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Evaluation of health hazards by exposure to

Wollastonite

and proposal of a health-based quality criterion for ambient air

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Evaluation of health hazards by exposure to Wollastonite and proposal of a health-based quality criterion for ambient air

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Preface

The Danish Environmental Protection Agency has requested an evaluation of health hazards by exposure to wollastonite and proposal of a health based quality criterion for ambient air. This resulted in 2006 in the present report, which was prepared by Elsa Nielsen and Ole Ladefoged, Department of Toxicology and Risk Assessment, Danish Institute for Food and Veterinary Research, i.e. the present Division of Toxicology and Risk Assessment, National Food Institute, Technical University of Denmark.

The report has been subjected to review and discussion and has been endorsed by a steering committee consisting of representatives from the following Danish authorities:

The Danish Working Environment Authority,
The Danish Ministry of Food, Agriculture and Fisheries (The Faculty of Agricultural Sciences),
The Danish Veterinary and Food Administration,
The National Board of Health, Denmark,
The Danish Environmental Protection Agency.

The Danish Environmental Protection Agency
Copenhagen, September 2013.

1 General description

Wollastonite has previously been reviewed in order to establish a health based quality criterion in air (Larsen & Ladefoged 1991). New data have become available since then; these data have been included in this document and taken into consideration in this evaluation and consequently, in the proposed health based quality criterion in air.

Natural wollastonite is an acicular (needle-like) calcium silicate mineral that occurs in triclinic and monoclinic varieties. When triclinic, the unit cell parameters are as follows: a = 0.79 nm, b = 0.73 nm and c = 0,71 nm; α = 90°02', β = 95°22' and γ = 103°26'. Wollastonite consists of chains of indefinite length containing three SiO_4 tetrahedra per unit cell. The tetrahedra are joined apex to apex, and one is orientated with an edge parallel to the axis of the chain. These chains are paired; slight offsetting (placing out of line) produces the different structural forms of the mineral. Also within the mineral structure are calcium atoms, which occur in octahedral coordination and alternate with layers composed of silica atoms between layers of oxygen atoms. Wollastonite has unique cleavage properties and breaks down during crushing and grinding into lath-like or needle-shaped particles (fibres) of varying acicularity. The acicularity of particles is defined by their aspect ratio, i.e., their length/width ratio or length/diameter ratio. For wollastonite, the individual particles commonly exhibit an aspect ratio of 7:1 or 8:1 and have an average diameter of 3.5 μm. (IARC 1997).

1.1 Identity

Molecular formula:	$CaSiO_3$
Molecular weight:	116.18
CAS-no.:	13983-17-0
Synonyms:	-

1.2 Physical / chemical properties

Description:	Triclinic crystals, which occurs as coarse-bladed masses and rarely shows good crystal form. White when pure; may be grey, pale green yellowish brown or red with impurities.
Purity:	Wollastonite has a theoretical composition of 48.3% CaO and 51.7% SiO_2, but aluminium, iron, magnesium, manganese, potassium or sodium may partially substitute for calcium. The chemical composition of commercial wollastonite products varies depending on the origin.
Melting point:	1540 °C

Density:	2.87 – 3.09 g/ml
Solubility:	Water: < 1 mg/ml at 21 °C
Stability:	Natural occurring wollastonite consists almost entirely of α-wollastonite, but can be converted to the metastable β-form, pseudowollastonite, by heating to temperatures of about 1120 °C.
Incompatibilities:	In general, wollastonite is inert chemically, but it can be decomposed in concentrated hydrochloric acid.
Other properties:	A 10 % wollastonite/water slurry has a pH of 9.9.
Fibre content:	The fibre content and fibre dimension varies and are dependent on the origin and processing of wollastonite.
References:	IARC (1997), IUCLID (2000), A&H (1992), NTP (2003).

1.3 Production and use

Wollastonite was probably first mined in California, US, in 1933 for mineral wool production. The principal wollastonite mines are located in the USA, Finland, China, India, and Mexico. More recently, synthetic wollastonite has been introduced, which predominantly plays a role in the wollastonite industries where purity and performance are required. All known production of synthetic wollastonite is as powder grade. (IARC 1997).

The markets can be divided into two main categories: 1) those for high-aspect ratio wollastonite and 2) those for low-aspect ratio wollastonite (powder or milled grades).
High-aspect ratio wollastonite (aspect ratios of 10:1 to 20:1) is used as a reinforcing and functional filler in a variety of applications, especially in plastics and rubber (20-25% of total consumption), as asbestos substitution (20-25%), and in paints and coatings (about 2-5%). These applications rely on the physical acicularity of wollastonite where it provides added hardness, flexural strength and impact resistance.
Low-aspect ratio wollastonite (aspect ratios of 3:1 to 5:1) is used as a source of both calcium oxide and silicon dioxide and has unique qualities as fillers and is primarily used in ceramics (40-45%) and in metallurgy (12-15%).
(IARC 1997).

1.4 Environmental occurrence

Wollastonite occurs most commonly in nature where limestone has reacted at high temperature with igneous rock and created either one of two principal mineral types. Wollastonite from skarn deposits is typically of high purity and accounts for most of the world's mined ores. This type is fine-grained and usually interspersed with other silicates. The other type, the carbonatitic wollastonite formed by magmatic process, is found to a much more limited extent in nature. Ores from the major wollastonite deposits contain 18-97% wollastonite. The associated minerals are most often calcite, quartz, garnet, epidote, apatite, sphene, idocrase and diopside. (IARC 1997).

Wollastonite in the environment also results from its use in industrial products.

No data on environmental concentrations have been found.

1.5 Environmental fate

No data have been found.

1.6 Human exposure

1.6.1 Non-occupational exposure

The general population can be exposed to airborne wollastonite emitted from production facilities. Non-occupational exposure can also occur from products that contain wollastonite, such as wallboard or paints (IARC 1997).
No exposure data have been found.

1.6.2 Occupational exposure

Airborne dust and fibre concentrations have been measured in a limestone-wollastonite quarry and flotation plant at Lappenranta, Finland, and Willsboro, N.Y., US; these localities represent, according to IARC (1997), the two largest wollastonite production sites in the world.

Table 1 presents the concentrations of total dust and fibres during different operational stages and the number of workers on one work shift (number in parentheses under the heading 'Operation') at Lappenranta, Finland. The respirable fraction of 12 dust samples from drilling, crushing, and sorting contained, in addition to calcite, 15% wollastonite and 3% quartz. The airborne dust in the flotation plant was mainly composed of wollastonite. The dust measurements were taken both in the breathing zones of the workers and within the working areas. Fibres were counted by phase-contract optical microscopy (PCOM) or by scanning electron microscopy (SEM) and all fibres over 5 μm in length, below 3 μm in diameter, and with an aspect ratio over 3:1 were counted. The different detection limits for PCOM and SEM (ca. 0.5 μm for PCOM and ca. 0.05 for SEM) should be noticed when comparing the fibre concentrations obtained by the two methods. (Huuskonen et al. 1983a).
When studied by SEM, the thinnest wollastonite fibres were characteristically 0.2-0.3 μm in diameter. The median fibre lengths and median diameters were 4 μm and 0.8 μm, respectively, in crushing operations and 2 μm and 0.4 μm, respectively, in bagging work. (Huuskonen et al. 1982, Tuomi et al. 1982 – quoted from IARC 1997).

Table 2 presents the mean concentrations of total dust during different operational stages at the US wollastonite production plant in Willsboro. The NIOSH surveys included personal breathing zone samples of respirable and total dust in the mine and mill occupations and were obtained over full working shifts. The results are reported as eight-hour time weighted averages (8-hour TWA). The mean concentration of total dust ranged from 0.9 to 12 mg/m^3. Airborne fibre counts (PCOM) showed 0.3 fibres/cm^3 in the mine, and 23.3 fibres/cm^3 in the mill. Fibrous particles had a median diameter of 0.22 μm and a median length of 2.5 μm. (Hanke et al. 1984).

Table 1. Concentrations of total dust and fibres during different operational stages (reproduced from Huuskonen et al. 1983a).

Operation	Concentration (mg/m³ total dust)			Concentration of fibers (fibers/cm³)[a]					
				Optical method			SEM		
	N	Mean	Range	*N*	Mean	Range	*N*	Mean	Range
Drilling (1–2)[b]									
By automatic machine (outside the cabin)							5	2,6	1–5
By handtools	6	27	11–59				5	5,8	1–21
Loading and transport (3–4)	3	0,3	0,2–0,4						
Primary crushing plant (1)									
Inside control room	6	3,8	2–6						
Outside control room	15	44	7–99	6	5,1	1–14	16	23	2–50
Manual sorting (13)	11	2,8	2–7				4	8,6	7–10
Automatic sorting (1)									
Inside control room	2	3,3	3–4						
Outside control room	3	67	48–84				3	6,4	4–10
Secondary crushing plant (1)									
Inside control room	2	10	10–11						
Outside control room	6	43	30–56	3	33	26–45	2	52	42–63
Fine crushing plant (1)									
Inside control room	2	11	2–20						
Outside control room	5	41	7–60	2	6,9	6–7	2	11	11–12
Flotation plant (2) (including fine milling)	6	22	15–30	5	21	8–37	4	30	15–45
Bagging (3)	2	27	25–28	2	19	15–23	3	36	27–42

Table 2. Mean total dust concentrations (in mg/m^3) (±SD) (reproduced from Hanke et al. 1984).

Job category	*NIOSH (1976 and 1982)*	*MSHA and company (1977–81)*	*All sources*
All mining except crushing	0·90 (n = 2)	0·93 ± 1·94 (n = 9)	0·90 ± 2·16 (n = 11)
All administrative activities in mill	2·30 (n = 2)	—	2·30 (n = 2)
All milling and crushing	5·24 ± 1·95 (n = 11)	3·33 ± 1·40 (n = 15)	4·10 ± 1·90 (n = 26)
Labourer and beneficiator	11·65 ± 1·85 (n = 8)	6·88 ± 1·60 (n = 9)	8·71 ± 1·80 (n = 17)
Mill maintenance and packers	10·30 ± 1·93 (n = 26)	9·73 ± 1·99 (n = 15)	10·00 ± 1·94 (n = 41)

Regarding occupational exposure to wollastonite during use, airborne respirable fibre (fibre > 5 μm, no further information available) levels in the range of 0.02-0.2 fibres/ml have been measured during stacking and mixing in the production of fibre-reinforced cement sheets, (SEM analysis) (AMI 1986 – quoted from IARC 1997, IUCLID 2000 and NOHSC 2001).

2 Toxicokinetics

2.1 Deposition, distribution, biopersistence and durability

Factors that determine the deposition, retention, and clearance of respirable fibres in biological systems have been considered by a WHO-IPCS Task Group (WHO 1993). The potential health effects of fibrous aerosols are a function of the internal dose to the target tissue, which is determined by airborne concentrations, pattern and amount of exposure, chemical composition, fibre size (length, diameter, aspect ratio, shape), electrostatic charge, biopersistence and durability. The term 'biopersistence' refers to the ability of a fibre to stay in the biological environment where it was introduced. The length of time that fibres persist in the tissue is also a function of their durability, which is directly related to their chemical composition and physical characteristics.

In the nasopharyngeal and tracheobronchial regions, fibres are generally cleared fairly rapidly via mucociliary clearance, while fibres deposited in the alveolar space appear to be cleared more slowly, primarily by phagocytosis and to a lesser extent via translocation and, possibly, by dissolution. Translocation refers to the movement of the intact fibre after initial deposition at foci in the alveolar ducts, and on the ciliated epithelium at the terminal bronchioles. These fibres may be translocated via ciliated mucous movement up the bronchial tree and removed from the lung or may be moved through the epithelium with subsequent migration to interstitial storage sites or along lymphatic drainage pathways or transport to pleural regions. Fibres short enough to be fully ingested are thought to be removed mainly by phagocytosis by macrophages, whereas longer fibres may be partly cleared at a slower rate, either by translocation to interstitial sites, breakage, or dissolution. A higher proportion of longer fibres are, therefore, retained in the lung. (WHO 1993).

The biopersistence of inhaled wollastonite in the lungs has been evaluated in male Crl:CD-BR rats exposed 6 hours/day for 5 days to wollastonite (origin not stated; 800 fibres/cm^3; 115 mg/m^3). Rats were examined after specific time intervals, up to 6 months after cessation of exposure. The lungs were digested to quantify dose, fibre dimensional changes over time, and clearance kinetics. Inhaled wollastonite fibres were cleared rapidly with a retention half time of less than one week. Within one month, mean fibre length decreased from 11 μm to 6 μm and mean fibre diameters increased from 0.5 μm to 1.0 μm. The authors suggested that the wollastonite fibres were readily solubilised and concluded that the low durability of wollastonite in the lungs might account for the less severe toxicity in comparison to more durable fibres. (Warheit et al. 1994 – quoted from IARC 1997, IUCLID 2000 and Toxline 2003).

Muhle et al. (1994 – quoted from IARC 1997, NOHSC 2001, IUCLID 2000 and Toxline 2003) compared the biodurabilities of wollastonite (origin not stated) and several man made mineral fibres as well as other natural fibres instilled intratracheally into Wistar rats. Serial sacrifices were done up to 24 months after exposure and the fibres were analysed by scanning electron microscopy (SEM). The half times of fibre elimination from the lung ranged from about 10 days for wollastonite to more than 300 days for crocidolite asbestos. Data suggested that the

biodurability of the fibres is a function of both their dimension and chemical composition.

The *in vivo* durability of coated wollastonite (Wollastocoat, origin not stated), uncoated wollastonite (origin not stated), and of a synthetic wollastonite (xonotlite) was investigated following intratracheal instillation (single dose, 2 mg test material in 0.3 ml 0.9% saline) into female Wistar rats. Crocidolite asbestos (high durability) was used as a positive control. Rats were sacrificed at 2 and 14 days, and at one, three and six months after instillation. The fibres were analysed by SEM. A relatively even distribution of fibres both in the bronchi as well as in the bronchioli and the alveoli was observed; no agglomerations or accumulations of fibres were found. The elimination of wollastonite fibres from the lung was relatively fast and was predominantly due to the dissolution of fibres, with half-times of 15 to 21 days. The coating had no effect. The elimination of xonotlite from the lung was very fast and up to about 90% was eliminated by two days after instillation. In comparison, the total number of crocidolite fibres decreased with a half time of 240 days, but the number of fibres > 5 μm in length was unchanged six months after exposure. (Bellman & Muhle 1994 – quoted from IARC 1997, HSDB 2003, Toxline 2003, NTP 2003 and IUCLID 2000).

2.2 Mode of action

In a review of the determinants of fibre toxicity and the health effects of exposure to man made fibres and non-asbestos fibrous silicates, it was reported that the main determinants of fibre toxicity are dose, fibre size, and fibre durability. Fibres of less than 3.5 μm in diameter and 200 μm in length were reported to be respirable and fibres from 0.25 to 1.5 μm in diameter and above 4-8 μm in length had the highest carcinogenic potential. Furthermore, fibre toxicity increased with increasing durability/biopersistence. (Lockey 1996 – quoted from Toxline 2003).

Warheit et al. (1988 – quoted from IARC 1997) have tested a number of inorganic particles and fibres, including wollastonite fibres (from Willsboro, USA), for complement activation *in vitro* and compared these data with results on particle-induced macrophage accumulation *in vivo*. Volcanic ash was used as a negative control. For complement activation, fresh serum was treated with a concentration of 25 mg/ml (the optimal particle/sera concentration for complement activation). For macrophage activation, male Sprague-Dawley rats were exposed by inhalation to aerosols at concentrations from 10 to 20 mg/m^3 for 1, 3, or 5 hours. The results showed that all of the particulates that activated complement *in vitro* also induced alveolar macrophage accumulation at sites of particle and fibre deposition *in vivo*. The negative control did not activate complement *in vitro* and did not elicit macrophage accumulation *in vivo*. According to IARC (1997) *"these results indicate that complement activation by inhaled particles is a mechanism through which pulmonary macrophages accumulate at sites of deposition"*.

3 Human toxicity

3.1 Single dose toxicity

No data have been found.

3.2 Irritation

No data have been found.

3.3 Sensitisation

No data have been found.

3.4 Repeated dose toxicity

A clinical study has been carried out among 46 men who had been exposed to wollastonite in a Finnish limestone-wollastonite quarry for an average duration of exposure of 21.5 years (10-41 years) and an average duration since initial exposure of 22.8 years (Huuskonen et al. 1983a). Concentrations of total dust and fibres are presented in Table 1, see section 1.6.2. Chronic bronchitis was found in 11/46 workers, including 3/15 non-smokers. Chest radiographs revealed slight lung fibrosis in 7 men, slight bilateral pleural thickening in 6 men, and both lung and pleural changes in 7 men. Among the 138 referents, 5 had pulmonary fibrosis only, 6 had pleural thickening only, and one had both lung and pleural changes. Their sputum specimens were normal. Lung function tests (spirometry and nitrogen single breath tests) indicated the possibility of small airways disease.

A follow-up study (Koskinen et al. 1997) to the study by Huuskonen et al. (1983a) included 49 workers (40 men and 9 women). Mean exposure of the workers was 25 years. The mean concentrations of total dust in the mine and mill varied in 1981 from 0.3 to 67 mg/m^3 and that of fibres from 5.1 to 33 fibres/cm^3 (PCOM) or from 2.6 to 52 fibres/cm^3 (SEM), see Table 1 (section 1.6.2) for further details. In addition to calcite, the average respirable fraction contained 15% wollastonite and 3% quartz. Later dust measurements (PCOM) revealed fibre concentrations ranging from 0.04 to 3.4 fibres/cm^3 for wollastonite mining and milling and from 0.09 to 1.2 fibres/cm^3 calcite mining and milling. The workers underwent a physical examination, and work histories and symptoms of chronic bronchitis were recorded. Chest radiographs were performed, and spirometry and diffusion capacity were measured. Four workers underwent high-resolution computerised tomography (HRCT – a type of X-ray) of the lungs, and bronchoalveolar lavage (BAL). Lung tissue specimens obtained at autopsy were available for two workers. Two workers had small irregular lung opacities; HRCT revealed no parenchymal fibrosis in those workers. Nine workers, five of whom had been exposed to asbestos, had pleural plaques; multivariate logistic regression analyses revealed no association of plaques with the duration of wollastonite or asbestos exposure. Wollastonite fibres or bodies were not found in any of the four workers who underwent BAL, nor in either of the workers whose lung tissue specimens were

available. The authors concluded that no evidence was found that long-term exposure to wollastonite causes parenchymal fibrosis of the lung and pleura. They further concluded that the findings indicate that wollastonite fibres are poorly retained in human lungs.

Medical surveys have been conducted in 1976 (Shasby et al. 1979 – quoted from IARC 1987, 1997), in 1982 (Hanke et al. 1984), and in 1990 (Davis & Emerson 1990 – quoted from IUCLID 2000) in a US wollastonite production plant in Willsboro. Analysis of dust showed less than 2% free silica, and fibrous particulates with a median length of 2.5 μm and a median diameter of 0.22 μm. Concentrations of total dust are presented in Table 2 (section 1.6.2). The mean concentration of total dust ranged from 0.9 to 12 mg/m^3. Airborne fibre counts (PCOM) showed 0.3 fibres/cm^3 in the mine, and 23.3 fibres/cm^3 in the mill.
In 1976, 104 men were included representing 72% of all men with at least one year of exposure since 1952. The prevalence of symptoms of chronic bronchitis (23%) was higher in the exposed group than in workers in non-dusty occupations but was not related to years of exposure. Pneumoconiosis was observed in 4/76 wollastonite workers.
In 1982, 108 men (102 current workers; 6 former workers) were included representing 89% among current workers and 25% among former workers. Pneumoconiosis was observed in 3/108 wollastonite workers, but none showed a significant progression from their 1976 radiographs. Lung function tests showed dust-related changes in forced expiratory volume in one second (FEV_1), FEV_1/FVC (forced vital capacity) ratio, and peak flow rate, which were independent of age, height, and smoking habits. Workers with higher dust exposure had a significantly greater decline in peak flow than workers with lower exposures. No pleural change was noted. The authors concluded that long-term cumulative exposure to wollastonite may impair ventilatory capacity.
In 1990, 112 workers had chest radiographs and 110 had pulmonary function tested in a detailed health survey. Few workers (not further specified) were reported to have abnormalities on chest radiograph or moderate abnormalities of lung function. Wollastonite exposure appeared to have an additional adverse effect on small airways function in smokers, but not in non-smokers. Neither the intensity nor duration of employment proved to have significant independent effects on pulmonary function test results. The authors concluded that there are little or no primary adverse effects of wollastonite exposure on the respiratory health of the workers at this factory.

3.5 *In vitro* studies

The effects of wollastonite (origin not stated) and of crocidolite asbestos on the production of the chemotactic cytokine interleukin-8 (IL-8) in the absence of endogenous stimuli were assessed in a human lung type II epithelial cell line and in human bronchial epithelial cells. Stimulation of the epithelial cells by crocidolite provoked the induction of IL-8 whereas stimulation by wollastonite did not. (Rosenthal et al. 1994 – quoted from IARC 1997 and IUCLID 2000).

A dose of 0.5 mg/ml of a naturally occurring fibrous wollastonite from the USA and of a natural, almost non-fibrous specimen from Finland induced haemolysis of human red blood cells *in vitro*; however, these samples caused less haemolysis than non-fibrous synthetic wollastonite or chrysotile asbestos (Skaug & Gylseth 1983 – quoted from IARC 1987, 1997 and A&H 1992).

3.6 Toxicity to reproduction

No data have been found.

3.7 Mutagenic and genotoxic effects

No data have been found.

3.8 Carcinogenic effects

A cohort study of mortality has been conducted among 238 workers (192 males and 46 females) employed for at least one year in a Finnish limestone-wollastonite quarry (Huuskonen et al. 1983b).
The study covered the period 1923-1980 and expected deaths were calculated from national age- and sex-specific deaths rates for 1952-1972. By the end of 1980, 79 deaths (67 among males, 12 among females) had occurred in the cohort versus 96 expected (79 among males, 17 among females) on the basis of the general Finnish mortality rate. The causes of death showed no significant deviations from expectations for malignancies, cardiovascular diseases, all natural causes, or all causes of death.
Death was due to malignant neoplasms (all sites combined) for 8 men (13.2 expected) and 2 women (2.6 expected). Mortality from bronchial cancer was the cause of death in 4 men (5.0 expected) but in no women (0.2 expected). Other cancers included two ventricular cancers, one cancer of the rectum, one cancer of the lower lip, one melanoma, and one malignant retroperitoneal mesenchymal tumour. The last-mentioned tumour occurred in a 73-year-old non-smoking woman 30 years after first exposure; a pathological re-examination of the tumour concluded that the tumour was a poorly differentiated epithelial tumour, but mesothelioma could not be ruled out.
The mean concentrations of total dust in the mine and mill varied from 0.3 to 67 mg/m^3 and that of fibres from 5.1 to 33 $fibres/cm^3$ (PCOM) or from 2.6 to 52 $fibres/cm^3$ (SEM); for further details, see Table 1, section 1.6.2.
The IARC Working Group (IARC 1997) has *"noted a low statistical power of this study"*.

3.8.1 IARC evaluation

Based on the data presented in section 3.8, IARC (1997) has evaluated *"There is inadequate evidence in humans for the carcinogenicity of wollastonite"*.

4 Animal toxicity

4.1 Single dose toxicity

No data have been found.

4.2 Irritation

No data have been found.

4.3 Sensitisation

No data have been found.

4.4 Repeated dose toxicity

4.4.1 Inhalation / intratracheal instillation

Rats (Crl:CD CR) were exposed by inhalation to wollastonite (from Willsboro, USA) at different fibre dimensions (mass median aerodynamic diameters (MMAD) of 2.6, 4.3, or 5.8 μm; mean diameters of 0.2-3.0 μm) and fibre concentrations (50 or 100 mg/m^3; 123-835 fibres/cm^3) for 6 hours/day, for 3 or 5 days. Crocidolite asbestos (MMAD 2.2 μm; 40 mg/m^3; 12800 fibres/cm^3) was used as a positive control. Fibre exposed rats and age-matched sham controls were evaluated at 0, 24 and 48 hours, 15 days, or 1 month after exposure by analysing the enzyme and protein levels in bronchoalveolar lavage (BAL) fluids and the *in vitro* phagocytic capacities of alveolar macrophages recovered from fibre exposed rats. (Warheit et al. 1991 – quoted from IARC 1997 and IUCLID 2000).
Wollastonite exposure resulted in transient granulocytic pulmonary inflammatory responses and corresponding increases in lavage fluid parameters only when the MMAD was sufficiently small (i.e., 2.6 μm) and the concentration exceeded 500 fibres/cm^3 (according to the authors). A 6-hour inhalation exposure to crocidolite fibres produced a transient influx of neutrophils and eosinophils which returned to near normal levels within 8 days after exposure; BAL fluid lactate dehydrogenase and protein values remained significantly elevated throughout the month after exposure.
Macrophage function in wollastonite exposed alveolar macrophages was not significantly different from controls whereas crocidolite exposed macrophages were impaired in their phagocytic responses.
The method of fibre aerosol generation, the fibre aerodynamic size, the aerosol concentration and corresponding fibre number, and the exposure duration were all critical factors in producing wollastonite-related lung injury.

Male Fisher 344 rats (78 per group) were exposed to 10 mg/m^3 (360 fibres/cm^3) commercial wollastonite (from Willsboro, USA) by inhalation for 6 hours/day, on 5 days/week for either 12 or 24 months. Two additional groups of 78 male rats per group served as controls, one as an untreated chamber control and the other as a positive control exposed to chrysotile asbestos for 12 months at a concentration of

10 mg/m^3 (about 1000 fibres/cm^3). Six rats from each exposure group were sacrificed after 3, 12 and 24 months; the remaining rats were held for lifetime observation (until 90% mortality). (McConnell et al. 1991).
The wollastonite sample taken from the inhalation chamber had a diameter range of 0.1 to 1.0 μm; 15% of the fibres had a length > 5 μm; and the concentration of fibres with a length ≥ 5 μm, a diameter ≤ 3 μm and aspect ratio ≥ 3:1 was 54 fibres/cm^3.
Survival of wollastonite- and chrysotile-exposed rats was comparable to that of controls. Wollastonite produced a minimal amount of pulmonary pathology. Lesions were restricted to the terminal bronchioles and proximal alveoli and were characterised by the influx of small numbers of pulmonary macrophages, which were present both on the epithelial lining and in the lumina in this region. The lesions in rats exposed for 24 months were no more severe than those exposed for 12 months. The incidence of interstitial fibrosis was 0/56 in the control group, 0/57 in the group exposed to wollastonite for 12 months and 1/60 in the group exposed to wollastonite for 24 months. The incidence of bronchoalveolar hyperplasia was 3/56 in the control group, 0/57 in the group exposed to wollastonite for 12 months, and 0/60 in the group exposed to wollastonite for 24 months. Chrysotile produced significant fibrosis (50/52) and hyperplasia (30/52). The authors related the lack of evidence for fibrogenic response to the biodegradability of wollastonite. Neoplastic findings are described in section 4.5.1.
The IARC Working Group (IARC 1997) has *"noted the low number of wollastonite fibres in the exposure atmosphere with a fibre length > 5 μm"* and *"that the small number of fibres measured (117) was insufficient for a sound characterisation of the wollastonite"*.

Two types of wollastonite as well as other respirable fibre materials, including crocidolite asbestos, was instilled intratracheally into the lungs of male Wistar rats at a gravimetric dose of 25 mg bolus in 1 ml saline, which was estimated to contain a minimum of 3 x 10^9 particles/sample. The animals were sacrificed 3 months after exposure and the lungs were evaluated for hydroxyproline content, an indicator of fibrosis. Results showed that the fibres were respirable and only fibres < 3.5 μm in diameter reached the alveolar spaces. In rats exposed to wollastonite from China (geometric mean fibre length of 11.6 μm and diameter of 1.3 μm), the lung wet weights, lipid content and hydroxyproline levels were significantly increased compared with those of unexposed controls and were generally comparable to the effects produced by crocidolite exposure. In rats exposed to wollastonite from Willsboro, USA (geometric mean fibre length of 9.2 μm and diameter of 1.2 μm), a small increase in hydroxyproline levels was observed compared with controls. (Cambelova & Juck 1994 – quoted from IARC 1997, NOHSC 2001, Toxline 2003 and IUCLID 2000).
A further review by another pathologist (McConnell 1995 – quoted from NOHSC 2001, IARC 1997 and IUCLID 2000) stated that the fibrotic changes found in the study by Cambelova & Juck (1994) were due to the relatively large (25 mg) mass of dust given in one dose, and fibrosis would not have occurred if the fibres had been given by inhalation.

4.4.2 Other routes

The relationship between the biopersistence of wollastonite and crocidolite asbestos and the induction of mesothelial cell proliferation was examined in male C57B1/6 mice that received intraperitoneal injection with 200 μg to 10 mg of wollastonite (origin not stated), 20 μg to 1 mg crocidolite, or saline. Wollastonite and crocidolite caused dose dependent increases in mesothelial cell proliferation and fibre deposition on the inferior surface of the diaphragm; crocidolite was more

potent than wollastonite. Mesothelial cell proliferation returned to background levels within 56 days following injection of wollastonite while enhanced proliferation continued for 6 months following injection of crocidolite. Wollastonite and crocidolite caused a dose dependent inflammatory response, initially characterised by activated macrophages, and later, the number of lymphocytes was significantly increased. The inflammatory response decreased after 21 days. The initial histopathological response to fibres deposited on the diaphragm consisted of macrophage accumulation and multinucleated giant cell formation. Crocidolite elicited a greater and longer inflammatory response than wollastonite. Three days after injection with wollastonite or crocidolite, there were about 20-25 x 10^3 fibres/mm^2 deposited on diaphragm; with time, the number of crocidolite fibres increased, peaking at day 21, whereas the number of wollastonite fibres decreased. The authors concluded that biopersistent fibres, such as crocidolite, cause sustained inflammation and chronic mesothelial cell proliferation. (McDonald & Kane 1997 – quoted from HSDB 2003, Toxline 2003).

Female Sprague-Dawley rats (5 animals) were exposed by a single intraperitoneal injection to 100 mg of wollastonite (from India). The omenta of these rats were examined microscopically for mesothelial changes 26-28 months after exposure. A low level of mesothelial proliferation was observed, but no tumours. (Friemann et al. 1990).

4.4.3 *In vitro* studies

The effects of wollastonite (from Finland; fibre diameter approximately 0.5 μm; length 2-5 μm) on rat alveolar macrophages have been studied *in vitro*. After exposure to 25 μg/ml wollastonite, cell viability (trypan blue exclusion) was reduced by 15% and release of cytoplasmic lactate dehydrogenase was increased by 125% within 24 hours. No significant effect was observed on β-glucuronidase release. Wollastonite was more toxic than titanium dioxide but less toxic than crocidolite asbestos. Macrophages took up less wollastonite than crocidolite one hour after exposure. (Pasanen et al. 1983 – quoted from IARC 1987 and IUCLID 2000).

The effects of wollastonite (from USA; most fibres 4-9 μm in length) and of crocidolite asbestos on the viability, morphology, and functional capacities of rat pulmonary macrophages were assessed *in vitro*. Wollastonite and crocidolite had little effect upon macrophage viability (about 95% viability). In crocidolite-exposed cells, the morphology was changed and the phagocytic capacity was impaired. The morphology of macrophages exposed to wollastonite was not altered whereas the phagocytic capacity was impaired, but to a lesser extent than crocidolite. Using a chemotaxis bioassay, wollastonite and crocidolite activated rat serum complement. (Warheit et al. 1984).

The cytotoxicity of samples of US wollastonite (50% of fibres > 10 μm in length) and Finnish wollastonite (3% of fibres > 7 μm in length) were assessed by lactate dehydrogenase and β-glucuronidase release by mouse peritoneal macrophages. Induction of a dose-dependent release of β-glucuronidase was observed for Finnish wollastonite and a lower induction by US wollastonite 18 hours after exposure. Concentrations of up to 40 μg/ml of US wollastonite did not induce release of lactate dehydrogenase whereas the Finnish sample induced a significant release. (Skaug et al. 1984 – quoted from IUCLID 2000).

Measurements of biochemical indices of cytotoxicity indicated that wollastonite (from USA; 98% ≤ 8 μm) caused no significant effects on rabbit alveolar macrophages *in vitro* whereas chrysotile asbestos was cytotoxic (Pailes et al. 1984).

When tracheal explants prepared from female Sprague-Dawley rats were exposed to cigarette smoke or air and then to wollastonite (origin not stated) dust, cigarette smoke did not significantly increase the epithelial uptake of wollastonite. In contrast, cigarette smoke increased the uptake of asbestos fibres. (Keeling et al. 1993 – quoted from IARC 1997 and IUCLID 2000).

Less lipid peroxidation (evaluated by malondialdehyde formation) occurred when rat hepatocytes were incubated *in vitro* with wollastonite (three different samples from India) compared with chrysotile asbestos (Aslam et al. 1992 – quoted from IARC 1997, HSDB 2003, Toxline 2003 and IUCLID 2000).
Similarly, less haemolysis and less lipid peroxidation occurred in human erythrocytes incubated *in vitro* with wollastonite (three different samples from India; dust concentrations of 1.0-5.0 mg/ml) compared with chrysotile asbestos (Aslam et al. 1995 – quoted from IARC 1997, Toxline 2003 and IUCLID 2000).

4.5 Toxicity to reproduction

No data have been found.

4.6 Mutagenic and genotoxic effects

4.6.1 *In vitro* studies

Wollastonite has been evaluated for mutagenicity in the Salmonella/microsome preincubation assay using the standard protocol approved by the National Toxicology Program in USA. Wollastonite was tested in *Salmonella typhimurium* strains TA98, TA100, TA1535, and TA1537 in the presence and absence of Arochlor-induced rat or hamster liver S9 at doses from 0 to 10,000 μg/plate. Wollastonite was negative in these tests and the highest ineffective concentration tested (not producing a precipitate) was 1000 μg/plate. (Zeiger et al. 1987).

Neither chromosomal aberrations nor polyploidy were induced in Chinese hamster CHL cells exposed to wollastonite (from Canada; mostly long and thick fibres) for 48 hours in the absence of an exogenous metabolic system at doses of up to 300 μg/ml (Koshi et al. 1991 – quoted from IARC 1997 and IUCLID 2000).

The genotoxic effect of wollastonite has been studied human primary mesothelial cells *in vitro*. Wollastonite was reported to increase the number of aberrant mesothelial cells in the dose range of 0.5 to 5 $\mu g/cm^2$; however, without a dose response. No further details are available (abstract). (Jantunen et al. 1989).

Wollastonite (from China; 62% of the fibres with a length > 5 μm; 62.5% < 1 μm in diameter) induced morphological transformation in Syrian hamster embryo cells after a single exposure without an exogenous metabolic system; the lowest effective dose was 20 μg/ml. The transformation rate induced by N-methyl-N-nitro-N-nitrosoguanidine was also elevated after several exposures to wollastonite. (Liu et al. 1993 – quoted from IARC 1997 and IUCLID 2000).

4.6.2 *In vivo* studies

No data have been found.

4.7 Carcinogenic effects

4.7.1 Inhalation

Male Fisher 344 rats (78 per group) were exposed to 10 mg/m^3 (360 fibres/ml) commercial wollastonite (from Willsboro, USA) by inhalation for 6 hours/day, on 5 days/week for either 12 or 24 months. Two additional groups of 78 male rats per group served as controls, one as an untreated chamber control and the other as a positive control exposed to chrysotile asbestos for 12 months at a concentration of 10 mg/m^3 (about 1000 fibres/cm^3). Six rats from each exposure group were sacrificed after 3, 12 and 24 months; the remaining rats were held for lifetime observation (until 90% mortality). (McConnell et al. 1991).
The wollastonite sample taken from the inhalation chamber had a diameter range of 0.1 to 1.0 μm; 15% of the fibres had a length > 5 μm; and the concentration of fibres with a length ≥ 5 μm, a diameter ≤ 3 μm and aspect ratio ≥ 3:1 was 54 fibres/cm^3.
Survival of wollastonite- and chrysotile-exposed rats was comparable to that of controls. The incidence of bronchoalveolar adenoma or carcinoma (combined) was 1/56 in the chamber control group, 0/57 in the group treated with wollastonite for 12 months, 1/60 in the group treated with wollastonite for 24 months, and 20/52 in the chrysotile-exposed group. The authors related their lack of evidence for carcinogenic response to the biodegradability of wollastonite. Non-neoplastic findings are described in section 4.2.1.
The IARC Working Group (IARC 1997) has *"noted the low number of wollastonite fibres in the exposure atmosphere with a fibre length > 5 μm"* and *"that the small number of fibres measured (117) was insufficient for a sound characterisation of the wollastonite"*.

4.7.2 Other routes

Osborne-Mendel rats (30-50 females per group) received 40 mg/animal wollastonite uniformly dispersed in hardened gelatine directly on the left pleural surface by open thoracotomy and were followed for two years. Four separate grades of wollastonite from the same Canadian mine, with a length 4-8 μm and a diameter < 0.25-2.5 μm were used except grade 4 which contained relatively few fibres of these dimensions. The 40-mg doses of these four grades were 140 x 10^6 fibres (grade 1), 10 x 10^6 fibres (grade 2), 200 x 10^6 fibres (grade 3), and 10.4 x 10^6 fibres (grade 4). The incidences of pleural sarcomas were 5/20 (grade 1), 2/25 (grade 2), 3/21 (grade 3), and 0/24 (grade 4) compared with 14/29 for a positive control group treated with 40 mg crocidolite asbestos, 3/488 for untreated controls, 9/432 in a control group receiving 'non-carcinogenic' pulmonary implants of 'non-fibrous materials', and 17/598 in a control group receiving 'noncarcinogenic'pleural implants of 'non-fibrous materials'. (Stanton et al. 1981).
According to IARC (1987) *"the incidence of pleural sarcomas was statistically significantly higher (p<0.05, Fisher exact test) in groups receiving grades 1 and 3 than in the controls receiving pleural implants"*; this comment was not included in IARC (1997).
The IARC Working Group (IARC 1997) has *"noted that the number of fibres was low"* and *"the lack of data on the composition and purity of the samples and on the survival of the rats, and that none of the grades of wollastonite contained fibres >*

8 μm in length and < 0.25 μm in diameter (the hypothetical range for maximal carcinogenesis)".

A group of 54 female Wistar rats received five intraperitoneal injections (once a week) of 20 mg/animal of wollastonite (from India) in saline. The number of fibres in this wollastonite sample (from India) with a length > 5 μm, diameter < 3 μm and aspect ratio > 5:1 was 430 x 10^6; the median fibre length was 8.1 μm and the median fibre diameter was 1.1 μm. No abdominal tumours (mesothelioma or sarcoma) were observed; the median life span was 107 weeks. In a positive control group treated with 0.05 mg actinolite asbestos, 15/36 abdominal tumours were observed; the median survival was 101 weeks. In a negative control group receiving the same number of injections of saline, 2/102 abdominal tumours were observed; the median survival was 111 weeks. (Pott et al. 1987, Pott et al. 1989 – quoted from IARC 1997 and IUCLID 2000).

In another study with intraperitoneal injection of wollastonite (obtained from a Belgian company), a group of 50 female Wistar rats was treated with two injections of a suspension of 30 mg wollastonite/animal in saline with a time interval of one week between injections. The median fibre length was 5.6 μm and the median fibre diameter was 0.71 μm. Surviving animals were killed 130 weeks after the start of treatment. No abdominal tumours were observed. In a positive control group treated with 3 mg crocidolite asbestos, abdominal tumours were observed in 32/50 rats. In a negative (saline) control group, no abdominal tumours were detected (0/50). (Muhle et al. 1991, Rittinghausen et al. 1991,1992 – quoted from IARC 1997, NOHSC 2001 and IUCLID 2000).

No tumours were observed in female Sprague-Dawley rats (5 animals) exposed by a single intraperitoneal injection of 100 mg of wollastonite (from India) and examined microscopically for mesothelial changes 26-28 months after exposure (Friemann et al. 1990).

4.7.3 IARC evaluation

Based on the data presented in section 4.7, IARC (1997) has evaluated "*There is inadequate evidence in experimental animals for the carcinogenicity of wollastonite"*.

5 Regulations

5.1 Ambient air

Denmark (C-value): 1300 fibre/m^3, Main Group 1 (MST 2002).

5.2 Drinking water

-

5.3 Soil

-

5.4 Occupational Exposure Limits

Denmark:	1 fiber/cm^3 (At 2005). This OEL was set in 1988 in accordance with the OEL for ceramic fibres.
ACGIH:	-
Germany:	-

5.5 Classification

-

5.6 IARC

Based on the data presented in sections 3.8 and 4.7, IARC (1997) has evaluated that *"Wollastonite cannot be classified as to its carcinogenicity to humans (Group 3). There is inadequate evidence in humans and in experimental animals for the carcinogenicity of wollastonite"*.

5.7 US-EPA

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6 Summary and evaluation

6.1 Description

Natural wollastonite is an acicular (needle-like) calcium silicate mineral that occurs in coarse-bladed crystal masses. It is white when pure; may be grey, pale green yellowish brown or red with impurities. The solubility in water is < 1 mg/ml.

6.2 Environment

Wollastonite occurs most commonly in nature where limestone has reacted at high temperature with igneous rock. Ores from the major wollastonite deposits contain 18-97% wollastonite. Wollastonite in the environment also results from its use in industrial products.

No data on environmental concentrations or fate have been found.

6.3 Human exposure

The general population can be exposed to airborne wollastonite emitted from production facilities and from products that contain wollastonite; no exposure data have been found.

Occupational exposure to wollastonite occurs during its mining, milling, production and use.
In a Finnish wollastonite production plant, the mean concentration of total dust in various operations ranged from 0.3 to 67 mg/m^3 and the mean concentration of fibres varied from 5.1 to 33 fibres/cm^3 (counting by PCOM) or from 23 to 52 fibres/cm^3 (counting by SEM, same sites as PCOM). The median fibre lengths and median diameters were 4 μm and 0.8 μm, respectively, in crushing operations and 2 μm and 0.4 μm, respectively, in bagging work; the thinnest fibres were characteristically 0.2-0.3 μm in diameter.
In a US wollastonite production plant, the mean concentration of total dust ranged from 0.9 to 12 mg/m^3 and airborne fibre counts (PCOM) showed 0.3 fibres/cm^3 in the mine, and 23.3 fibres/cm^3 in the mill. Fibrous particles had a median diameter of 0.22 μm and a median length of 2.5 μm.
Regarding occupational exposure to wollastonite during use, airborne respirable fibre levels in the range of 0.02-0.2 fibres/cm^3 have been reported.

6.4 Toxicokinetics

In one study, inhaled wollastonite fibres were cleared rapidly from the lungs of rats with a retention half time of less than one week. Within one month, mean fibre lengths decreased from 11 μm to 6 μm and mean fibre diameters increased from 0.5 μm to 1.0 μm indicating that the wollastonite fibres were readily solubilised and of low durability and biopersistence. In another study with intratracheal instillation of wollastonite into rats, elimination of wollastonite fibres from the lung

of rats was relatively fast (half-times of 15-21 days) and was predominantly due to the dissolution of fibres.

No other data regarding the toxicokinetics of wollastonite in experimental animals or in humans have been found.

6.5 Human toxicity

6.5.1 Single dose toxicity, irritation and sensitisation

No data have been found.

6.5.2 Repeated dose toxicity

In a clinical study of 46 men exposed to wollastonite in a Finnish wollastonite production plant (10-41 years), chest radiographs revealed slight lung fibrosis among 14 men, and slight bilateral pleural thickening among 13 men. Spirometry and nitrogen single breath tests indicated the possibility of small airways disease. The mean concentrations of total dust in the mine and mill varied from 0.3 to 67 mg/m^3 and that of fibres from 5.1 to 33 fibres/cm^3 (PCOM) or from 2.6 to 52 fibres/cm^3 (SEM).
In a follow-up study among 49 workers (40 men and 9 women), two workers had small irregular lung opacities; high-resolution computerised tomography revealed no parenchymal fibrosis in those workers. Nine workers, five of whom had been exposed to asbestos, had pleural plaques; no association of plaques with the duration of wollastonite or asbestos exposure was revealed. Wollastonite fibres or bodies were not found in any of the four workers who underwent BAL, nor in either of the workers whose lung tissue specimens were available. Dust measurements (PCOM) revealed fibre concentrations ranging from 0.04 to 3.4 fibres/cm^3 for wollastonite mining and milling and from 0.09 to 1.2 fibres/cm^3 for calcite mining and milling.
The median fibre lengths and median diameters in the production plant were 4 μm and 0.8 μm, respectively, in crushing operations and 2 μm and 0.4 μm, respectively, in bagging work; the thinnest fibres were characteristically 0.2-0.3 μm in diameter.

Medical surveys have been conducted in 1976, 1982, and in 1990 in a US wollastonite production plant in Willsboro. Analysis of dust showed fibrous particulates with a median length of 2.5 μm and a median diameter of 0.22 μm. The mean concentration of total dust ranged from 0.9 to 12 mg/m^3. Airborne fibre counts (PCOM) showed 0.3 fibres/cm^3 in the mine, and 23.3 fibres/cm^3 in the mill.
In 1976, the prevalence of symptoms of chronic bronchitis (23%) was higher in the exposed group (104 men) than in workers in non-dusty occupations but was not related to years of exposure. Pneumoconiosis was observed in 4/76 wollastonite workers.
In 1982, pneumoconiosis was observed in 3/108 wollastonite workers (men). Workers with higher dust exposure had a significantly greater decline in peak flow than workers with lower exposures. No pleural change was noted.
In 1990, few workers (not further specified) were reported to have abnormalities on chest radiograph (112 workers examined) or moderate abnormalities of lung function (110 workers examined). Wollastonite exposure appeared to have an additional adverse effect on small airways function in smokers, but not in non-smokers.

6.5.3 Toxicity to reproduction

No data have been found.

6.5.4 Mutagenic and genotoxic effects

No data have been found.

6.5.5 Carcinogenic effects

In a cohort study of mortality conducted among 192 male and 46 female workers at the Finnish wollastonite production plant, 79 deaths had occurred in the cohort versus 96 expected. Death was due to malignant neoplasms (all sites combined) for 8 men (13.2 expected) and two women (2.6 expected). Mortality from bronchial cancer was the cause of death in 4 men (5.0 expected) but in no women (0.2 expected). There was one rare abdominal tumour; mesothelioma could not be ruled out. The mean concentrations of total dust in the mine and mill varied from 0.3 to 67 mg/m^3 and that of fibres from 5.1 to 33 fibres/cm^3 (PCOM) or from 2.6 to 52 fibres/cm^3 (SEM).

6.6 Animal toxicity

6.6.1 Single dose toxicity, irritation and sensitisation

No data have been found.

6.6.2 Repeated dose toxicity

The pulmonary effects of short-term (6 hours/day for 3 or 5 days) high-dose inhalation exposure to wollastonite (from Willsboro, USA) at different fibre dimensions (MMAD of 2.6, 4.3, or 5.8 μm; mean diameters of 0.2-3.0 μm) and fibre concentrations (50 or 100 mg/m^3; 123-835 fibres/cm^3) have been evaluated by analysing the enzyme and protein levels in bronchoalveolar lavage (BAL) fluids and the *in vitro* phagocytic capacities of alveolar macrophages recovered from fibre exposed rats. Wollastonite exposure resulted in a transient pulmonary inflammatory response only when the MMAD was 2.6 μm and the concentration exceeded 500 fibres/cm^3. Macrophage function in wollastonite exposed alveolar macrophages was not significantly different from controls.

In a study in rats exposed to wollastonite (from Willsboro, USA) at 10 mg/m^3 (360 fibres/cm^3) by inhalation for 6 hours/day, on 5 days/week for either 12 or 24 months, wollastonite produced a minimal amount of pulmonary pathology which was restricted to the terminal bronchioles and proximal alveoli and were characterised by the influx of small numbers of pulmonary macrophages; the lesions in rats exposed for 24 months were no more severe than those exposed for 12 months. The incidence of interstitial fibrosis was 0/56 in the control group, 0/57 in the group exposed to wollastonite for 12 months and 1/60 in the group exposed to wollastonite for 24 months. The incidence of bronchoalveolar hyperplasia was 3/56 in the control group, 0/57 in the group exposed to wollastonite for 12 months, and 0/60 in the group exposed to wollastonite for 24 months.

6.6.3 Toxicity to reproduction

No data have been found.

6.6.4 Mutagenic and genotoxic effects

A sample of wollastonite from China induced morphological transformation of Syrian hamster cells (lowest effective dose: 20 μg/ml). Wollastonite has also been reported to increase the number of aberrant human primary mesothelial cells *in vitro* (dose range of 0.5 to 5 μg/cm^2); however, without a dose response. Neither chromosomal aberrations nor polyploidy were induced in cultured Chinese hamster lung cells (doses of up to 300 μg/ml). Wollastonite was negative in Ames tests (highest ineffective concentration tested (not producing a precipitate): 1000 μg/plate).

6.6.5 Carcinogenic effects

In a study in rats, no increase in tumour incidence was observed following exposure to wollastonite at 10 mg/m^3 (360 fibres/cm^3) wollastonite by inhalation for 6 hours/day, on 5 days/week for either 12 or 24 months. The wollastonite had a diameter range of 0.1 to 1.0 μm; 15% of the fibres had a length > 5 μm. The number of fibres with a length ≥ 5 μm, a diameter ≤ 3 μm and aspect ratio ≥ 3:1 would be approximately 54 fibres/cm^3.

Four grades of wollastonite (length 4-8 μm and a diameter < 0.25-2.5 μm were used except grade 4 which contained relatively few fibres of these dimensions) were tested for carcinogenicity in a study in rats by intrapleural implantation of 40 mg/animal. The incidences of pleural sarcomas were 5/20 (grade 1), 2/25 (grade 2), 3/21 (grade 3), and 0/24 (grade 4) compared with 14/29 for a positive control group treated with 40 mg crocidolite asbestos. According to IARC (1987) *"the incidence of pleural sarcomas was statistically significantly higher ($p<0.05$, Fisher exact test) in groups receiving grades 1 and 3 than in the controls receiving pleural implants"*; this comment was not included in IARC (1997).

In female rats, which received either five intraperitoneal injections (once a week) of 20 mg/animal wollastonite or two injections of a suspension of 30 mg wollastonite in saline with a time interval of one week between injections, no abdominal tumours were observed. In the positive control groups treated with either 0.05 mg actinolite asbestos or 3 mg crocidolite asbestos, 15/36 or 32/50 abdominal tumours were observed, respectively. The median fibre lengths were 8.1 μm or 5.6 μm, respectively, and the median fibre diameters were 1.1 μm or 0.71 μm, respectively.

6.7 Evaluation

Generally, the main determinants of fibre toxicity are considered to be the internal dose to the target tissue, fibre size, and fibre biopersistence/durability. Numerous studies on fibres indicate that fibre toxicity increases with increasing durability. The length of time that fibres persist in the tissue is a function of their durability, which is directly related to their chemical composition and physical characteristics. Fibres of less than 3.5 μm in diameter and 200 μm in length have been reported to be respirable and fibres from 0.25 to 1.5 μm in diameter and

above 4-8 μm in length have been reported to possess the greatest carcinogenic potential.

For wollastonite, the individual particles commonly exhibit an aspect ratio of 7:1 or 8:1 and have an average diameter of 3.5 μm (IARC 1997); no information about the average length was given. Based on this information, wollastonite fibres are considered to respirable to some extent, whereas the carcinogenic potential is expected to be low.
At the two major wollastonite production sites (Lappenranta, Finland, and Willsboro, N.Y., US), the median fibre lengths and diameters of wollastonite fibres in the Finnish plant were 2-4 μm and 0.4-0.8 μm, respectively, and the thinnest fibres were characteristically 0.2-0.3 μm in diameter. In the US plant, a median length of 2.5 μm and a median diameter of 0.22 μm of wollastonite fibres were reported. Based on this information, most of the wollastonite fibres in the dust samples are considered as being respirable. The median diameters, but not the median lengths, of wollastonite fibres in these two plants may point at a carcinogenic potential.

Results obtained in a recent follow-up study among workers in the Finnish wollastonite production plant (Koskinen et al. 1997) indicate that wollastonite fibres are poorly retained in human lungs. This finding is supported by the available studies (inhalation, intratracheal instillation) in experimental animals (only rat studied), which indicate that wollastonite fibres are cleared rapidly from the lungs with a retention half-time of less than one week following inhalation; the elimination was reported to be predominantly due to the dissolution of fibres and it was concluded that wollastonite has a low durability in the lungs of rats.

One cohort mortality study of workers in the Finnish wollastonite production plant is available in which the observed number of deaths from all cancers combined as well as from lung cancer were lower than expected. There was one rare abdominal tumour for which a mesothelioma could not be ruled out. IARC (1997) has *"noted a low statistical power of this study"*.
Only one long-term inhalation study in rats is available, which showed no increase in tumour incidence following exposure at 10 mg/m^3 (360 fibres/cm^3) wollastonite. According to IARC (1997) *"this study only has a limited value for an evaluation of carcinogenicity"* because *"the number of fibres with a length > 5 μm and a diameter < 3 μm was relatively low (about 54 fibres/cm^3)"*. A slight increase in the incidence of pleural sarcomas has been observed in female rats with three grades of wollastonite (fibres > 4 μm in length and < 0.5 μm in diameter) following intrapleural implantation; pleural sarcomas were not observed following implantation of a grade that contained relatively few fibres with these dimensions. According to IARC (1987) *"the incidence of pleural sarcomas was statistically significantly higher (p<0.05, Fisher exact test) in groups receiving grades 1 and 3 than in the controls receiving pleural implants"*; this comment was not included in IARC (1997). In two studies in rats in which wollastonite (median fibre lengths of 8.1 μm and 5.6 μm, respectively, and median fibre diameters of 1.1 μm or 0.71 μm, respectively) was administered by intraperitoneal injection, no abdominal tumours were observed.
Based on these data on carcinogenicity, IARC (1997) has evaluated that "*Wollastonite cannot be classified as to its carcinogenicity to humans (Group 3)*" (inadequate evidence in humans and in experimental animals for the carcinogenicity of wollastonite).
Whether wollastonite may possess a carcinogenic potential to humans cannot be fully excluded based on the available data; however, the potential is considered to be low because wollastonite seems to be cleared fairly rapidly from the lungs of

humans (and rats) predominantly due to the dissolution of the fibres and consequently, to be of low durability/biopersistence. Furthermore, the fibre dimensions of wollastonite at the two major production sites also point at a low carcinogenic potential of wollastonite fibres.

Data on health effects in workers at the two major wollastonite production sites (Lappenranta, Finland, and Willsboro, N.Y., US) indicate that occupational exposure may cause impaired respiratory function and slight lung fibrosis (pneumoconiosis). The mean concentrations of total dust in the Finnish wollastonite production plant varied from 0.3 to 67 mg/m^3 and that of fibres from 5.1 to 33 fibres/cm^3 (PCOM) or from 2.6 to 52 fibres/cm^3 (SEM). In the US wollastonite production plant in Willsboro, the mean concentration of total dust ranged from 0.9 to 12 mg/m^3 and airborne fibre counts (PCOM) showed 0.3 fibres/cm^3 in the mine, and 23.3 fibres/cm^3 in the mill.
In a recent follow-up study among workers in the Finnish plant (Koskinen et al. 1997), no evidence was found that long-term exposure to wollastonite causes parenchymal fibrosis of the lung and pleura; dust measurements (PCOM) revealed fibre concentrations ranging from 0.04 to 3.4 fibres/cm^3 for wollastonite mining and milling. Similarly, a medical survey conducted in the US wollastonite production plant in Willsboro in 1990 only reported a few workers (not further specified) to have abnormalities on chest radiograph or moderate abnormalities of lung function; no information about dust or fibre concentrations was given.

One long-term inhalation study in rats exposed to wollastonite (10 mg/m^3; 360 fibres/cm^3) indicated that wollastonite is slightly toxic to the lung and produced an alveolar macrophage response, which resolved after cessation of exposure; no significant inflammation or fibrosis was observed. The wollastonite sample taken from the inhalation chamber had a diameter range of 0.1 to 1.0 μm; 15% of the fibres had a length > 5 μm; and the concentration of fibres with a length ≥ 5 μm, a diameter ≤ 3 μm and aspect ratio ≥ 3:1 was 54 fibres/cm^3.
Following short-term (3-5 days) high-dose (50 or 100 mg/m^3; 123-835 fibres/cm^3) inhalation exposure of rats to wollastonite at different fibre dimensions (MMAD of 2.6, 4.3, or 5.8 μm; mean diameters of 0.2-3.0 μm) resulted in a transient pulmonary inflammatory response only when the MMAD was 2.6 μm and the concentration exceeded 500 fibres/cm^3; macrophage function in wollastonite exposed alveolar macrophages was not significantly different from controls.

No data are available for an evaluation of the acute toxicity, irritative effects or sensitising potential of wollastonite to humans or to experimental animals. However, these effects are not considered to be of particular significance to humans following exposure to wollastonite as no symptoms indicative of such effects have been reported among workers at the two major wollastonite production sites (Lappenranta, Finland, and Willsboro, N.Y., US).

No data are available in order to evaluate the reproductive or developmental toxicity of wollastonite to humans or to experimental animals. However, such effects are not expected to occur following inhalation exposure to wollastonite because the fibres will predominantly be retained in the respiratory tract rather than being absorbed and consequently, no exposure of the reproductive tissues or foetus.

Equivocal results have been reported in the few *in vitro* tests available regarding mutagenicity and genotoxicity; therefore, no conclusion can be drawn for these end-points. However, such effects are not expected to occur systemically following inhalation exposure to wollastonite because the fibres will predominantly be retained in the respiratory tract rather than being absorbed. Whether cells in the respiratory tract may be affected cannot be excluded based on the available data;

however, wollastonite fibres are generally not expected to enter cells with the exception of macrophages, which have phagocytic properties.

6.7.1 Critical effect and NOAEL

The critical effect following inhalation exposure to wollastonite is considered to be the effects observed in the respiratory tract (impaired respiratory function and slight lung fibrosis) of workers at the two major wollastonite production sites (Lappenranta, Finland, and Willsboro, N.Y., US) and of rats (transient inflammation and very slight signs of fibrosis) in the long-term inhalation study.

In the Finnish plant, mean concentrations of total dust in 1981varied from 0.3 to 67 mg/m^3 and that of fibres from 5.1 to 33 $fibres/cm^3$ (PCOM) or from 2.6 to 52 $fibres/cm^3$ (SEM) at that time where the effects in the respiratory tract of the workers were observed (Huuskonen et al. 1983a). In the US plant, the mean concentration of total dust ranged from 0.9 to 12 mg/m^3 and airborne fibre counts (PCOM) showed 23.3 $fibres/cm^3$. However, in the follow-up study of workers in the Finnish plant (Koskinen et al. 1997), no evidence was found that long-term exposure to wollastonite caused parenchymal fibrosis of the lung and pleura; dust measurements (PCOM) revealed fibre concentrations ranging from 0.04 to 3.4 $fibres/cm^3$ for wollastonite mining and milling. For the purpose of establishing a health base quality criterion in ambient air, the fibre concentration of 3.4 $fibres/cm^3$ is considered as a NOAEC for effects observed in the respiratory tract of humans. The rationale behind this choice is that respiratory tract effects were not observed in the more recent study at fibre concentrations ranging from 0.04 to 3.4 $fibres/cm^3$.

7 Quality criterion in ambient air

The quality criterion in air QC_{air} is calculated based on a NOAEC of 3.4 fibres/cm^3 observed for effects observed in the respiratory tract of humans in the study by Koskinen et al. (1997). The NOAEC is adjusted to a continuous NOAEC of 0.8 fibres/cm^3 assuming that the workers in the Finnish plant have been exposed 8 hours per day for 5 days per week:

$$QC_{air} = \frac{NOAEC}{UF_I * UF_{II} * UF_{III}} = \frac{0.8 \text{ fibres/cm}^3}{1 * 10 * 20}$$

$$= 0.004 \text{ fibres/cm}^3 = 4000 \text{ fibres/m}^3$$

The uncertainty factor UF_I is set to 1 as human data are used. The UF_{II} accounting for intraspecies variability is set to 10 reflecting the range in biological sensitivity within the human population. The UF_{III} is set to 20 because of the uncertainty related to the NOAEC and because only a limited number of workers (49) have been examined at the Finnish plant; a factor of 20 is considered adequate because the carcinogenic potential of wollastonite is considered to be very low, if any, as wollastonite seems to be cleared fairly rapidly from the lungs of humans (and rats) predominantly due to the dissolution of the fibres and consequently, to be of low durability/biopersistence.

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Evaluation of health hazards by exposure to Wollastonite and proposal of a health-based quality criterion for ambient air

The Danish Environmental Protection Agency has requested an evaluation of health hazards by exposure to Wollastonite. This resulted in 2006 in the present report which includes a health-based quality criterion for the substance in ambient air.

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