

5.5 Evaluation

There is *sufficient evidence* in humans for the carcinogenicity of inhaled crystalline silica in the form of quartz or cristobalite from occupational sources

There is *inadequate evidence* in humans for the carcinogenicity of amorphous silica.

There is *sufficient evidence* in experimental animals for the carcinogenicity of quartz and cristobalite.

There is *limited evidence* in experimental animals for the carcinogenicity of tridymite.

There is *inadequate evidence* in experimental animals for the carcinogenicity of uncalcined diatomaceous earth.

There is *inadequate evidence* in experimental animals for the carcinogenicity of synthetic amorphous silica.

Overall evaluation

In making the overall evaluation, the Working Group noted that carcinogenicity in humans was not detected in all industrial circumstances studied. Carcinogenicity may be dependent on inherent characteristics of the crystalline silica or on external factors affecting its biological activity or distribution of its polymorphs.

Crystalline silica inhaled in the form of quartz or cristobalite from occupational sources *is carcinogenic to humans (Group 1)*.

Amorphous silica *is not classifiable as to its carcinogenicity to humans (Group 3)*.

For definition of the italicized terms, see [Preamble Evaluation](#).

Previous evaluation: Suppl. 7 (1987) (p. 341)

Synonyms for crystalline silica

- Agate
- Chalcedony
- Chert
- Clathrasil
- Coesite
- α, β Cristobalite
- CSQZ
- DQ 12
- Flint
- Jasper
- Keatite
- Min-U-Sil
- Moganite
- Novaculite
- Porosil
- α -Quartz
- α, β Quartz
- Quartzite
- Sandstone
- Sil-Co-Sil
- Silica sand
- Silica W
- Snowit
- Stishovite
- Sykron F300
- Sykron F600
- α, β_1, β_2 Tridymite
- Zeosil

Synonyms for amorphous silica

- Aerosil
- Art Sorb
- Baykisol
- Bindzil
- Biogenic silica
- Britesorb
- Cab-O-Sil
- Celatom
- Celite
- Clarcel
- Colloidal silica
- Decalite
- Diamantgel
- Diatomaceous earth (flux-calcined)
- Diatomaceous earth (uncalcined)
- Diatomite
- Fina/Optima
- FK
- Fused silica
- Gasil
- HDK
- Hi-Sil
- Hispacil
- KC-Trockenperlen
- Ketjensil

- Kieselguhr
- Lucilite
- Ludox
- Nalcoag
- Neosyl
- Nipsil
- Nyacol
- Opal
- Precipitated silica
- Quartz glass
- Reolosil
- Seahostar
- Sident
- Silcron
- Silica fibres (biogenic)
- Silica-Perlen
- Silica-Pulver
- Sipernat
- Skamol
- Snowtex
- Spherosil
- Suprasil
- Sylobloc
- Syloid
- Sylopute
- Syton
- TAFQ
- Tixosil
- Tripolite
- Trisyl
- Ultrasil

PALYGORSKITE (ATTAPULGITE)
Long palygorskite (attapulgitite) fibres (> 5 micrometers): Group 2B
Short palygorskite (attapulgitite) fibres (< 5 micrometers): Group 3

For definition of Groups, see [Preamble Evaluation](#).

VOL.: 68 (1997) (p. 245)

CAS No.: 12174-11-7

Chem. Abstr. Name: Palygorskite

5. Summary of Data Reported and Evaluation

5.1 Exposure data

Palygorskite is a hydrated magnesium aluminium silicate, which occurs as a fibrous chain-structure mineral in clay deposits in several areas of the world. There is a major deposit of commercial importance in the United States. Palygorskite fibre characteristics vary with the source, but fibre lengths in commercial samples are generally less than 5 micrometers. Palygorskite has been mined since the 1930s and is used mainly as an absorbent for pet wastes and oils and greases and as a component of drilling muds. Occupational exposure to palygorskite occurs during its mining, milling, production and use. General population exposures also may occur in its use as pet waste absorbent, in fertilizers and pesticides and by ingestion of antidiarrhoeal preparations.

5.2 Human carcinogenicity data

A single cohort study of palygorskite (attapulgitite) miners and millers was available. It showed small excesses of mortality from lung cancer and stomach cancer, but no indications of any exposure-response for either cancer.

5.3 Animal carcinogenicity data

Samples of palygorskite from different regions vary considerably with regard to their fibre lengths. Results of studies in experimental animals suggest that carcinogenicity is dependent on the proportion of long fibres (> 5 micrometers) in the samples.

In one inhalation study in rats with palygorskite from Leicester, United Kingdom, in which about 20% of the fibres were longer than 6 micrometers, bronchoalveolar hyperplasia and a few benign and malignant alveolar tumours and mesotheliomas were observed. The same sample induced a high incidence of pleural mesotheliomas in rats after intrapleural administration. One sample from Torrejon, Spain, in which 0.5% of the fibres were longer than 6 micrometers, produced a significant increase in the incidence of pleural mesotheliomas after intrapleural injection.

In rats, intraperitoneal injection of a palygorskite sample (of unspecified origin and in which 30% of the fibres were longer than 5 micrometers) produced a high incidence of malignant abdominal tumours. A sample from Caceres, Spain, in which 3% of the fibres were longer than 5 micrometers, induced malignant abdominal tumours in rats after intraperitoneal injection.

Several studies involving exposures of rats by inhalation, intrapleural or intraperitoneal injection using samples originating from Lebrija (Spain), Mormoiron (France) and Attapulgitite (GA, United States) employed materials with relatively short fibres (less than or 0.5% were longer or equal to 5 micrometers). In these studies, no significant increase in the incidence of tumours was observed.

5.4 Other relevant data

Intratracheal instillation studies with palygorskite (attapulgit) fibres in sheep demonstrated significant and sustained inflammatory changes as measured in bronchoalveolar lavage fluids. These effects were mild compared to UICC chrysotile B but comparable to short chrysotile fibres. Intratracheal instillation studies in rats demonstrated that palygorskite (attapulgit) was less active than short chrysotile, UICC chrysotile B or aluminium silicate fibres but was more active than calcium silicate fibres. In-vitro studies have indicated that palygorskite can be toxic to mouse peritoneal and rat and rabbit alveolar macrophages.

In a single study, palygorskite did not show evidence for induction of sister chromatid exchange in rat pleural mesothelial cells.

5.5 Evaluation

There is *inadequate evidence* in humans for the carcinogenicity of palygorskite (attapulgit).

There is *sufficient evidence* in experimental animals for the carcinogenicity of long palygorskite (attapulgit) fibres (> 5 micrometers).

There is *inadequate evidence* in experimental animals for the carcinogenicity of short palygorskite (attapulgit) fibres (< 5 micrometers).

Overall evaluation

Long palygorskite (attapulgit) fibres (> 5 micrometers) are *possibly carcinogenic to humans (Group 2B)*.

Short palygorskite (attapulgit) fibres (< 5 micrometers) cannot be classified as to their carcinogenicity to humans (Group 3).

For definition of the italicized terms, see [Preamble Evaluation](#).

Previous evaluation: Suppl. 7 (1987) (p. 117)

Synonyms

- Actapulgit
- Attaclay
- Attacote
- Attagel
- Attapulgit
- Attapulgit
- Attapulgit
- Attasorb
- Basco
- Diasorb
- Diluex;
- Donnagel
- Fert-o-Gel
- Florex
- Florigel H-Y
- Gastropulgit
- Kaopectate
- Min-U-Gel

- Mucipulgite
 - Permangel
 - Pharnasorb-colloidal
 - Zeogel
-

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SEPIOLITE (Group 3)

For definition of Groups, see [Preamble Evaluation](#).

VOL.: 68 (1997) (p. 267)

CAS No.: 18307-23-8

Chem. Abstr. Name: Sepiolite ($\text{Mg}_3\text{H}_2(\text{SiO}_3)_4 \cdot x\text{H}_2\text{O}$)

CAS No.: 15501-74-3

Chem. Abstr. Name: Sepiolite ($\text{Mg}_2\text{H}_2(\text{SiO}_3)_3 \cdot \text{H}_2\text{O}$)

CAS No.: 63800-37-3

Chem. Abstr. Name: Sepiolite ($\text{Mg}_2\text{H}_2(\text{SiO}_3)_3 \cdot x\text{H}_2\text{O}$)

5. Summary of Data Reported and Evaluation

5.1 Exposure data

Sepiolite is a hydrated magnesium silicate that occurs as a fibrous chain-structure mineral in clays in several areas of the world. The major commercial deposits of sepiolite are in Spain. Sepiolite fibre characteristics vary with the source, but fibre lengths in commercial samples are generally less than 5 μm . Sepiolite has been mined since the 1940s, finding its greatest use as an absorbent, particularly for pet waste, and oils and greases. It is also used as a drilling mud and as a carrier for fertilizers and pesticides. Meerschaum, a compact form of sepiolite, has been used for centuries for the production of smokers' pipes. Occupational exposure occurs during the mining, milling, production and use of sepiolite.

5.2 Human carcinogenicity data

No data were available to the Working Group.

5.3 Animal carcinogenicity data

In one inhalation study in rats using sepiolite from Vicálvaro-Vallecas, Spain, in which all fibres were shorter than 6 μm , no significant increase in tumour incidence was found.

In one study by intrapleural injection to rats, sepiolite from China (fibre length, 1-100 μm) induced pleural mesotheliomas. In similar studies by intrapleural injection using samples from Turkey and Vicálvaro-Vallecas (all fibres shorter than 6 μm), no increases in tumour incidence were observed.

In two studies in rats by intraperitoneal injection using samples (0.9% of fibres > 5 μm) from Vicálvaro-Vallecas, no significant increases in the incidences of abdominal tumours were found.

In one study in mice by intraperitoneal injection, sepiolite from China (fibres, 1-100 μm in length) produced a small increase in the incidence of peritoneal mesotheliomas but sepiolite from Turkey (fibre length, 3-5 μm) did not.

5.4 Other relevant data

One study in sepiolite-exposed workers demonstrated clinical evidence of pulmonary function deficits. The results of one in-vitro study indicated that sepiolite was relatively potent in inducing superoxide anion release from both hamster and rat alveolar macrophages. Sepiolite is strongly haemolytic in some in-vitro assays.

In a single study, samples of sepiolite from China, Japan, Spain and Turkey induced polyploidy, but not chromosomal aberrations, in cultured Chinese hamster lung cells.

5.5 Evaluation

There is *inadequate evidence* in humans for the carcinogenicity of sepiolite.

There is *limited evidence* in experimental animals for the carcinogenicity of long sepiolite fibres (> 5 µm).

There is *inadequate evidence* in experimental animals for the carcinogenicity of short sepiolite fibres (< 5 µm).

Overall evaluation

Sepiolite *cannot be classified as to its carcinogenicity to humans (Group 3)*.

For definition of the italicized terms, see [Preamble Evaluation](#).

Previous evaluation: Suppl. 7 (1987) (p. 71)

Synonyms

- Aid Plus
- Ecume de mer
- Hexal
- Meerschaum
- Milcon
- ML 70DSA
- Pangel
- Pansil
- Quincite
- SP

WOLLASTONITE

(Group 3)

For definition of Groups, see [Preamble Evaluation](#).

VOL.: 68 (1997) (p. 283)

CAS No.: 13983-17-0

Chem. Abstr. Name: Wollastonite

5. Summary of Data Reported and Evaluation

5.1 Exposure data

Wollastonite is a calcium silicate mineral that occurs naturally in deposits in several areas of the world. Wollastonite has been mined in commercial quantities since the 1950s and its production is increasing with its use as a replacement for asbestos. Wollastonite breaks down during processing (crushing and grinding) into fibres of varying aspect ratios. High-aspect ratio wollastonite is used mainly as an asbestos replacement in construction and insulation board and automotive friction products, and in plastics and rubber. Powdered (milled) wollastonite, including small amounts of synthetic wollastonite, is used mainly in ceramics (the major current application of wollastonite) and in metallurgy. Occupational exposure to wollastonite occurs during its mining, milling, production and use.

5.2 Human carcinogenicity data

In the only available small cohort mortality study of workers in a wollastonite quarry, the observed numbers of deaths from all cancers combined and lung cancer were lower than expected.

5.3 Animal carcinogenicity data

Wollastonite was tested for carcinogenicity in an inhalation study in rats. No increase in tumour incidence was observed, but the number of fibres with a length $> 5 \mu\text{m}$ and a diameter $< 3 \mu\text{m}$ was relatively low (about 54 fibres/mL). Therefore, this study has only a limited value for an evaluation of carcinogenicity.

Four grades of wollastonite of different fibre sizes were tested for carcinogenicity in one experiment in rats by intrapleural implantation. There was no information on the purity of the four samples used. A slight increase in the incidence of pleural sarcomas was observed with three grades, all of which contained fibres greater than $4 \mu\text{m}$ in length and less than $0.5 \mu\text{m}$ in diameter. Pleural sarcomas were not observed after implantation of the grade that contained relatively few fibres with these dimensions.

In two studies by intraperitoneal injection in rats using two samples of wollastonite (one from India and one of unspecified origin with median fibre lengths of $8.1 \mu\text{m}$ and $5.6 \mu\text{m}$, respectively), no intra-abdominal tumours were found.

5.4 Other relevant data

Evidence from wollastonite miners suggests that occupational exposure can cause impaired respiratory function and pneumoconiosis. However, animal studies have demonstrated that wollastonite fibres have low biopersistence and induce a transient inflammatory response compared to various forms of asbestos. A two-year inhalation study in rats at one dose showed no significant inflammation or fibrosis.

A sample of wollastonite from China produced morphological transformation of Syrian hamster embryo cells. A sample of wollastonite from Québec, Canada, induced polyploidy but not chromosomal aberrations in cultured Chinese hamster lung cells.

5.5 Evaluation

There is *inadequate evidence* in humans for the carcinogenicity of wollastonite.

There is *inadequate evidence* in experimental animals for the carcinogenicity of wollastonite.

Overall evaluation

Wollastonite *cannot be classified as to its carcinogenicity to humans (Group 3)*.

For definition of the italicized terms, see [Preamble Evaluation](#)

Previous evaluation: Suppl. 7 (1997) (p. 377)

Synonyms

- Aedelforsite
- Cab-O-Lite
- Casiflux
- F1
- FW50
- FW200
- FW325
- Gillebächite
- Kemolite
- NYAD
- Nyad G
- NYCOR
- Okenite
- Rivaite
- Schalstein
- Tabular spar
- Tremin
- Vansil
- Vilnite
- WIC10
- WIC40
- Wollastocoat
- Wollastokup

ZEOLITES OTHER THAN ERIONITE (Group 3)

For definition of Groups, see [Preamble Evaluation](#).

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CAS No.: 1318-02-1
Chem. Abstr. Name: Zeolites

CAS No.: 12173-10-3
Chem. Abstr. Name: Clinoptilolite

CAS No.: 12271-42-0
Chem. Abstr. Name: Clinoptilolite (Na(AlSi₅O₁₂ · xH₂O))

CAS No.: 67240-23-7
Chem. Abstr. Name: Clinoptilolite (AlNaH₁₆(SiO₄) · 4H₂O)

CAS No.: 12173-98-7
Chem. Abstr. Name: Mordenite

CAS No.: 12445-20-4
Chem. Abstr. Name: Mordenite (AlNaH₆(SiO₃)₅)

CAS No.: 66732-10-3
Chem. Abstr. Name: Mordenite (Al₂CaH₁₂(SiO₃)₁₀ · H₂O)

CAS No.: 68652-75-5
Chem. Abstr. Name: Mordenite (Na(AlSi₅O₁₂))

CAS No.: 12174-18-4
Chem. Abstr. Name: Phillipsite

CAS No.: 61027-84-7
Chem. Abstr. Name: Phillipsite (CaK[Al₃O(SiO₃)₅] · 6H₂O)

CAS No.: 66733-09-3
Chem. Abstr. Name: Phillipsite (AlNa(SiO₄) · 6H₂O)

CAS No.: 68989-22-0
Chem. Absr. Name: Zeolite A

CAS No.: 68989-23-1
Chem. Abstr. Name: Zeolite X

CAS No.: 79982-98-2
Chem. Abstr. Name: ZSM-5

5. Summary of Data Reported and Evaluation

5.1 Exposure data

Zeolites are crystalline aluminosilicate minerals with cage-like crystal structures. Zeolites have been used extensively since the late 1940s in a variety of applications. Naturally occurring zeolites, some of which are fibrous, occur worldwide and many are used in materials for the construction industry, in paper, in agriculture and in other applications. A large number of zeolites have been synthesized for use in detergents, as catalysts and as adsorbents and desiccants. Exposures may occur during the mining, production and use of zeolites.

5.2 Human carcinogenicity data

No data were available to the Working Group.

5.3 Animal carcinogenicity data

Clinoptilolite with a particle size in the respirable range was tested for carcinogenicity in rats by intratracheal instillation. No significant increase in the incidence of tumours was found.

No adequate study was available to the Working Group on *phillipsite*.

Mordenite was studied for carcinogenicity in one experiment in mice by intraperitoneal injection. No peritoneal tumours were found.

Non-fibrous Japanese zeolite was tested for carcinogenicity in one experiment in rats by single intrapleural injection. No increase in pulmonary tumours was found.

Synthetic zeolite A was tested for carcinogenicity in one experiment in rats by oral administration in the diet. No increase in tumour incidence was found.

Synthetic non-fibrous zeolite was tested for carcinogenicity in rats by inhalation exposure. No increase in pulmonary tumours was found.

Synthetic zeolite 4A was tested for carcinogenicity in mice by single intraperitoneal injection. No abdominal tumour was observed.

Synthetic zeolites MS4A and MS5A were tested for carcinogenicity in rats by intraperitoneal, intrapleural and subcutaneous injection. No increase in the incidence of tumours was found.

5.4 Other relevant data

Oral administration of natural and synthetic zeolite particles produced little toxicity in a variety of species. Intratracheal instillation of mordenite in rats produced mild fibrosis and hyperplasia.

Inhalation studies in rats and hamsters of synthetic zeolite A produced no significant pulmonary inflammation or interstitial fibrosis

Mordenite exhibited low cytotoxicity *in vitro*. A sample of natural zeolite particles from Chonguruu, Russia, induced aberrant metaphases in human whole blood cultures *in vitro*. This zeolite sample also induced aberrant metaphases in cells collected by peritoneal lavage of mice after intraperitoneal injection.

No data were available to the Working Group on the genetic and related effects of synthetic zeolite.

5.5 Evaluation

There is *inadequate evidence* in humans for the carcinogenicity of zeolites other than erionite.

There is *inadequate evidence* in experimental animals for the carcinogenicity of clinoptilolite, phillipsite, mordenite, non-fibrous Japanese zeolite and synthetic zeolites.

Overall evaluation

Clinoptilolite, phillipsite, mordenite, non-fibrous Japanese zeolite and synthetic zeolites *cannot be evaluated as to their carcinogenicity to humans (Group 3)*.

For definition of the italicized terms, see [Preamble Evaluation](#).

Synonyms for Clinoptilolite

- Klinosorb
- 1010A

Synonyms for Mordenite

- Prilolite
- 2020A
- Alite 150
- Astonite
- Jinyunite
- Zeolon 100

Synonyms for zeolites

- Abscents 3000
- Adsorbents, zeolites
- Agrolithe 15/25
- Aid Plus OCMA
- Aluminosilicates, zeolites
- Bactekiller BM 101A
- Bactekiller BM 102A
- Bactekiller BM 102B
- Bactekiller BM 501A
- Bactekiller BM 503
- Bactekiller MB
- Baylith AC 6184
- Ca EH 4B
- Calsit
- Coratyl G
- Crystal structure types, zeolitic
- Crystals, zeolitic
- CS 100
- CS 100 (zeolite)
- CS 100S
- EZA Zeolite A
- Filtering materials, zeolites

- Filters and Filtering materials, mol. sieves
- GRZ 1
- Harmony 70
- HSD 640NAD
- Ionsiv
- JE 15P
- KC-Perlkator D 10E
- KKh 100
- LM 104
- LM 108
- LM 204
- LM 208
- LM 208 (zeolite)
- LMS 9611
- LP zeolites
- Microzeokar 8
- Mol. sieves, zeolites
- Molecular sieves, zeolitic
- MZ 3
- NA 100
- NC 300
- Neounizeon SP 3000
- Radiolite
- SGK 1
- Sieves, mol.
- Silicates, alumino
- Siliporite NK 10
- Siltan B 50
- Siltan B-MZ 260
- Siltan CPT 30
- T 134 (zeolite)
- Wessalith NaP
- Wessalith P
- Zeolite 3A
- Zeolite 4A
- Zeolite 5A
- Zeolite L
- Zeolite Y
- Zeolite 1014
- Zeolite 1424
- Zeolite 24P

COAL DUST (Group 3)

For definition of Groups, see [Preamble Evaluation](#).

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5. Summary of Data Reported and Evaluation

5.1 Exposure data

Coal is a generic term for a heterogeneous, carbonaceous rock of varying composition and characteristics. It is mined in over 70 different countries around the world, and utilized in many more for electricity generation, heating, steel making and chemical processes. It varies in type from the soft and friable lignite to the hard and brittle anthracite. The term 'rank', which reflects the percentage carbon content, is used conventionally for its classification.

Coal typically contains variable but substantial amounts of mineral matter, of which quartz is an important component. The major exposures to coal dust occur during mining and processing of coal. In these operations the exposure includes dusts generated not only from the coal but also from adjacent rock strata and other sources. These may increase the quartz component of the airborne dust to about 10% of the total mixed dust, or to even greater levels if significant rock cutting is being undertaken.

Before 1970, in Germany, the United Kingdom and the United States, levels of respirable mixed dust in underground mines were typically 12 mg/m³ or less, depending on occupation and mine. More recently, regulations in some countries have brought these levels down to 3 mg/m³ or less. Dust concentrations in surface (strip, opencast) coal mines are generally lower than those found in underground mining. However, owing to the need to disturb overlying rock strata in surface mining, quartz exposures can be significant in some jobs, e.g. in rock drilling.

Exposure to coal dust also occurs during bulk loading and transfer, and at sites where coal is stored and used, such as power stations, steel and coke works, chemical plants, and during domestic use.

5.2 Human carcinogenicity data

There have been no epidemiological investigations on cancer risks in relation to coal dust *per se*. There is, however, a large body of published literature concerning cancer risks potentially associated with employment as a coal miner, including a small number of exposure-response associations with coal mine dust.

Cancers of the lung and stomach have been investigated most intensively among coal miners, with sporadic reports for other sites, such as urinary bladder. The absence of information on levels of the specific components of coal mine dust (e.g. coal, quartz, metals) further hindered interpretation of the epidemiological literature.

The evidence from occupational cohort studies for an association between coal mine dust and lung cancer has not been consistent; some studies revealed excess risks, whereas others indicated cohort-wide lung cancer deficits. There is no consistent evidence supporting an exposure-response relation for lung cancer with any of the customary dose surrogates, including duration of exposure, cumulative exposure or radiographic evidence of pneumoconiosis.

In contrast to the lung cancer findings, there have been reasonably consistent indications of stomach cancer

excess among coal miners, detected both in occupational cohort studies and in community-based case-control studies. However, there is no consistent evidence supporting an exposure-response gradient for coal mine dust and stomach cancer.

5.3 Animal carcinogenicity data

Coal dust was tested for carcinogenicity both separately and in combination with diesel particle aerosols by inhalation in one adequate experiment in rats. The incidence of tumours was not increased compared to controls.

In one study in rats, single intrapleural injection of coal dust did not increase the incidence of thoracic tumours.

5.4 Other relevant data

The biological effects of coal mine dust in coal miners include simple coal workers' pneumoconiosis, progressive massive fibrosis, emphysema, chronic bronchitis and accelerated loss of lung function. Fibrotic endpoints in animals are attributable either to its quartz, clay or ash content; the age and dimensions of the particles probably also play a role. Human studies suggest that coal dust contains stable radicals and is able to induce reactive oxygen species that may cause DNA damage. Coal mine dust can cause cytotoxicity and induce the release of mediators from inflammatory cells; however, these effects are not predictable from its quartz content alone. *In vitro*, the cytotoxicity of quartz is clearly inhibited by the presence of coal dust, while the inflammatory activity is dependent on yet unidentified parameters. The release of cytokines and growth factors most probably contributes to pneumoconiosis development. Reactive oxygen species also can inactivate α -1-antitrypsin and bronchoalveolar leukocytes from rats inhaling coal mine dust had increased secretion of connective tissue proteases, leading to the development of emphysema.

Non-nitrosated extracts of a variety of coal dust samples were not mutagenic to *Salmonella typhimurium*. Non-nitrosated extracts of sub-bituminous coal dust induced mammalian cell transformation in one study; these extracts also induced chromosomal aberrations and sister chromatid exchange in human lymphocyte cultures. These extracts also induced sister chromatid exchange in Chinese hamster ovary cells.

Exposure of rodents to coal dust by inhalation or oral gavage did not produce any evidence of mutagenicity.

5.5 Evaluation

There is *inadequate evidence* in humans for the carcinogenicity of coal dust.

There is *inadequate evidence* in experimental animals for the carcinogenicity of coal dust.

Overall evaluation

Coal dust *cannot be classified as to its carcinogenicity to humans (Group 3)*.

For definition of the italicized terms, see [Preamble Evaluation](#).

***para*-ARAMID FIBRILS (Group 3)**

For definition of Groups, see [Preamble Evaluation](#).

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CAS No.: 24938-64-5

Chem. Abstr. Name: Poly(imino-1,4-phenyleneiminocarbonyl-1,4-phenylenecarbonyl)

CAS No.: 25035-37-4

Chem. Abstr. Name: 1,4-Benzenedicarboxylic acid, polymer with 1,4-benzenediamine

CAS No.: 26125-61-1

Chem. Abstr. Name: 1,4-Benzenedicarbonyl dichloride, polymer with 1,4-benzenediamine

5. Summary of Data Reported and Evaluation

5.1 Exposure data

para-Aramid fibres are long-chain synthetic polyamides, most commonly poly(*para*-phenyleneterephthalamide), and have been produced commercially since the early 1970s. The combination of high strength, high temperature resistance and light weight make these fibres useful in the reinforcement of composite materials for the aerospace and sports equipment industries, in woven fabrics used in protective apparel and in automotive brake pads and gaskets.

During abrasive processing operations, small-diameter respirable fibrils can be released into the air. Highest occupational exposures to *para*-aramid fibrils have been measured in the processing of shorter (staple) fibres in yarn.

5.2 Human carcinogenicity data

No data were available to the Working Group.

5.3 Animal carcinogenicity data

para-Aramid fibrils were tested for carcinogenicity in one study in rats by inhalation exposure. An increased incidence of cystic keratinizing squamous-cell carcinomas was reported. However, subsequent re-examinations and evaluation of these lesions revealed a diagnosis of pulmonary keratinizing cysts. The biological significance of these lesions is unclear. *para*-Aramid fibrils were also tested in two experiments in rats by intraperitoneal injection. No intra-abdominal tumours were observed.

5.4 Other relevant data

Inhalation exposure of rats to *para*-aramid fibrils for two years produced minimal pulmonary fibrosis. Chronic inhalation studies demonstrate that inhaled *para*-aramid fibrils are biodegradable in the lungs of rats. Similarly, two-week inhalation studies in rats and hamsters demonstrate transient pulmonary inflammatory and cell proliferative responses and biodegradability of inhaled fibrils in the lungs of exposed animals. *para*-Aramid fibrils demonstrate some cytotoxic activity to cells under in-vitro conditions.

para-Aramid fibril extracts were not mutagenic to *Salmonella typhimurium* or to Chinese hamster V79 fibroblasts.

5.5 Evaluation

There is *inadequate evidence* in humans for the carcinogenicity of *para*-aramid fibrils.

There is *inadequate evidence* in experimental animals for the carcinogenicity of *para*-aramid fibrils.

Overall evaluation

para-Aramid fibrils *cannot be classified as to their carcinogenicity to humans (Group 3)*.

For definition of the italicized terms, see [Preamble Evaluation](#).

Synonyms

- 1,4-Benzenediamine-terephthalic acid copolymer
- Aramica
- Kevlar
- Kevlar 29
- Kevlar 49
- *para*-Phenylenediamine, polyamide with terephthalic acid
- *para*-Phenylenediamine-terephthalic acid chloride copolymer
- *para*-Phenylenediamine-terephthalic acid copolymer
- *para*-Phenylenediamine-terephthaloyl chloride copolymer
- Poly(imino-*para*-phenyleneiminocarbonyl-*para*-phenylenecarbonyl)
- Poly(imino-*para*-phenyleneiminoterephthaloyl)
- Poly(1,4-phenylene terephthalamide)
- Poly(*para*-phenylene terephthalamide)
- Poly(*para*-phenylenediamine-terephthalic acid amide)
- PPD-T
- PPTA
- Twaron