Danish Ministry of the Environment
Environmental Protection Agency

Mineral wools (glass, stone/slag, HT)

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

Environmental Project No. 1515, 2013

Title:

Evaluation of health hazards by exposure to Mineral wools (glass, stone/slag, HT) and proposal of a health-based quality criterion for ambient air

Author:

Elsa Nielsen
Pia Nørhede
Ole Ladefoged
Lea Tobiassen
Division of Toxicology and Risk Assessment
National Food Institute, Technical University of Denmark

Published by:

The Danish Environmental Protection Agency
Strandgade 29
1401 Copenhagen K
Denmark
www.mst.dk/english

Year:

Authored in 2010
Published in 2013

ISBN no.

978-87-93026-68-1

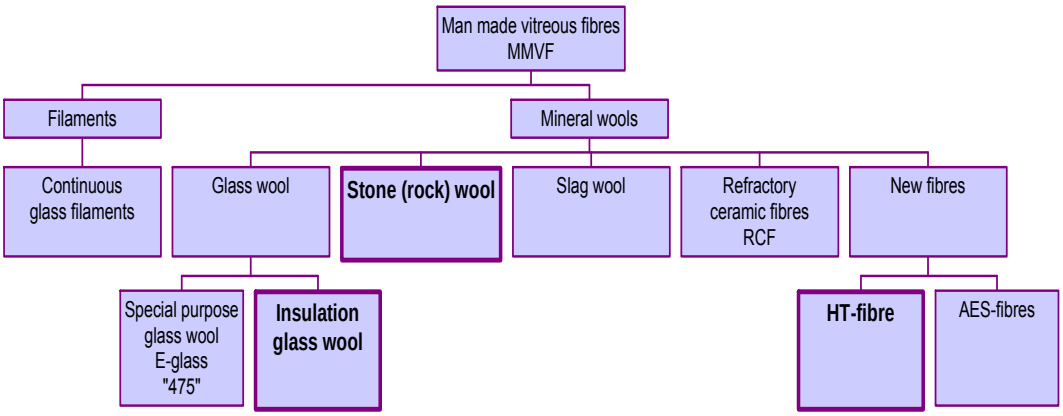
Content

1 General description

1.1 Identity

"Mineral wool" designates a subgroup of man made vitreous (or mineral) fibres composed of tangled, discontinuous fibres. Man-made vitreous fibres (MMVF) are inorganic, non-crystalline fibrous materials manufactured from glass, stone (rock), slag or other processed minerals. The most common types of MMVF are insulation wools, (glass, stone and slag wool), continuous glass filaments, special purpose glass fibres and refractory (ceramic) fibres. The term "mineral wool" is used in Europe to cover glass, stone (rock) and slag wool and new fibre types. In the USA however, this term covers only stone (rock) wool. In this document, the European meaning of "mineral wool" is used.

Diagram 1: Categories of Man-made vitreous fibres



This evaluation includes the mineral wools produced in Denmark, that is insulation glass wool, stone (and slag) wool and the new HT-fibre (high-alumina, low-silica wool used for insulation). These fibre types are indicated in bold in Diagram 1.

No CAS numbers have been attributed to the elder types of mineral wools. The HT-fibre has CAS no. 287922-11-0.

1.1.1 Terminology

Definitions of categories of fibres, synonyms and product names are listed below:

Man-made vitreous fibres: Man made mineral fibres, synthetic vitreous fibres.

Glass fibres: Continuous glass filaments, glass wool and special purpose glass fibres.

Continuous glass filaments: E-glass, textile glass.

Glass wool: TEL; fibreglass insulation; Fiberglas®; MMVF10 (= Manville 901 glass wool); MMVF10a; MMVF11(= Certain Teed B glass wool).

Special purpose glass: glass micro fibres; Micro-Fiber®; fine fibres; ultra fine fibres; A diameter fibres; B diameter fibres, AA diameter fibres.

Stone(rock) wool: Rockwool®; basalt wool; mineral wool (US); M-stone wool; R-stone wool-E3; MMVF21(Rockwool International basalt-based stone wool).

Slag wool: MMVF22 (USG Interiors blast-furnace slag wool).

HT-fibre: HT stone wool; HT-wool; MMVF34.

WHO-fibre = respirable fibre: Fibre with a length > 5 μm, a diameter < 3 μm and a length-diameter ratio > 3:1.

1.2 Physical / chemical properties

1.2.1 Composition

SiO_2 is the principal constituent of most MMVFs. Lesser amounts of "intermediate oxides" such as Al_2O_3, TiO_2 and ZrO_2 are used as stabilizers. These oxides increase the chemical and heat resistance of the fibres. "Modifiers" (or fluxes) as CaO, MgO, BaO, Na_2O, K_2O and Li_2O decrease the durability of fibres. (CEPA 2001). In the 1990's, the traditional composition of fibres has been modified in order to obtain less biopersistent fibres: The content of alkali oxide and borate has been increased in glass wools, alkaline earth oxides has been substituted to alumina in stone wools and developing high-temperature resistant alkaline earth silicate wools (AES) as an alternative to aluminosilicate refractory ceramic fibres. (IARC 2002)

Table 1.1 gives the typical compositional ranges of oxides for different types of mineral wool.

1.2.2 Fibre dimensions

Fibre diameters vary with the fibre type and the manufacturing process employed. The wools have average diameters of 3-10 μm, with a range from 1 to 20 μm. Also, "shots", rounded particles of approximately 60 μm in diameter are formed in some wool production processes. Sizes of fibres are often referred to as length-weighted diameters (LWD). Normally the length-width ratio of fibres is of at least 3:1. (IARC 2002).
Table 1.2 lists dimensions and shot content for various MMVFs.

The fibrous character and the aerodynamics of MMVFs (depending upon fibre length, shape and density) lead to comparison with asbestos, which is a known carcinogen by inhalation. However, unlike asbestos, MMVFs break transversely rather than cleaving along the fibre axis. This difference is important for the clearance of the fibres from the lungs. (IARC 1988; IARC 2002).

Table 1.1. Compositional ranges for MMVF categories expressed as weight percentage of oxides (from IARC 2002).

Fiber type / Chemical component	Conti-nuous glass filaments	Special purpose glass fibres	Insula-tion glass wool	Stone (rock) wool	Slag wool	RCF	HT-fibre	AES-wool
SiO_2	52-75	54-69	55-70	43-50	38-52	47-54	33-43	50-82
Al_2O_3	0-30	3-15	0-7	6-15	5-16	35-51	18-24	<2
CaO+MgO	1-25	0-25.5	5-18	16-41	24-57	<2	23-33	18-43
BaO	0-1	0-5.5	0-3					
ZnO	2-5	0-4.5						
Na_2O+K_2O	0-21	0-31	12-20.5	1.5- 5.5	0.3-3	<2	1-10	<1
B_2O_3	0-24	4-11	0-12	<1	<1			<1
Fe_2O_3	0-5	0-0.4	0-5		0-5	0-1	3-9	<1
FeO				3-8				
TiO_2	0-12	0-8	0-0.5	0.5-3.5	0.3-1	0-2	0.5-3	
ZrO_2	0-5	0-4				0-17		0-6

RCF: Refractory Ceramic Fibres; HT-fibre: High alumina, low silica wool; AES-wool: Alkaline earth silicate wool (New refractory fibre). Columns on grey background refer to fibre types described in this document.

Table 1.2. Dimensions and shot content for different MMVF categories (compiled from CEPA 2001 and IARC 2002).

Fibre type	Typical diameter (μm)	Length (μm)	Average LWD	Shot content (w%)	Density
Continuous glass filaments	3-25	3-10			2.1-2.7
Special purpose fibres	0.2-4				
Insulation glass wool	3-10	Most > 3	0.6-7.7	0-5	2.4-2.6
Stone/slag wool	2-6		2.4-5.3	16-55	2.7-2.9
RCF	1.2-3.5		2.4-3.8	20-43	2.6-2.7
HT			4.6	30	2.8
AES			2.2-3.0	35-40	2.6

RCF: Refractory Ceramic Fibres; HT-fibre: High alumina, low silica wool; AES-wool: Alkaline earth silicate wool. The rows on grey background refer to fibre types described in this document.

1.2.3 Additives

Mineral wools may contain oils and other lubricants, added during processing to reduce dust generation from the product. An organic binder may be applied to the wools after primary fiberising in order to hold the fibres together. The binder is often a phenol-formaldehyde resin in aqueous solution, but in the recent years, alternatives such as melamine and acrylic resins have been used. For insulation wool (glass and stone wool), these binders can account for up to 5-10 % of the mass of the final product. (IARC 2002).

1.2.4 Other physico-chemical properties

The melting point of MMVFs is around 500 °C; the fibres crystallise from 900°C. MMVFs are generally more water soluble than naturally occurring asbestiform minerals. The solubility of MMVFs in water varies considerably as a function of their chemical composition and fibre size distribution, alkali-content and fine-diameters increasing solubility (WHO 1988).

1.3 Production and use

Stone and slag wool have been produced in a small scale from around 1840 and in larger scale from the 1920's. Glass wool production started around 1940.
In 1999, glass, stone and slag wool represented over half of the world demand for insulation, amounting to 10683 thousand tonnes. Glass wool accounted for 3493 thousand tonnes and stone and slag wool for 3090 thousand tonnes. Newer fibre types (Alkaline earth silicate wool, HT-fibre), often with lower biopersistence have been developed in the last decade. In 2000, Europe produced 1300 thousands tonnes glass wool in 30 plants and 1200 thousands tonnes stone/slag wool and HT-fibre in 30 plants. USA had 32 glass wool plants and 12 stone wool/slag plants producing 1950 thousands tonnes and 746 thousands tonnes, respectively. The new HT-fibre, introduced in 1995, has been produced in more than 1 million tonnes for the European market in 2000. (IARC 2002).

Three technological phases have been defined in the history of the European insulation wool: The early phase (1933-68) when MMVFs were manufactured by discontinuous batch production and/or oil was not added during production.
The intermediate phase (1940-69) in which all mixed production processes occurred. The late phase (1951-1978) in which modern production techniques including the addition of binders and/or oil were used. (Dogson et al. 1987 – quoted from IARC 2002).

The production process of MMVF can be divided into three steps: The raw materials are melted and mixed in a furnace (fusion), the fibres are formed by directing a jet of hot gas at the liquid stream or by centrifugal attenuation and finally, the fibres are converted into a commercial product. This step includes spraying of a binder (often an urea-formaldehyde or phenol- formaldehyde resin, but melamine resins, silicone compounds are also used) and a lubricating oil (soluble and emulsified oil, surfactants) on the raw fibres to reduce breakage and prevent dustiness. Silicon compounds are used to make the fibres water repellent. The fibres are then cured by heating, and then converted into commercial products by shaping and cutting. (IARC 1988).
The production processes for glass and stone wool are schematically presented in Figures 1 and 2, respectively.

Most mineral wool is used as thermal and acoustic insulation and/or fire protection. Eighty eight percent of glass wool production and 80 % of stone/slag wools are used in building construction, while 12 % of glass and 20 % of stone/slag wools are used in industrial applications as heating, ventilation and air conditioning, household appliances and transportation. A small proportion of glass and stone wools are used as growing media and soil conditioning in gardening and agriculture. The HT-fibre has replaced traditional stone wool in many of its applications. (IARC 2002).

Figure 1: Rotary process for manufacturing glass wool fibres (from IARC 2002).

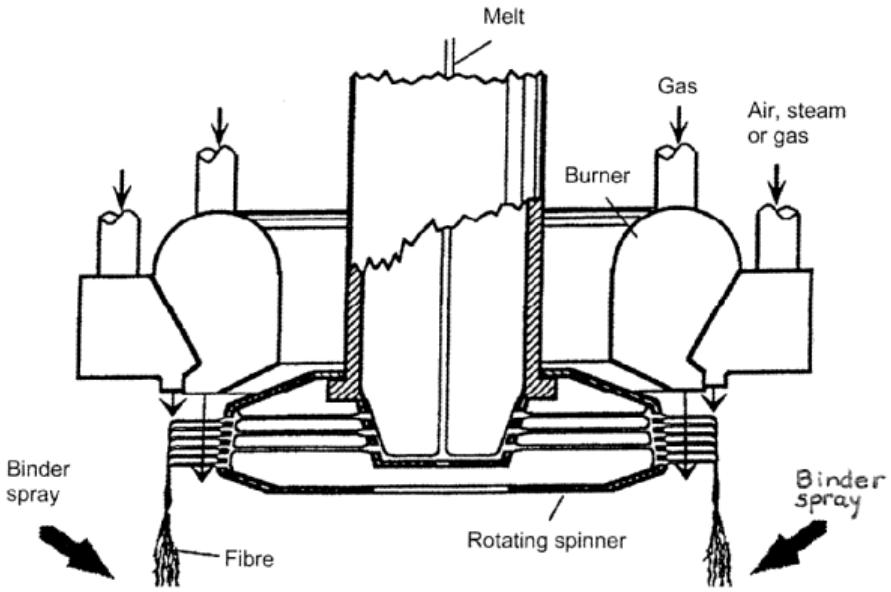
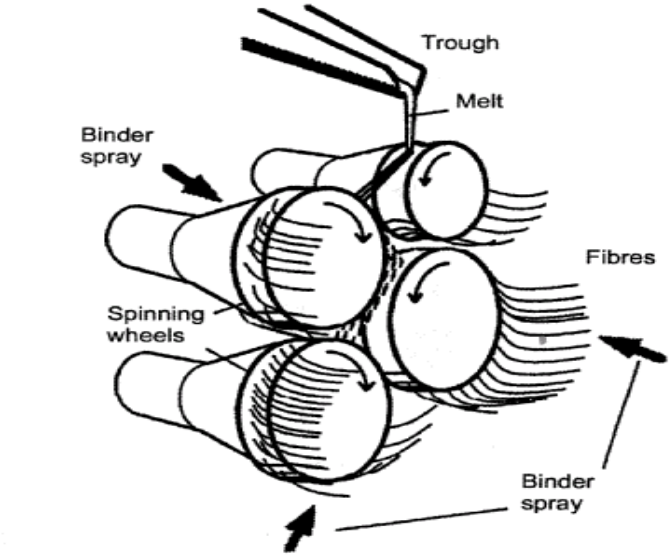


Figure 2. Wheel centrifuge or spinning process for manufacturing stone and slag wool. (from IARC 2002).



1.4 Environmental occurrence

MMVF may be released into the environment during their production, installation, erosion, removal and/or disposal. Studies quantifying fibre concentrations in air, however, often fail to distinguish between MMVFs and "other inorganic fibres", and the fibre size or chemical composition are not specified.

1.4.1 Air

1.4.1.1 Outdoor

Emissions from fibrous glass and stone wool plants in Germany were of the order of 10^{-2} fibres/cm^3 (10^4 fibres/m^3) (Tiesler 1982 – quoted from WHO 1988).

The mean fibrous glass content in outdoor air was determined at the rooftop of 3 buildings of the University of California in Berkeley to be 2.7 x 10^{-4} fibres/cm^3 (2.7 x 10^2 fibres/m^3). Levels at other sites averaged 4.5 x 10^{-3} fibres/cm^3 (4.5 x 10^3 fibres/m^3). (Balzer et al. 1971 – quoted from WHO 1988).

Friedrichs and co-workers reported glass fibre concentration in ambient air in 3 cities in Germany to range from 0.00036 - 0.00249 fibres/cm^3 (3.6 x 10^2 - 2.5 x 10^3 fibres/m^3), the average being 1.23 x 10^3 fibres/m^3. The levels were higher during the week than in the weekends. (Friedrichs et al. 1983 – quoted from IARC 2002).

Mean airborne glass fibre concentrations ranged from 40 fibres /m^3 (4 x 10^1 fibres/m^3) at 1 rural location to 1700 fibres/m^3 (1.7 x 10^3 fibres/m^3) in 1 out of 3 cities in the Ruhr-district in the Federal Republic of Germany in 1981-82. The median diameters of the glass fibres ranged from 0.25 to 0.89 µm and median lengths from 2.54 to 3.64 µm. (Höhr 1985).

Measurements of outdoor background values in 18 locations in Paris showed medians of 2 total fibres/m^3 (ranging from 3 x 10^{-1} to 2.2 x 101 fibres/m^3) and 1 respirable fibre/m^3 < 3 µm in diameter (ranging from "not detectable" to 1.5 x 10^1 fibres/m^3). (Gaudichet et al. 1989).

Rockwool A/S, Hedehusene has performed several measurements on emission from the production plant. For respirable fibres, concentrations up to about 100.000 fibres/normal m^3 were observed and for non-respirable fibres, the concentrations were a little bit lower. OML-calculations based on the limit value given in the 'Environmental Permit' showed an immission for respirable fibres of about 700 fibres/m^3 (99 percentile); the actual immission was evaluated by Rockwool A/S to be about 300-400 respirable fibres/m^3. Respirable fibres are, according to Rockwool A/S, fibres with a diameter < 3 µm, length > 5 µm, and length:diameter ratio > 3:1; and the non-respirable fibres are fibres with a diameter > 3 µm, length > 9 µm, and length:diameter ratio > 3:1.
The dimensions of the Rockwool respirable fibre are identical with the WHO respirable fibre, see section 1.1.1.

1.4.1.2 Indoor

Indoor measurements were made in 16 schools and one office building in Greater Copenhagen. The concentrations of airborne respirable MMVFs ranged from non-

detectable to 0.08 fibres/cm^3 (8 x 10^4 fibres/m^3). (Schneider 1986 – quoted from IARC 2002).

Measurements in 105 rooms containing acoustical ceiling tiles showed average concentrations of airborne respirable MMVFs of less than 0.0001 fibres/cm^3 (1 x 10^2 fibres/m^3), ranging from none detected to 0.002 fibres/cm^3 (2 x 10^3 f/ibresm^3). (Nielsen 1987 and Schneider et al. 1990 – quoted from IARC 2002).

Gaudichet and co-workers measured levels of airborne fibre levels in 79 buildings containing MMVF products in France. Locations with different types of MMVF application gave a large variation in results. Fibre concentrations were reported to be 0.2 - 6778 total fibres/m^3 (2 x 10^{-1} – 6.8 x 10^3 fibres/m^3. Respirable fibres accounted for 0 - 6230 fibres/m^3 (0 – 6.23 x 10^3 fibres/m^3). (Gaudichet et al. 1989).

Concentrations of airborne MMVFs were measured in 51 residential and commercial buildings throughout the USA. The data were analysed by phase contrast microscope and showed a mean concentration of all respirable fibres to be 0.008 fibres/cm^3, only 3 % of which were inorganic. The concentration of respirable MMVFs was thus found to be less than 0.0001 fibres/cm^3 (1 x 10^2 fibres/m^3) (Carter et al. 1999 – quoted from IARC 2002).

1.4.2 Water

Quantitative data on the MMVF content of water supplies were not found. However, glass fibres have been identified by optical microscopy in samples of sewage sludge from 5 cities in the USA (Bishop et al. 1985 - quoted from WHO 1988).

1.4.3 Soil

No data were found.

1.4.4 Foodstuffs

No data were found.

1.5 Environmental fate

MMVF can be removed from the environment by breakage into smaller fragments, thus loosing their fibre characteristics, by dissolution, by sedimentation and subsequent burial in soil or by thermal destruction (e.g. incineration of waste) (WHO 1988).

1.5.1 Air

Mineral fibres with small diameters are most likely to remain airborne for long periods. Marconi and co-workers reported that airborne fibres become shorter and thinner with increasing distance from working areas. The respirable fraction of airborne fibres accounted for about 67 % of the total airborne fibres in areas where stone wool blankets were installed, whereas 90 % of the fibres were respirable at

about 5 m from the working area. This is attributable to the sedimentation of larger diameter fibres. (Marconi et al. 1988 – quoted from WHO 1988).

1.5.2 Water

Solubility of MMVF in water varies with the chemical composition and the fibre size distribution. Degradation increases with alkali and fine fibre content. Removal from water occurs most likely by dissolution and deposition and subsequent burial in sediments. (WHO 1988).

1.5.3 Soil

No data were found.

1.5.4 Bioaccumulation

No data were found.

1.6 Human exposure

IARC (1988) has made an overall summary (see Table 1.3) of estimated respirable fibre concentrations generated during the production and use of man-made vitreous fibres, as well as typical levels in non-industrial environments and outdoor air.

Human exposure to fibres occurs through contaminated air, primarily in occupational settings in production or application areas. MMVF products can release airborne respirable fibres during their production, use and removal. In general, as the nominal diameter of MMVF products decreases, both the concentration of respirable fibres and the ratio of respirable to total fibres increase. Although exposure to MMVFs during their production, processing and use is thought to have been higher in the past, current average exposure levels are generally less than 0.5×10^6 respirable fibres/m^3 as an 8 hour time-weighted average. Higher levels have been measured in production of special-purpose glass fibres and refractory ceramic fibres, installation of loose-fill insulation without binder, and removal of insulation products. The concentration of MMVFs measured in outdoor and indoor air in non-occupational settings have been found to be much lower than in occupational settings related to their production, use or removal. (IARC 2002).

Measurements of airborne respirable as well as non-respirable MMVFs in user industries in Scandinavia showed that there was no direct relation between respirable fibre concentration and non-respirable fibre concentration. The concentration and average length of the non-respirable fibres varied with type of fibre and way of application. (Schneider 1979).

See chapter 3 for specific humane exposure data for the included human studies.

Table 1.3. Range of airborne respirable fibre concentrations in typical exposure situations. (from IARC 1988).

Fibre concentration (fibres/cm³)	Location/use	Reference
Ultralow (<0.0001)[a]	Outdoor: rural area Buildings: thermal insulation	Höhr (1985)
Extremely low (0.0001–0.001)[a]	Outdoor: large cities Buildings: ceiling boards Ventilation systems	Höhr (1985) Rindel *et al.* (1987) Balzer (1976)
Very low (0.001–0.01)		
Glass continuous filament	Production and use	Cherrie *et al.* (1986)
Coarse glass fibre	Production and use	
Ceiling boards	Buildings: some damage, some ventilation ducts	Schneider (1986)
Low (0.01–0.1)		
Glasswool	Production and most secondary production	Höhr (1985)
Rockwool	Production and most secondary production	
Rock-/slagwool	Production and most secondary production	
Ceiling boards	Buildings: severe damage	Schneider (1976)
Medium (0.1–1.0)		
Fine glass fibre	Production	Höhr (1985)
Rockwool	Some secondary production and user industry	
Ceramic	Primary production and user industry	
Glasswool	User industry	
High (>1.0)		
Very fine glass fibre	Production and use	
Glass-/rockwool, loose	User industry: blowing into attic	
Glass-/rockwool, without dust suppressants	Production and use	
Ceramic	Secondary production and some user industry	

[a]Estimated from transmission electron microscopic measurements

2 Toxicokinetics

2.1 Deposition

Deposition of airborne fibrous and non-fibrous particles is defined as the active loss of these particles from the air during respiration, as a result of inelastic encounter of the airborne particles with the respiratory epithelium. The deposition of inhaled fibres in the respiratory tract is a function of their physical characteristics (size, shape and density) and of the anatomical and physiological parameters of the airways. Fibres tend to orient parallel to the direction of airflow, thus the diameter is the primary factor influencing respirability. It has been suggested that the upper respirability limit of fibres in man is 3.5 µm in diameter (5 µm by mouth breathing) and that there is a rapid decrease in the respirability of fibres of > 1 µm in diameter in rats. (WHO 1988 and IARC 2002).

2.2 Clearance

Clearance of fibres depends on physical (dimensions) as well as on chemical composition. Mucociliary movement in the nasopharyngeal and tracheobronchial regions and alveolar macrophage phagocytosis in the alveolar region are the main mechanisms of fibre clearance.
The retention of fibres differs in different regions of the respiratory tract. For the nasal region, ciliary motion-mediated movement of deposited particles has been observed to occur mostly towards the pharynx, with clearance within 24 h. (ICRP 1994 – quoted from IARC 2002). For the tracheobronchial region, the main clearance mechanism is the mucociliary escalator of macrophage phagocytised fibres or of the free fibres. This process takes less than 24 h, but can be prolonged if the fibres are caught by a thin surfactant layer, thus been embedded in the epithelial cells, from which the fibres can eventually be translocated into the interstitial cells. In the alveolar region, phagocytosis is the most important clearing clearance mechanism. Short MMVF (< 5µm in length) are efficiently cleared by alveolar macrophages, but the macrophages cannot phagocytise fibres 10-20 µm long. Incompletely phagocytised fibres are likely to come into contact with alveolar cells and translocated to interstitial sites and to be transported via lymphatic channels to pleural sites. (IARC 2002.)

Alveolar macrophage-mediated clearance is significantly slower in humans than in rats, with retention half-times of particles or fibres of several hundred days and about 70 days in rats. (Bailey et al. 1982 and Snipes 1989 – quoted from IARC 2002.)

Chemical dissolution and breakage in the extracellular fluid (pH of 7.4) of the incompletely phagocytised, long fibres also contribute to clearance (IARC 2002).

Particle overload occurs when high doses of poorly soluble particles of low cytotoxicity are repeatedly deposited in the lung so that their daily rate of deposition exceeds the normal rate of macrophage-mediated clearance. In rats, this causes persistent alveolar inflammation, fibrosis and lung tumours (Donaldson 2000; ILSI 2000 - quoted from IARC 2002).

2.3 Biopersistence

Biopersistence refers to the capacity of fibres to persist and conserve their chemical physical features over time in the lung. It is determined by physiological clearance (by alveolar macrophage translocation to the larynx or via the lymphatic system into the interstitium and the pleura) and by physiochemical clearance such as dissolution, leaching and breaking. Biopersistence reflects the pulmonary retention of the fibres and plays an important role in the potential chronic effects on health of man-made vitreous fibres. (IARC 2002.)

The biopersistence of several MMVFs and asbestos has been evaluated in rat studies (see Table 2.1). The rats were exposed to the fibres by nose-only inhalation 6 h/day for five days and were then kept without further exposure up to one year. The rat lungs were analysed at intervals during this year for number of fibres in the lungs, dimensions, morphology and chemical composition. Asbestos fibres cleared much more slowly than the MMVFs. For asbestos and the more biopersistent MMVFs, the number of short fibres tended to decrease more rapidly than the number of long fibres. The investigators suggested that this was a likely result of macrophage-mediated lung clearance, which is more efficient for shorter fibres. However, for the less biopersistent MMVFs, the number of long fibres decreased more rapidly than the number of short fibres. The investigators suggested that this could be a result of a rapid rate of transverse breakage of long, biosoluble fibres into short fibres. (Hesterberg et al. 1996, 1998, 2002 – quoted from IARC 2002). Transverse fragmentation of MMVFs has been demonstrated in *in vitro* studies (Bauer 1998 – quoted from IARC 2002).

The *in vitro* dissolution of several MMVFs and asbestos has been evaluated in cell free systems using salt solutions simulating lung fluids (see Table 2.1). The dissolution was tested at pH 7.4 which simulated the pH of extracellular fluid and pH 4.5 which simulated the acidic pH of the phagolysosome of macrophages. (Several authors quoted from IARC 2002).

Table 2.1. Lung biopersistence and *in vitro* dissolution of selected fibres from inhalation studies in rats (adapted from IARC 2002).

Fibre		Biopersistence: fibres > 20 μm in length; lung clearance rates			*In vitro* dissolution, k_{dis}, at pH 7.4 and *pH 4.5* (ng/cm^2/h)
		$T_{½}$ of slower pool (days)	$WT_{½}$ (days)	T_{90} (days)	
Amosite	Asbestos	1160	418	2095	< 1
Crocidolite	Asbestos	0	817	2770	< 1
MMVF21	Stone wool	95-613	67-91	206-264	20, *72*
MMVF22	Slag wool	35	9	37	400, *459*
MMVF10	Glass wool	0	37	123	300, *329*
MMVF10,1	Glass wool	30	14.5	69	
MMVF11	Glass wool	31	9	38	100, *25*
MMVF10B	Glass wool	20	8	38	500
MMVF35	Glass wool	18	7	33	150
MMVF34	HT-fibre	24	6	19	59, *620*

$T_{½}$: Retention half-time of slow clearance phase (if bi-exponential) or of one clearance phase (if mono-exponential)
$WT_{½}$: Weighted retention half-time
T_{90}: Number of days to clear 90% of fibres

A case-control study of autopsies from 112 production workers in the US cohort (described in chapter 3) showed no significant difference in retention of MMVFs in the lung between the exposed workers and the controls. The mean duration of exposure was 11 years and the mean time elapsed since the end of exposure was 12 years. (McDonald et al. 1990 – quoted from IARC 2002).

3 Human toxicity

3.1 Single dose toxicity

No data have been found.

3.2 Irritation

3.2.1 Dermal irritation

MMVFs may cause dermal irritation following occupational exposure or exposure in contaminated buildings. The irritative effect on the skin results from fibres with a diameter greater than 4-5 μm. The skin irritation potential depends on the fibre diameters: <5 μm slight, if any, 5-7.5 μm moderate and 7.5-10 μm high, but also on other factors e.g. the presence of shots. The effect is a mechanical one, as pulverized fibres do not have any effect. The irritative effect appears as itching, and as erythemas with papules and vesicles. Other occasional manifestations are urticaria, petechiae, erosions, and, rarely, nummular eczema. The fibres can penetrate the stratum corneum and occasionally deeper into the epidermis. It has been suggested that skin penetration is directly proportional to fibre diameter and inversely proportional to fibre length. Secondary lesions include bacterial infections, which develop as a result of scratching. (Several authors quoted from Björnberg 1985, IARC 1988, 2002, Lockey and Ross 1994, Petersen and Sabroe 1991, Schneider 1979, Stam-Westerveld et al. 1994, and WHO 1988).

Data concerning the incidence or prevalence of dermatitis in workers exposed to MMVFs are sparse. Up to 65 % of workers had cutaneous lesions and/or symptoms from exposure to glass or stone wool. Clinical as well as experimental studies have reported the itching to disappear after 1-4 weeks of exposure, with a tolerance developing. However, when the workers resumed work after a 1-month break in the exposure, the itching started again. No exposure levels have been reported for any of these studies. (Several authors quoted from Björnberg 1985, Petersen and Sabroe 1991, and WHO 1988).

A total of 63 cases of occupational dermatosis caused by MMVF were reported to the Finnish Register of Occupational Diseases during 1990-99. Of these 56 were diagnosed as irritant contact dermatitis (ICD). Carpenters, building workers and insulation workers had the highest risk of ICD from MMVF with annual incidences of 1.6×10^{-5}, 2.7×10^{-5} and 9.1×10^{-5}, respectively. Glass, stone or slag wool was estimated to cause about 23 of the ICD cases. (Jolanki et al. 2002).

Twenty-five percent of 315 people (not stone or glass wool workers) exhibited skin reactions when patch tested with stone wool (Björnberg and Löwhagen 1977).

3.2.2 Dermal, eye and respiratory irritation

In Danish end-users (construction workers) a dose-response correlation was found between duration of exposure and rate of dermal irritation (stinging or itching skin, skin eruption/rash), eye irritation (stinging or itching eyes) and upper respiratory

symptoms (cough, burning, stinging throat and nose, running and stuffed nose). Two thirds of the workers working daily with mineral wool had some of these symptoms once a week or more. The occurrence was 2-3 times higher compared with worker not working with mineral wool. The data were adjusted for smoking, age and co-exposure to organic solvents whereas potential co-exposures of other kinds were not included. (Petersen and Sabroe 1991).

Children and adults in 24 kindergartens in Denmark were evaluated for irritation of the skin, eye and upper respiratory tract and diseases of the eye, respiratory tract, and middle ear. In kindergartens with visible MMVF (type not specified) ceilings compared to kindergartens without (control institutions), the frequency of eye and nose irritation in adults, skin irritation, common cold and sore throat in adults and children, and otitis media in children was statistically significantly higher. No significant differences were found between the kindergartens with regard to amount of settled fibres on regularly or occasionally cleaned surfaces or with regard to mean concentration of respirable fibres (97-110 fibres/m^3 in kindergartens with visible MMVF ceilings, 41 fibres/m^3 in control institutions). For non-respirable fibres the mean concentration was 23-40 fibres/m^3 in kindergartens with visible MMVF ceiling. In the control institutions, the level of non-respirable fibres was often lower than the analytical detection limit (40-80 fibres/m^3). Among children, no correlation was found between symptoms/diseases and the results of measurements on the MMVFs. Among adults, the concentrations of airborne respirable and non-respirable MMVFs were positively correlated with eye irritation, and the presence of settled non-respirable MMVFs on surfaces occasionally cleaned was positively correlated with skin and nose irritation. Control for confounder (e.g. socioeconomic parameters, concentration of airborne dust, carbon dioxide, volatile organic components and formaldehyde, thermal environment, air change rate, cleaning standards) influence was performed. (Rindel et al. 1989).

Employees in a German administrative building with sound absorbing mineral fibre (type not specified) boards complained of skin irritation (mainly itching and/or redness), eye irritation (mainly flow of tears, redness and/or burning) and respiratory irritation (mainly nasal catarrh, dry nose, sneezing and/or coughing). The fibre content in the air was measured to be 1000-3500 fibres/m^3 < 3 μm in diameter and 100-200 fibres (not stated if total count or concentration) >3 μm in diameter. (Thriene et al. 1996).

3.2.3 Eye irritation

The frequency of eye symptoms increased significantly and the number of micro epithelial defects on the medial bulbar conjunctiva and, in some cases, the neutrophil count of the conjunctival fluid were increased after 4 days of exposure in 15 Danish stone wool workers (employed for > 6 months) compared with controls. While there were no ophthalmological differences between exposed workers and controls on Monday morning, an excess of mucous was found in exposed workers, suggesting that the effect was not completely reversible over the weekend. (Stokholm et al. 1982 – quoted from Lockey and Ross 1994, and WHO 1988)

3.2.4 Respiratory irritation

In reports that appeared in the early literature, several cases of acute irritation of the upper respiratory tract (and more serious pulmonary diseases) were attributed

to occupational exposure to various MMVFs. On the basis of reviews of these reports, several authors have concluded that exposure to MMVF was probably incidental rather than causal in most of these cases, since the reported conditions have not been observed in most of the more recently conducted epidemiological studies. (WHO 1988). The results of epidemiological studies reported after 1987 are described in the chapter on respiratory diseases.

3.3 Sensitisation

A few cases of allergic contact dermatitis in workers exposed to MMVFs have been described. Upon patch testing, epoxy resins or phenol-formaldehyde resins used to bind mineral fibres together were shown to be the allergens. (Several authors quoted from Conde-Salazar et al. 1985, Jolanki et al. 2002, WHO 1988).

3.4 Repeated dose toxicity

3.4.1 Inhalation

Numerous studies are available regarding adverse health effects due to inhalation exposure to MMVFs. Two large cohorts, one in Europe (Section 3.4.1.1) and another in the USA (Section 3.4.1.2), have been followed for many years; the data from these cohorts are reviewed below. Afterwards, data on respiratory diseases from other studies are summarised (Section 3.4.1.3).

No data were found for the HT-fibres.

3.4.1.1 European cohort

3.4.1.1.1 Introduction

IARC has coordinated a large European cohort study which focused on the mortality and cancer incidence among production workers in a total of 13 MMVF factories in Denmark, Finland, Norway, Sweden, United Kingdom, Germany and Italy. The cohort consisted of 7 stone/slag wool factories, 4 glass wool factories, and 2 continuous filament factories (one of which also produced glass wool during 1946-1960). The population under study was the workforce ever employed in the 13 factories (with at least one year of employment for some of the factories) from the year of start of production to 1977 (see Table 3.1). A first follow-up was published in 1984 and covered mortality and, where possible, cancer incidence up to December 31st 1977. A second and more informative follow-up, up to at least December 31st 1982, was published in 12 articles in Scand J Work Environ Health 12, suppl 1 in 1986. These articles reviewed the experimental evidence for carcinogenicity (Davis 1986) and the prior epidemiologic evidence for chronic respiratory diseases and lung cancer (Saracci 1986) of MMVF. The results of the whole cohort (Simonato et al. 1986) as well as of each of the seven national components (Olsen et al. 1986, Claude and Frentzel-Beyme 1986, Teppo and Kojonen 1986, Bertazzi et al. 1986, Andersen and Langmark 1986, Westerholm and Bolander 1986, Gardner et al. 1986) were described. The articles also covered the results of measurements of level and size distribution of airborne fibres under present-day conditions (Cherrie et al. 1986) and results of a historical investigation to reconstruct past conditions of exposure (Cherrie and Dodgson 1986). Simonato et al. 1987 presented further results in relation to other potential confounding risk factors present in the working environment. In an updating of cancer (Boffetta et

al. 1997) and non-neoplastic (Sali et al. 1999) mortality, the exposed workers were followed up until 1990-1992 (depending on the country). One study estimated the individual cumulative exposure to stone/slag wool fibres in workers who had died from lung cancer and analysed the relative risk for lung cancer in relation to e.g. fibre exposure (Consonni et al. 1998 - quoted from IARC 2002). A study followed a subset of the workers (from factories in Denmark, Finland, Norway and Sweden) included in the European cohort for cancer incidence up until 1994-1995 (Boffetta et al. 1999 – quoted from IARC 2002). Two nested case-control studies were performed with workers with lung cancer at one glass wool factory (Gardner et al. 1988 - quoted from IARC 2002) and all 7 stone/slag wool factories (Kjaerheim et al. 2002 - quoted from IARC 2002) as the cases.

Table 3.1. Factories and population included in the study (adapted from Boffetta et al. 1997).

Production process Factory no. and country		Year*			Number of exposed workers
		BP	BIP	BLP	
Stone/slag wool					
1	Denmark	1937	1941	1954	4585
3	Norway	1950	1955	1957	473
4	Norway	1940	1947	1956	460
5	Norway	1948	1948	1961	875
8	Sweden	1943		1951	384
9	Sweden	1938	1946	1950	1194
12	Germany	1941		1941	2137
Total stone/slag wool					**10108**
Glass wool					
2	Finland	1941		1960	924
6	Norway	1935		1961	644
7	Sweden	1933		1961	2022
10	UK	1943	1946	1950	4145
14	Italy	1946	1946		600
Total glass wool					**8335**
Continuous filament					
11	UK		Not available		1837
14	Italy		Not available		1722
Total continuous filament					**3559**
Total cohort					**22002**

*BP = beginning of production; BIP = beginning of intermediate technological phase; BLP = beginning of late technological phase. See the chapter on human exposure for further explanation.

3.4.1.1.2 Human exposure

From 1977 to 1980 scientist measured the concentrations and size of airborne fibres in 6 of the 7 stone/slag wool factories (no data from the German factory) and all 4 glass wool factories in the European cohort (Ottery et al. 1984 – quoted from Cherrie et al. 1986). The workforce at each factory was classified into occupational groups (see Table 3.2) on the basis of job and work zone. Some members of each group were selected at random for personal sampling. The samples were analysed by phase contrast optical microscopy (PCOM) for evaluation of fibre concentrations and by scanning electron microscopy (SEM) for assessment of fibre size. Upon reanalysis to harmonize the results with the WHO-European MMVF reference counting level, the concentrations of respirable fibres originally reported were determined to be too low and were therefore corrected (Cherrie et al. 1986).

Respirable fibres were defined as those of length (L) $\geq$ 5 μm, diameter (D) < 3 μm, and aspect ratio (L:D) $\geq$ 3 (Gardner et al. 1986).
For different occupational groups the arithmetic mean respirable fibre concentrations in the 6 stone/slag wool factories was in the range of (0.01 - 0.67) x 10^6 fibres/m^3 (geometric mean = (0.01-0.51) x 10^6 fibres/m^3). The highest concentrations were observed in certain specialist secondary production groups. The arithmetic mean respirable fibre concentration in the main production and secondary production groups was in the range of (0.05 – 0.12) x 10^6 fibres/m^3. See Table 3.2 for fibre concentrations in the different occupational groups. For the different factories, the median lengths of stone wool fibres ranged from 10 to 20 μm and the median diameters ranged from 1.2 to 2 μm. (Cherrie et al. 1986).
For different occupational groups the arithmetic mean respirable fibre concentrations in the 4 glass wool factories was in the range of (0.01 – 1.00) x 10^6 fibres/m^3 (geometric mean = (0.01-0.77) x 10^6 fibres/m^3). The highest concentrations were associated with the manufacture of special fine fibre earplugs. The arithmetic mean respirable fibre concentration in the main production and secondary production groups was in the range of (0.01 – 0.16) x 10^6 fibres/m^3. See Table 3.2 for fibre concentrations in the different occupational groups. For the different factories, the median lengths of glass wool fibres ranged from 8 to15 μm and the median diameters ranged from 0.7 to 1 μm. Compared to the stone wool fibres, glass wool fibres tended to be shorter and thinner. (Cherrie et al. 1986).

Table 3.2. Respirable fibre concentrations (10^6 fibres/m^3) in combined occupational groups in the European cohort (adapted from Cherrie et al. 1986).

Combined occupational groups	Number of measurements	Range of arithmetic means	Lowest value measured	Highest value measured
Stone/slag wool				
Preproduction	25	0.01 – 0.08	< 0.01	0.22
Production	183	0.05 – 0.12	0.01	0.37
Maintenance	68	0.03 – 0.08	0.01	0.18
General	69	0.04 – 0.08	0.01	0.37
Secondary production 1	166	0.06 – 0.12	0.01	0.39
Secondary production 2	39	0.25 – 0.67	0.06	1.40
Cleaning	37	0.06 – 0.14	0.01	0.44
Total	587	0.01 – 0.67	< 0.01	1.40
Glass wool				
Preproduction	23	0.01 – 0.01	< 0.01	0.03
Production	153	0.01 – 0.05	< 0.01	0.62
Maintenance	63	0.02 – 0.07	< 0.01	0.60
General	47	0.02 – 0.03	< 0.01	0.06
Secondary production 1	131	0.02 – 0.05	< 0.01	0.21
Secondary production 2	70	0.07 – 1.00	0.02	4.02
Cleaning	4	0.01	0.01	0.02
Total	491	0.01 – 1.00	< 0.01	4.02

An historical investigation based on questionnaires has been conducted to reconstruct past conditions of exposure in the European cohort. The investigation resulted in a division of the production into three technological phases. See Table

3.1 for information on when each factory entered the different technological phases. In the *early technological phase*, no dust-suppressing agent (mainly mineral oil) was used and/or a batch process involving labour-intensive and hand-operated production methods were in operation. The period when oil and resin binders were in use with modern mechanized production methods was called the *late technological phase*. The intermediate phase with exposure during the use of processes both with and without dust suppressors was called the *intermediate technological phase*.
The two factors identified as most important to fibre emission levels from MMVF were nominal fibre size (= length-weighted average fibre diameter in the bulk product) and the use of dust-suppressing agents. It was estimated that both factors could produce differences of approximately ten times. Changes in nominal fibre size have generally been associated with changes in the production process. The nominal fibre size of stone/slag wool has not changed substantially but the early glass wool processes produced larger nominal fibre diameters. These changes would have tended to result in lower airborne fibre concentrations in the early glass wool factories than in current production processes but would have had little effect on stone/slag wool production. The period with no oil added would give rise to higher fibre levels. For the glass wool factories this meant that the airborne fibre concentration was probably similar in the early technological phase to the measurements in the late technological phase. For the stone/slag wool factories, the airborne fibre concentration was higher in the early than in the late technological phase. Based on data obtained from samples collected in a modern production plant manufacturing stone wool without the addition of oil or binder, it was estimated that the airborne fibre concentration was about 1 x 10^6 fibres/m^3 and possibly as high as 10-25 x 10^6 fibres/m^3 in the early technological phase. (Cherrie and Dodgson 1986).

The historical exposure investigation in the European cohort also provided information on possible exposure to other agents in the factories included in the study. The authors conclude that the agents that could potentially present a risk for lung cancer in the epidemiologic study were the use of asbestos in factory 12 and the contamination of olivine and exposure to coal-tar pitch volatiles at factory 4. In the following more details on exposure to other agents are provided:
Factories with a history of more than an occasional processing of **asbestos** were excluded from the European cohort. However, asbestos has been used in some form in all of the included factories. The primary uses have been personal protective equipment and as thermal insulation. One of the factories (4) used olivine potentially contaminated with fibres with a chemical composition similar to tremolite asbestos as a raw material. Two stone/slag wool (1 and12) and two glass wool (2 and10) factories had used small quantities of asbestos products in secondary production. For most of the uses, the exposure level was low, the number of workers directly involved in handling asbestos was low, and/or the exposure was of short duration. In one factory (12) calcium silicate bricks containing 4% of chrysotile asbestos were manufactured, which may have caused relatively high airborne asbestos fibre levels for the 10-20 workers employed in this process.
Formaldehyde has been used in all of the glass and stone/slag wool factories in the production of resin binders. Exposure levels were probably high in the initial period of use since most factories reported that the odour of formaldehyde was frequently detected and occasionally it was reported as causing severe irritation. Most factories reported that the concentrations of formaldehyde were currently less than the occupational exposure limit.
The exposure to **polycyclic aromatic hydrocarbons** (PAH) from bitumen used as a binder and mineral oil used as an additive was considered to be low. Exposure to PAH from coal-tar pitch used in an electric furnace at factory 4 until 1967 would

have been high for workers in the furnace area. In this factory the workers rotated jobs from MMVF production to work in the furnace area so most would have had some periodic exposure to these conditions.
Transformer oil containing **polychlorinated biphenyls** were used occasionally as a substitute for mineral oil at factory 4 between about 1940 and the early 1950s.
Slag as raw material has been used in five of the seven stone/slag wool factories. Most of the material used was iron slag, some lead and copper slag being used occasionally. (Cherrie and Dodgson 1986).

3.4.1.1.3 Respiratory diseases

Neither in the second follow-up (Simonato et al. 1986) nor in the updating of non-neoplastic mortality (Sali et al. 1999) in the European cohort, evidence of an increased risk for non-malignant respiratory diseases was found in exposed workers. In both of the studies, the standardized mortality ratio (SMR) and the 95% confidence interval (CI) was calculated but no record was made of the incidence of non-malignant respiratory diseases. Non-malignant diseases of the respiratory system were subdivided into acute infections, influenza, pneumonia, and bronchitis, emphysema and asthma. No statistically significant increase in SMR was observed for any of these subgroups either. See Table 3.3 for more details. Sali et al. (1999) reported five deaths from pneumoconiosis including one from asbestosis but no statistics was applied.

Table 3.3. SMR and 95 % CI for non-malignant respiratory diseases in exposed workers in the European cohort.

Cause of death	SMR	95 % CI
Simonato et al. 1986:		
Diseases of the respiratory system	1.00	0.85 – 1.17
Acute infections	0.79	0.10 – 2.87
Influenza	1.24	0.53 – 2.44
Pneumonia	0.95	0.73 – 1.21
Bronchitis, emphysema and asthma	0.90	0.70 – 1.14
Sali et al. 1999:		
Diseases of the respiratory system	1.09	0.95 – 1.25
Pneumonia	1.18	0.95 – 1.47
Bronchitis, emphysema and asthma	1.03	0.82 – 1.28

When the exposed workers were divided into groups of exposure to stone/slag wool or glass wool, the SMR for non-malignant respiratory diseases was slightly higher in the glass wool group than in the stone/slag wool group but none of the SMRs were statistically significantly elevated (Sali et al. 1999). See Table 3.4 for more details.

The relative risk (RR) of mortality from bronchitis, emphysema, and asthma according to time since first employment, duration of employment, and technological phase at first employment among stone/slag wool and glass wool workers was calculated. The mortality was slightly higher among stone/slag wool workers with more than 30 years since first employment than among other stone/slag wool workers. A trend in the opposite direction was suggested among glass wool workers. However, none of the RRs or the trends were statistically significant. (Sali et al. 1999). See Table 3.5 for more details.

Table 3.4. SMR and 95 % CI for non-malignant respiratory diseases in stone/slag wool and glass wool workers in the European cohort. Data from Sali et al. (1999).

Cause of death	Stone/slag wool		Glass wool	
	SMR	95 % CI	SMR	95 % CI
Diseases of the respiratory system	0.97	0.76 – 1.23	1.18	0.98 – 1.40
Pneumonia	1.00	0.66 – 1.45	1.25	0.93 – 1.63
Bronchitis, emphysema and asthma	0.96	0.66 – 1.35	1.12	0.82 – 1.49

Table 3.5. Relative risks (RR)of mortality from bronchitis, emphysema, and asthma according to time since first employment, duration of employment, and technological phase at first employment among stone/slag wool and glass wool workers. Data from Sali et al. 1999.

	Stone/slag wool		Glass wool	
	RR	95 % CI	RR	95 % CI
Years since first employment				
1 – 19[+]	1	-	1	-
20 - 29	0.9	0.3 – 2.6	0.7	0.3 – 1.6
≥ 30	1.8	0.7 – 7.0	0.4	0.1 – 1.1
Trend[*]	0.5		0.08	
Duration of employment in years				
1 – 4[+]	1	-	1	-
5 - 9	0.9	0.3 – 2.2	1.6	0.7 – 3.3
10 - 19	1.1	0.4 – 2.8	1.4	0.7 – 3.2
≥ 20	0.6	0.2 – 2.6	0.5	0.1 – 2.5
Trend[*]	0.7		0.9	
Technological phase at first employment				
Late[+]	1	-	1	-
Intermediate	0.4	0.1 – 1.6	3.4	0.9 – 13.2
Early	0.9	0.2 – 3.9	1.8	0.4 – 7.7
Trend[*]	0.7		0.2	

[*] p-value in test for linear trend. [+] Reference category.

Exposed workers with short-term employment (less than 1 year) had a statistically significant increased mortality (SMR = 1.50) from non-malignant respiratory diseases. No further details were given. (Simonato et al. 1986).

3.4.1.1.4 Non-respiratory diseases

Mortality from non-malignant renal diseases in stone/slag wool and glass wool workers from the European cohort were not statistically significantly increased. See Table 3.6 for more details. Although results were based on small numbers of men (6 deaths among stone/slag wool workers and 9 deaths among glass wool workers), mortality was somewhat higher among workers with more than 20 years between first employment and death. The authors made a suggestion of an increasing risk of death from non-malignant renal diseases among stone/slag wool workers with duration of employment or employment in the early technological phase. No such relation was found in the glass wool sub-cohort. The few deaths,

however, limited the power of the analyses so no statistically significant trends were observed. See Table 3.7 for more details. (Sali et al. 1999).

Table 3.6. SMR and 95 % CI for non-malignant renal diseases in exposed workers in the European cohort. Data from Sali et al. 1999.

Cause of death	Stone/slag wool		Glass wool		Total	
	SMR	95 % CI	SMR	95 % CI	SMR	95 % CI
Non-malignant renal diseases	0.97	0.36 – 2.11	1.11	0.51 – 2.10	1.04	0.59 – 1.69

Table 3.7. SMR and 95 % CI for non-malignant renal diseases according to time since first employment, duration of employment, and technological phase at first employment among stone/slag wool and glass wool workers. Data from Sali et al. 1999.

	Stone/slag wool		Glass wool	
	SMR	95 % CI	SMR	95 % CI
Years since first employment				
0 – 19	0.56	0.07 – 2.09	0.66	0.14 – 1.92
20 - 29	1.43	0.17 – 5.16	2.04	0.56 – 5.23
≥ 30	1.49	0.18 – 5.39	1.16	0.14 – 4.18
Trend*	0.3		0.4	
Duration of employment in years				
1- 9	0.52	0.06 – 1.86	1.07	0.39 – 2.33
10 - 19	1.38	0.17 – 4.98	1.09	0.13 – 3.95
≥ 20	2.30	0.28 – 8.30	1.41	0.04 – 7.85
Trend*	0.1		0.7	
Technological phase at first employment				
Late	0.68	0.14 – 2.00	0.78	0.02 – 4.35
Intermediate	1.14	0.03 – 6.33	1.85	0.80 – 3.64
Early	2.17	0.26 – 7.85	0	0 – 1.46
Trend*	0.2		0.2	

* p-value in test for linear trend.

Mortality from ischemic heart disease in stone/slag wool and glass wool workers from the European cohort were not statistically significantly increased. See Table 3.8 for more details. A trend was seen for an increasing risk of ischemic heart disease in stone/slag wool workers with years since first employment and in glass wool workers with technological phase at first employment. See Table 3.9 for more details. In the whole cohort, the risk of ischemic heart disease was higher among maintenance workers (SMR = 1.18, 95 % CI = 1.00 – 1.38) than among other workers. (Sali et al. 1999).

The stone/slag wool workers experienced a statistically significant increased mortality from mental disorders (SMR = 1.94, 95 % CI = 1.20 – 2.97) such as alcoholism, senile dementia or psychoses, and from external causes (SMR = 1.26, 95 % CI = 1.05 – 1.49) such as suicide, motor vehicle accidents, injuries of undetermined origin, and accidental falls. The risk of death from external causes decreased steadily with duration of employment, and no deaths from mental disorders occurred among workers with more than 20 years of employment. (Sali et al. 1999). Exposed workers with short-term employment (less than 1 year) had a statistically significant increased mortality from non-malignant diseases of the

digestive system (SMR = 1.71). Deaths from liver cirrhosis were about four times more frequent than for longer-term employees. No further details were given. (Simonato et al. 1986).

Table 3.8. SMR and 95 % CI for ischemic heart disease in exposed workers in the European cohort. Data from Sali et al. 1999.

Cause of death	Stone/slag wool		Glass wool		Total	
	SMR	95 % CI	SMR	95 % CI	SMR	95 % CI
Ischemic heart disease	0.97	0.87 – 1.08	1.05	0.95 – 1.15	1.03	0.96 – 1.11

Table 3.9. RR and 95 % CI for ischemic heart disease according to time since first employment, duration of employment, and technological phase at first employment among stone/slag wool and glass wool workers. Data from Sali et al. 1999.

	Stone/slag wool		Glass wool	
	RR	95 % CI	RR	95 % CI
Years since first employment				
0 - 9[+]	1	-	1	-
10 - 19	0.9	0.6 – 1.3	1.0	0.7 – 1.5
20 - 29	1.0	0.6 – 1.6	0.8	0.5 – 1.2
≥ 30	1.6	0.9 – 3.0	0.8	0.5 – 1.3
Trend[*]	0.05		0.2	
Duration of employment in years				
1 - 4[+]	1	-	1	-
5 - 9	1.0	0.7 – 1.3	0.8	0.7 – 1.1
10 - 19	0.9	0.6 – 1.2	1.0	0.8 – 1.4
≥ 20	0.7	0.5 – 1.0	1.2	0.8 – 1.7
Trend[*]	0.07		0.5	
Technological phase at first employment				
Late[+]	1	-	1	-
Intermediate	1.0	0.7 – 1.4	1.3	0.9 – 1.9
Early	1.0	0.7 – 1.5	1.6	1.0 – 2.5
Trend[*]	0.9		0.04	

[*] p-value in test for linear trend. [+] Reference category.

3.4.1.2 US cohort

3.4.1.2.1 Introduction

Since 1975, the University of Pittsburgh, Graduate School of Public Health, Department of Biostatistics has been conducting a large historical cohort study of production and maintenance workers from the 17 of the oldest and largest fibre glass and stone/slag wool factories in the United States. The main objective of their study was to evaluate the total and cause-specific mortality risks among these workers with a focus on the possible association between fibre exposure and the risk of malignant and non-malignant respiratory disease. Esmen et al. 1979 reported the results of measurements of level and size of airborne fibres at 16 of the factories included in the cohort. The cohort consisted of 6 stone/slag wool factories and 11 fibreglass factories (including glass wool, glass filament, and special application glass fibres). The original population under study was (with a few exceptions) the male workforce employed for at least 1 year between 1945 and

1963 in the 17 factories. A first follow-up (Enterline et al. 1983) covered mortality for respiratory diseases up to 1977. A second follow-up (Enterline et al. 1987) covered mortality up to 1982. A third follow-up (Marsh et al. 1990) covered mortality up to 1985. In 1987 the cohort was expanded to include workers employed until 1978, female employees, and workers from additional manufacturing sites. In the following follow-ups covering stone/slag wool workers until 1989 (Marsh et al. 1996) and glass fibre workers until 1992 (Marsh et al. 2001c), efforts were made to characterize more completely the work histories of exposure and co-exposures (Smith et al. 2001, Quinn et al 2001), racial composition, and smoking patterns (Buchanich et al. 2001, Marsh et al. 2001a) of the cohort. Nested case-control studies were performed with 631 male workers with lung cancer at the glass fibre factories as the cases (Stone et al. 2001, Youk et al. 2001) and with 54 male workers with lung cancer at the stone/slag wool factories as the cases (Marsh et al. 1996). Special attention was paid to mortality from mesothelioma in workers in the cohort (Marsh et al. 2001b). See Table 3.10 for further details on the cohort.
In 1979 a cross-sectional investigation was begun with respiratory health assessment of 1028 workers employed in 7 of the factories (Glass fibre factories no. 1, 4, 6, 10, and 15; Stone/slag wool factories no. 8 and 12) in the US cohort (Weill et al. 1983). This study was followed up until 1986 with 1444 workers using a modified study design including e.g. comparison with blue-collar workers, without exposure to fibre or other materials known to be hazardous to respiration, from the local communities (Hughes et al. 1993).

In Europe most stone/slag wool plants began using stone instead of slag after the mid-1940s and currently most European factories continue to melt stone. In the USA, the production of stone wool dominated until the late-1930s when several of the factories converted to the use of slag, which was a cheap waste product from the production of iron. (TIMA 1993 – quoted from IARC 2002). According to Esmen et al. 1979, the stone/slag wool factory no. 3 produced stone wool, no. 8, 12, and 13 produced slag wool, and factory no. 17 produced stone and slag wool. According to Marsh et al. 1990, factories 7, 12, 13, and 17 were always slag wool plants. This slag was predominantly from a copper smelter (factory 7), a lead smelter (factory 17), and steel mills and iron foundries (factories 12 and 13). At factory 3 and 8 both stone and slag wool has been produced but the stone wool production only occurred for a brief period during the 1940s (Marsh et al. 1996). According to Quinn et al. 2001, the stone/slag wool factories no. 3, 7, 12, and 13 produced stone wool, and no. 8 produced stone and slag wool.

3.4.1.2.2 Human exposure

From 1975 to 1978 scientists measured the concentrations and size of airborne fibres in 16 of the 17 factories (no data from stone/slag wool factory no. 7) in the US cohort. The workforce at each factory was classified into occupational groups (see Table 3.11) on the basis of similarities in dust generation mechanisms and work tasks performed. Some members of each group were selected at random for personal sampling for 7-8 hours. The samples were analysed by phase contrast optical microscopy (PCOM) (fibres > 0.56 μm) and transmission electron microscopy (TEM) (fibres < 1 μm) for evaluation of fibre concentrations and by TEM for assessment of fibre size.

For different occupational groups the arithmetic mean fibre concentrations in the 5 stone/slag wool factories was in the range of (0.02 - 0.58) x 10^6 fibres/m^3 as measured by PCOM and (0.004 – 0.12) x 10^6 fibres/m^3 as measured by TEM. The overall arithmetic mean fibre concentration from each factory was in the range of

(0.02 - 0.34) x 10^6 fibres/m^3 as measured by PCOM and (0.01 – 0.04) x 10^6 fibres/m^3 as measured by TEM. See Table 3.11 for fibre concentrations in the different occupational groups. For the different factories, the nominal diameters (= median diameter to which the fibrous product is manufactured) of stone/slag wool fibres ranged from 5 to 8 μm. No data was given specifically on fibre length.

Table 3.10. Factories and population included in the study (adapted from Enterline et al. 1983, 1987, Marsh et al. 1990, 1996, 2001c).

Principal production process (according to Marsh et al. 2001c) Factory no. and other production		Original cohort size 1977, 1982, and 1985 follow-up	Expanded cohort size 1989 (stone/slag wool) and 1992 (fibre glass) follow-up
Stone/slag wool			
3		595	1084
7		120	299
8		308	950
12		193	369
13		185	333
17		445	
Total stone/slag wool		**1846**	**3035**
Glass wool (and limited amounts of continuous filament)			
1	Special application glass or quartz fibres.	682	1032
4		1874	3692
6	Special application glass or quartz fibres.	1167	2680
11	Classified as continuous filament and glass wool factory in Enterline et al. 1987 and Marsh et al. 1990.	865	2281
14		335	1276
15*		710	
Total glass wool		**5633**	**10961**
Continuous filament and glass wool			
9	Special application glass or quartz fibres.	5651	9856
10	Special application glass or quartz fibres. Classified as glass wool factory in Enterline et al. 1987 and Marsh et al. 1990.	96	1892
15 + 16*			3970
Total continuous filament and glass wool		**5747**	**15718**
Continuous filament			
2		1404	2853
5		897	2578
16*		1134	
Total continuous filament		**3435**	**5431**
Total cohort		**16661**	**35145**

* In the 1992 follow-up, the two factories 15 and 16 were combined as the workers moved freely between the adjacent manufacturing facilities.

For different occupational groups the arithmetic mean fibre concentrations in the 5 factories mainly producing glass wool was in the range of (0.003 – 0.38) x 10^6 fibres/m^3 as measured by PCOM and (0.002 – 0.73) x 10^6 fibres/m^3 as measured by TEM. The overall arithmetic mean fibre concentration from each factory was in the

range of (0.01 - 0.04) x 10^6 fibres/m^3 as measured by PCOM and (0.01 – 0.38) x 10^6 fibres/m^3 as measured by TEM. See Table 3.11 for fibre concentrations in the different occupational groups. For the different factories, the nominal diameters of glass wool fibres ranged from 3 to 15 μm. No data was given specifically on fibre length.
The amount of respirable fibres (< 3 μm in diameter, < 50 μm long) varied with different nominal diameters. In general, approximately 60 – 90 % of measured fibre lengths were less than 50 μm long. From a figure in the article it was read that approximately 85 % of airborne fibres were respirable when 5 μm nominal diameter fibre was produced, and approximately 40 % of airborne fibres were respirable when 14 μm nominal diameter fibre was produced. (Esmen et al. 1979).

Table 3.11. Fibre concentrations (10^6 fibres/m^3) in occupational groups and overall in the US cohort (data from Esmen et al. 1979).

Occupational groups	Range of arithmetic means measured by PCOM	Range of arithmetic means measured by TEM
Stone/slag wool (factories 3, 8, 12, 13, and 17)		
Forming	0.02 – 0.58	0.01 – 0.12
Production	0.03 – 0.24	0.01 – 0.04
Manufacturing	0.03 – 0.43	0.004 – 0.03
Maintenance	0.02 – 0.44	0.01 – 0.04
Quality control	0.03 – 0.19	0.01 – 0.07
Shipping	0.03 – 0.15	0.01 - 0.01
Overall	0.02 – 0.34	0.01 – 0.04
Glass wool (factories 1, 4, 6, 11, and 14 singled out based on Marsh et al. 2001)		
Forming	0.003 – 0.05	0.002 – 0.01
Production	0.01 – 0.38	0.004 - 0.73
Manufacturing	0.01 – 0.04	0.004 – 0.12
Maintenance	0.01 – 0.07	0.01 – 0.20
Quality control	0.01– 0.07	0.01 – 0.45
Shipping	0.004 – 0.02	0.002 – 0.01
Overall	0.01 – 0.04	0.01 – 0.38

Based on the above measurements by Esmen et al. 1979, and on work histories for individual workers, Enterline et al. 1983, and 1987 estimated the mean average intensity of exposure to respirable fibres (< 3 μm in diameter). Exposure to fibreglass (mean: 0.04 x 10^6 fibres/m^3) was lower than exposure to stone/slag wool (mean: 0.35 x 10^6 fibres/m^3). See Table 3.12 for more details. Historical data were estimated based on discussions with factory personnel about changes in the production and on dust levels. For fibreglass factories past exposures were believed to differ little from current levels, while exposure levels to stone/slag wool were evaluated to be 1.5 x 10^6 fibres/m^3 prior to 1945, 0.3 x 10^6 fibres/m^3 for the years 1945-60 and 0.03 x 10^6 fibres/m^3 after 1960. (Enterline et al. 1983, and 1987).

Table 3.12. Average intensity of exposure (data from Enterline et al. 1983, and 1987).

Factory no.	Respirable fibres (10^6 fibres/m^3)		
	Mean	Minimum	Maximum
Stone/slag wool			
3	0.43	0.0	1.41
7	0.20	0.0	0.34
8	0.37	0.0	1.34
12	0.22	0.0	1.07
13	0.24	0.0	0.89
17	0.39	0.0	1.36
All stone/slag wool factories	0.35		
Glass wool			
1	0.03	0.0	0.03
4	0.01	0.0	0.03
6	0.06	0.0	0.32
11	0.01	0.0	0.03
14	0.02	0.0	0.03
All fibreglass factories (including factories producing continuous filament)	0.04		

Table 3.13. Exposure estimates and number of workers in the study for each factory (data from Hughes et al. 1993 and Weill et al. 1983).

Factory no.	Mean concentration of fibre exposure (10^6 fibres/m^3) in follow-up	Number of workers in original study	Number of workers in follow-up*
Stone/slag wool			
12	0.03	34	86 (81)
8	0.03	56	99 (74)
Glass fibre			
4 Ordinary	0.003	260	313 (208)
15 Ordinary	0.04	244	269 (174)
1 Ordinary and fine	0.31	110	220 (155)
6 Ordinary and fine	0.03	217	335 (210)
10 Very fine	1.41	107	122 (128)
Total	0.03	1028	1444 (1030)

* Number of workers with chest x ray film (Number with both a health interview and repeatable spirometry)

For the studies on respiratory health assessment, the authors derived individual exposure estimates based on the survey made by Esmen et al. 1979 combined with job histories. In the original study only workers with a minimum of 5-10 years of employment were included but in the follow-up no minimum employment time was required. Excluded from the study were female employees and male employees with more than a month in the batch or binder areas (because of potential exposure to free crystalline silica and phenol-formaldehyde in these areas). The glass fibre factories were classified as ordinary (nominal fibre diameter > 3 μm), ordinary and fine (nominal diameter 1-3 μm), or very fine (nominal fibre diameter < 1 μm) depending on the nominal diameter of the fibres produced. See Table 3.13 for more details. The workers were questioned on their smoking habits and on previous employment in jobs potentially harmful to respiratory health. (Hughes et al. 1993, Weill et al. 1983).

In 1988, the North American Insulation Manufacturer's Association initiated an environmental project at the Harvard School of Public Health and the University of Massachusetts at Lowell to provide comprehensive data on respirable MMVF exposures and on exposure to other workplace contaminants for the 11 fibreglass factories and five of the six stone/slag wool factories (no data from stone/slag wool factory no. 17). Historical individual worker exposure profiles were estimated using an approach that integrates industrial hygiene and epidemiologic methods. Exposures were estimated quantitatively for respirable fibres (defined as those of length (L) $\geq$ 5 μm, diameter (D) < 3 μm, and aspect ratio (L:D) $\geq$ 3), formaldehyde, and silica, and qualitatively for arsenic, asbestos, asphalt, epoxy, polycyclic aromatic hydrocarbons (PAHs), phenolics, styrene, urea, and radiation. Each of the participating factories had airborne fibre and other exposure data for their work areas during approximately 1970 to 1990. Data on about 1600 of these samples were used for the exposure analysis. The fibre measurements made by Esmen et al. 1979 were discarded because there were no supporting data and they could not be coded for detailed work locations and job titles. Historical exposures were estimated based on the changes that had occurred in the production in nominal fibre diameters, use of oil, production rate, use of local ventilation, and manual handling.
After the exposure estimates were linked to individual members of the cohort via the detailed work histories, the job location-specific exposure values for a given time period, factory, department and job title were summarised to form a job location-weighted exposure (JLWE) measure (see Table 3.14). For quantitative exposures, JLWE represents a job location-weighted arithmetic average exposure measure, and for qualitative exposures, JLWE represents a job location-weighted duration of potential exposure measure. For respirable fibres, formaldehyde and silica, the JLWE values were used to compute e.g. average intensity of exposure (see Table 3.15). (Marsh et al. 1996, 2001c and Smith et al. 2001).

According to Marsh et al. 1996, asbestos has also been used in stone/slag wool factory no. 17.

A survey has been conducted to estimate smoking rates in the total MMVF cohort through a stratified random sample of workers (n = 899) from the total cohort. The prevalence of ever smoking and current smoking among male workers in both the fibreglass and stone/slag wool factories was higher than in the US population. Among female workers in the stone/slag wool factories, the prevalence of ever smoking and current smoking was also higher than in the US population but among females in the fibreglass factories, the prevalence was slightly lower than in the US population. See Table 3.16 for more details. Except for fibreglass factory 1, in each fibreglass and stone/slag wool factory the rate of ever smoking was greater than the home state rate, and except for fibreglass factories 1 and 2, and stone/slag wool factory 17, the factory rates of current smoking were also greater than the corresponding state rates. The authors are stating that these findings suggest that at least part of the elevated externally SMRs for respiratory system cancer among fibreglass and stone/slag wool workers were due to uncontrolled positive confounding by smoking. Ongoing analyses of the US MMVF cohort include adjustment for smoking. (Buchanich et al. 2001).

3.4.1.2.3 Respiratory diseases

In the expanded US cohort a statistically significant excess in mortality from non-malignant respiratory disease excluding influenza and pneumonia (NMRD excluding IP) was observed in fibreglass workers when compared to US rates but

when compared to local county rates a deficit in deaths were observed. See Table 3.17 for more details.

For the 5 factories that mainly produced glass wool (1, 4, 6, 11, and 14), the SMR (compared to local county rates) for NMRD excluding IP was reported to be 1.10 (95% CI: 0.91 – 1.32) for all workers and 0.94 (95% CI: 0.72 – 1.20) for long-term workers (employed for more than 5 years) , thus not significantly elevated. For fibreglass workers, a statistically significant excess in mortality from NMRD excluding IP compared to local rates was only observed at factory 4 (SMR: 1.34; 95% CI: 1.03-1.72) among all workers but among long-term workers the excess was not statistically significant. No evidence of an increased mortality risk for NMRD excluding IP by duration of employment or time since first employment was observed.

Table 3.14. Respirable fibre exposure and potential co-exposures expressed as person-years of JLWE by factory, 1946 to 1987 (data from Marsh et al. 1996, 2001c and Smith et al. 2001).

Exposure agent	Stone/slag wool factories					Glass wool factories				
	3	7	8	12	13	1	4	6	11	14
Quantitative exposures:										
Respirable fibres	8668	1443	3591	1884	1980	11276	31337	17868	21927	9532
Formaldehyde	1*	1354	3107	1532	1544	11391	26234	17148	21649	9101
Silica	2924	< 1*	377	97	36	10084	1487	1656	5414	938
Qualitative exposures:										
Arsenic	0	276	0	0	0	0	0	0	0	0
Asbestos	1065	188	209	186	390	1680	6269	3912	1691	1395
Asphalt	3965	4*	714	0	58	256	9815	7979	592	164
Epoxy	No data					0	0	442	0	0
PAHs	0	145	0	0	0	0	0	0	0	0
Phenolics	1*	1348	2647	1532	1544	8577	26198	16726	19941	7071
Styrene	No data					0	0	0	5	0
Urea	< 1*	518	823	255	458	3835	17638	10826	18001	6781
Radiation	0	175	< 1*	0	0	No data				

* Factory study population including employee(s) transferred from exposed factories, otherwise unexposed

Table 3.15. Mean average intensity of exposure (data from Marsh et al. 1996, 2001c and Smith et al. 2001).

Factory no.	Respirable fibres (10^6 fibres/m^3)	Formaldehyde (ppm)	Crystalline silica dust (mg/m^3)
Stone/slag wool			
3	0.27		
7	0.29		
8	0.07	No data in articles	No data in articles
12	0.13		
13	0.66		
Glass wool			
1	0.05	0.06	
4	0.06	0.06	
6	0.21	0.15	No data in articles
11	0.10	0.08	
14	0.05	0.15	
All fibreglass factories (including factories producing continuous filament)	0.07	0.08	0.07 (Range 0.01 to 0.18 for individual factories)

Table 3.16. Estimated point prevalence rates (95 % confidence interval) of ever and current smoking (cigarettes only) as of 1/1/80 showing US (1980) comparison.

	Ever smoking			Current smoking		
	Fibreglass	Stone/slag wool	US (1980)	Fibreglass	Stone/slag wool	US (1980)
All male	76.3 (71.2 - 81.4)	74.2 (69.1 - 79.3)	65.6	42.5 (36.6 - 48.4)	44.5 (38.7 - 50.3)	37.6
All female	41.8 (32.7 - 50.9)	60.2 (52.3 - 68.1)	44.5	24.5 (16.5 - 32.5)	42.9 (34.9 - 50.9)	29.3

For stone/slag wool workers, an excess in mortality from NMRD excluding IP was observed both when compared to US rates and local rates but none of the numbers were statistically significant. See Table 3.17 for more details.
The excess in mortality from NMRD excluding IP for stone/slag wool workers was observed at all factories except factory no. 8. None of the 39 deaths were coded to an underlying cause of death suggestive of an occupational aetiology (such as pneumoconiosis). For stone/slag wool workers, relative risk regression modelling of internal cohort rates for NMRD excluding IP revealed no consistent evidence of an association with any of the respirable fibre measures considered with or without adjustment for potential confounding factors (no further details were given).
The cohort was not expanded for workers from stone/slag wool factory no. 17 but nevertheless a follow-up was conducted for these workers. A statistically significant excess in mortality from NMRD excluding IP occurred when compared to local county rates (SMR: 1.83). Only one of the 20 observed deaths was coded to an underlying cause suggesting a specific occupational aetiology (that was asbestosis). (Marsh et al. 1996 and 2001c).

Table 3.17. Observed death (OBS), SMR (based on US and local county rates) and 95 % CI for non-malignant respiratory diseases in exposed stone/slag wool and fibreglass workers in the expanded US cohort (data from Marsh et al. 1996 and 2001c).

Cause of death	US rates (1946-1989/1992)			Local county rates (1960-1989/1992)		
	OBS	SMR	95 % CI	OBS	SMR	95 % CI
Stone/slag wool:						
Non-malignant respiratory diseases (NMRD)	50	1.03	No data	49	1.07	No data
Influenza and pneumonia (IP)	11	0.60	No data	10	0.65	No data
NMRD excluding IP	39	1.31	0.93-1.79	39	1.27	0.90-1.74
Fibreglass:						
Non-malignant respiratory diseases (NMRD)	629	0.94	0.87-1.02	593	0.86**	0.79-0.93
Influenza and pneumonia (IP)	163	0.66**	0.56-0.77	153	0.72**	0.61-0.84
NMRD excluding IP	466	1.10*	1.01-1.21	440	0.92	0.84-1.02

* $p < 0.05$; ** $p < 0.01$

The pattern of findings for NMRD excluding IP mortality in the expanded cohort was generally consistent with those observed in previous follow-ups based on the original cohort data. In all three follow-ups with the original cohort, the SMR for NMRD excluding IP was statistically significantly elevated for all workers in the cohort when compared to US rates. A greater excess mortality from NMRD excluding IP was observed among stone/slag wool workers than among fibreglass workers (only statistically significant for fibreglass workers in the 1977 follow-up when compared to US rates). In the 1977 follow-up the authors are stating that out of the 150 deaths caused by NMRD excluding IP, 11 were due to pneumoconiosis of which 10 were due to silicosis (8 deaths occurred among workers at fibreglass factory no. 9). (Enterline et al. 1983, 1987, Marsh et al. 1990).

For the studies on respiratory health assessment, workers from 7 of the factories in the US cohort were questioned on respiratory symptoms, were tested for pulmonary function by spirometry, and had chest radiographs taken (which were read by 3 readers in the original study and 5 readers in the follow-up). In both the original study and in the follow-up, respiratory symptoms and the level of pulmonary function were related to cigarette smoking and not to fibre exposure.
In the original study, chest x-ray revealed small opacities (shadows) in low profusion categories in 10 % of the workers. Their prevalence increased significantly with age and smoking and they were associated with lower lung function. The prevalence of opacities was highest among employees at the two factories (no. 1 and 6) manufacturing both ordinary and fine fibres. Among current smokers, after accounting for age, pack-years of smoking, and two factory categories (ordinary and fine fibre or not), presence of small opacities was significantly related to several measures of fibre exposure including cumulative exposure to fine fibres. The authors concluded that exposure to MMVF with small diameters may lead to low-level profusion of small opacities in the lungs, even though the authors did not regard the findings as clinically significant.
In the follow-up study, a lower prevalence of small opacities was found than in the original study. The presence of opacities was not related to lung function, to cigarette smoking, or to previous occupational exposures but it was significantly related to film quality. Ninety three percent of the workers with small opacities worked at the two factories (no. 1 and 10) with the highest exposures to fine glass fibres, resulting in a dose-response relation across plants. For factory no. 1 the prevalence of opacities for the MMVF and comparison workers were not significantly different (5.9% v 3.1%). No comparison x-ray films were obtained for the factory (no. 10) with the highest prevalence (6.6%), so a second phase of the study was conducted with pre-employment films from these two factories. On this second reading, the prevalence of opacities was lower; there were no significant differences between the two groups of films, and no relation between opacities and exposure indices. The authors concluded that the results indicated no adverse clinical, functional or radiographic signs of effects of exposure to MMVFs in these workers. (Hughes et al. 1993, Weill et al. 1983).

3.4.1.2.4 Non-respiratory diseases

In the expanded US cohort no statistically significantly elevated mortality risks were observed among the non-malignant non-respiratory diseases (including nephritis and nephrosis, and all heart diseases) in fibreglass workers (Marsh et al. 2001c). For stone/slag wool workers, the mortality from nephritis and nephrosis was statistically significantly elevated. The excess was observed in all study factories except factory no. 12. The authors are stating that to some extent, these excesses may be associated with reported long-term exposures to airborne lead,

cadmium or arsenic in factory no. 7. (Marsh et al. 1996). See Table 3.18 for more details.

Table 3.18. Observed deaths (OBS), SMR and 95 % CI for nephritis and nephrosis in exposed workers in the expanded US cohort compared to local county rates. Data from Marsh et al. 1996 and 2001c.

Cause of death	Stone/slag wool			Glass fibre		
	OBS	SMR	95 % CI	OBS	SMR	95 % CI
Nephritis and nephrosis	11	2.02*	No data	70	1.04	0.81 – 1.32

* $p < 0.05$

In the follow-ups made in the original US cohort, SMRs for non-respiratory diseases were only reported as compared to US rates and for fibreglass and stone/slag wool workers combined. Mortality from nephritis and nephrosis was elevated in both the 1982 (SMR: 1.26) and 1985 (SMR: 1.46) follow-up and reached statistical significance in the 1985 follow-up. (Enterline et al. 1987, Marsh et al. 1990).

A case-control study of fibreglass workers in the US reported no association between exposure to respirable fibreglass or respirable silica and nephritis or nephrosis. (Chiazze et al. 1999).

3.4.1.3 Other studies on respiratory diseases

See Table 3.19 for an overview of available data and exposure levels in recent studies on respiratory diseases in MMVF workers. The results of these studies are described in the following based on IARC 2002 and on some of the original articles. The study by Hughes et al. (1993) is described in more detail under the US cohort.

3.4.1.3.1 Pneumoconiosis

Pneumoconiosis is the condition of permanent deposition of particulate matter in the lungs and by the tissue reaction to its presence. Pneumoconiosis may lead to fibrosis. (Dorland 1988).

The data available on pneumoconiosis mainly come from radiological studies and are limited to standard thoracic x-rays that have low sensitivity and low specificity. All of the recent studies (including the one by Hughes et al. (1993)) found no significant excess of small opacities on chest autoradiographs except two studies of glass fibre production workers (Kilburn and Warshaw 1991) and end-users (Kilburn et al. 1992). However, as stated by the authors, previous exposure to asbestos could have affected the observed results. Moreover, severe methodological limitations were reported by other authors and agreed on by the IARC working group, which considers the data from these two studies uninterpretable.

3.4.1.3.2 Pleural abnormalities

As for pneumoconiosis the data on pleural abnormalities come from standard thoracic radiography. Pleural abnormalities were detected in the studies by Kilburn and Warshaw (1991) and Kilburn et al. (1992) but as for pneumoconiosis data from these studies were considered uninterpretable by the IARC working group. In the other studies no statistically significant excess of pleural abnormalities were observed. Moreover, a nested case-control study in the study by Järvholm et al. (1995) failed to demonstrate a relationship with exposure to fibres.

3.4.1.3.3 Respiratory symptoms

Respiratory symptoms were assessed by questionnaires. In the production studies from USA (Hughes et al. 1993) and Japan (Yano and Karita 1998) no statistically significant association was found between respiratory symptoms and exposure to fibres.
Kilburn et al. (1992) and Hunting and Welch (1993) reported a high rate of chronic bronchitis among end-users and Kilburn and Warshaw (1991) reported nose bleed and throat irritation among production workers. According to IARC 2002, the interpretation of these results was hampered by the absence of a control group and the potential for co-exposure to air contaminants including asbestos.
In one of the French production studies (Moulin et al. 1988) odds ratios (ORs) (compared to never exposed workers) for cough and phlegm were significantly increased (but no trend with duration of exposure) after adjustment for smoking and age among glass wool workers at one factory that contained 51% of the study population but not among workers in the other four factories (2 glass wool and 2 stone wool). In the same factory, complaints of sinuses and nasal cavities occurring after hiring showed a statistically significant trend with duration of employment and the OR for pharyngeal and laryngeal symptoms was statistically significantly elevated among the group of workers employed for 11-20 years. A few percent of the workers had co-exposure to formaldehyde-phenol or ureaformaldehyde resins. Among these a statistically significant OR for pharyngeal and laryngeal symptoms were observed. In the other French production study (Moulin et al. 1987) a significant excess for dyspnoea and nasal congestion was revealed among exposed workers.
In Danish production workers (Hansen et al. 1999) the prevalence of reported emphysema was 3.8% in the workers (9 cases) versus 0.9% in the control group (2 cases), resulting in a relative risk of 4.5 (95% CI: 1.0-20.6). No significant difference was found between the workers and the control group in the frequency of reported asthma and chronic bronchitis or in the reported symptoms (cough, phlegm, and dyspnoea).
In Swedish end-users (construction workers) (Albin et al. 1998) high exposure to insulation wool, silica, or asbestos was associated with statistically significant increased odds ratios for persistent cough of the same magnitude as current smoking. Clear dose-response associations were found for all three types of dust when exposure was cross classified according to a job exposure matrix and self reported exposure.
The results of the study with Danish end-users (construction workers) (Petersen and Sabroe 1991) are described in the chapter on irritation.

3.4.1.3.4 Pulmonary function

Pulmonary function was measured by spirometry. In the production studies from USA (Hughes et al. 1993), France (Moulin et al. 1987) and Australia (Brown et al. 1996) no statistically significant association was found between pulmonary function and exposure to fibres.

The IARC working group considered the data for pulmonary function uninterpretable in the studies by Kilburn et al. (1992) and Kilburn and Warshaw (1991).
In Danish production workers (Hansen et al. 1999) there were no significant differences in means of forced expiratory volume in one second (FEV_1) or forced vital capacity (FVC) between the workers and the control group (general population matched on age and social class), but the FEV_1/FVC ratio was statistically significantly lower in the workers, indicating obstructive lung disease, also when adjusting for self-reported exposure to asbestos and for asthma. Subgroup analysis showed that the elevated risk of airway obstruction was restricted to heavy smokers (> 40 packs-years). The authors speculated that there might be an additive or synergistic action between smoking and fibre exposure on airflow obstruction.
In Danish end-users (insulators) (Clausen et al. 1993) there were no significant differences in FVC between the workers and the control group (bus drivers), but the FEV_1 was statistically significantly lower in the workers independent of smoking habits. No statistics were performed on the FEV_1/FVC ratio but it was reported that 66% of the insulation workers had a ratio of under 70%, whereas only 9% of the control group had such low values, indicating obstructive lung disease in the workers. Comparison with measurements made 6 or 8 years earlier showed a significantly higher decline in FEV_1 and FVC in insulation workers than in the control group. The decline in FEV_1 was significant independent of smoking habits whereas the decline in FVC only was significant for current smokers. Over two thirds of the insulation workers indicated that they had been exposed to asbestos in connection with their work but no difference in lung function was found between exposed and unexposed workers. Insulation workers occasionally used lime containing tetrahydrofuran and polyurethane type insulation material that contain isocyanates.
In Swedish end-users (construction workers) (Albin et al. 1998) there were no significant differences in means of vital capacity (VC) and FEV_1 between construction workers exposed to insulation wool and construction workers not exposed to insulation wool. Comparison with measurements made on average 3.9 years later showed no statistically significant difference in yearly change of VC and FEV_1 between exposed and unexposed construction workers. For all the analysis no consistent effects were found from exposure to silica, asbestos or isocyanates.

3.4.2 Oral intake

No data were found.

3.4.3 Dermal contact

No data were found.

3.5 Toxicity to reproduction

No data were found.

Table 3.19. Recent studies on respiratory diseases in MMVF workers (data from IARC 2002 and from some of the original articles).

Reference	Country	Industry	No. of subjects*	Exposure (10^6 fibres/m^3) and size of fibres	Available data		
					Pneumoconiosis and/or pleural abnormalities by thoracic x-rays	Respiratory symptoms by questionnaire	Pulmonary function by spirometry
Glass fibre (excluding continuous filament)							
Hughes et al. 1993	USA	Production	1259/875	0.03 (estimated mean for airborne fibres)	Yes	Yes	Yes
Hunting and Welch 1993	USA	End-users (sheet-metal workers)	333	No data in IARC 2002	No	Yes	No
Kilburn and Warshaw 1991	USA	Production	175	No data	Yes	Yes	Yes
Kilburn et al. 1992	USA	End-users (insulation of refrigerators)	284/214	< 0.1-0.4 (measured) 3-7 μm diameters predominated	Yes	Yes	Yes
Moulin et al. 1987	France	Production	524	0.05-0.18 (mean for airborne fibres >5μm long and < 3 μm in diameter measured in different work areas). (Kauffer et al. 1987)	Yes	Yes	Yes
Moulin et al. 1988	France	Production	1839	0.05-0.12 (mean for airborne fibres >5μm long and < 3 μm in diameter measured in different work areas in on factory covering 1041 of the workers). (Kauffer et al. 1987)	No	Yes	No
Stone/slag wool							
Hansen et al. 1999	Denmark	Production	377/235	0.1-0.2 (estimated average for airborne respirable fibres in the European stone/slag wool industry in the examined period calculated based on an experimental model)	No	Yes	Yes
Hughes et al. 1993	USA	Production	185/155	0.03 (estimated mean for airborne fibres)	Yes	Yes	Yes
Järvholm et al. 1995	Sweden	Production	933	No data in IARC 2002	Yes	No	No
Moulin et al. 1988	France	Production	185	No data	No	Yes	No
Yano and Karita 1998	Japan	Production	440/493	No data in IARC 2002	Yes	Yes	No

Reference	Country	Industry	No. of subjects*	Exposure (10^6 fibres/m^3) and size of fibres	Available data		
					Pneumoconiosis and/or pleural abnormalities by thoracic x-rays	Respiratory symptoms by questionnaire	Pulmonary function by spirometry
Glass and stone/slag wool							
Albin et al. 1998	Sweden	End-users (construction workers)	96004	0.06 – 0.91 (mean airborne concentration of respirable fibres monitored by personal sampling for different occupations within the Swedish construction industry 1978-90). Values up to 5.08 were measured in insulators, which generally were exposed to the highest values.	No	Yes	Yes
Brown et al. 1996	Australia	Production	533/687	No data	Yes	Yes	Yes
Clausen et al. 1993	Denmark	End-users (insulators)	340	Usually 0.03-1 but up to 10 (individual measurements at Danish worksites since 1988)	No	No	Yes
Petersen and Sabroe 1991	Denmark	End-users (construction workers)	2654	< 0.05 - > 3, with about 80 % of the fibres being thinner than 1 μm (range for airborne fibres for Danish insulation workplaces reported by Schneider (1979))	No	Yes	No

* For some of the studies, number of subjects differed among the different parts of the study

3.6 Mutagenic and genotoxic effects

No data were found.

3.7 Carcinogenic effects

3.7.1 Inhalation

Two large cohort studies and case-control studies nested within these cohorts from the USA and Europe provided the epidemiological evidence on respiratory and other cancers associated with occupational exposure to glass fibres and stone/slag wool. No human carcinogenicity data were available for HT-fibres.

See chapter 3.4.1.1.1 and 3.4.1.2.1 for an introduction to the cohorts and 3.4.1.1.2 and 3.4.1.2.2 for exposure estimates in the cohorts.

3.7.1.1 European cohort

Both in the second follow-up (Simonato et al. 1986) and in the updating of neoplastic mortality (Boffetta et al. 1997) in the European cohort, the standardized mortality ratio (SMR) for lung cancer (including tracheal, bronchial and lung cancer) in exposed workers was statistically significantly elevated compared to a national reference population. The SMR for lung cancer was still elevated but not statistically significantly when compared to a local reference population (a region or county for most factories). The standardized incidence ratio (SIR) for lung cancer, which was only calculated in Simonato et al. 1986, was also elevated but not statistically significantly. The SIR but not the SMR for cancer of the buccal cavity and pharynx were statistically significantly elevated. See Table 3.20 and Table 3.21 for more details. The SMR and SIR were not statistically significantly elevated for other types of malignant neoplasms. Five mesothelioma deaths occurred in the exposed workers.

Table 3.20. SMR (based on national and local rates) for selected malignant neoplasms in exposed workers in the European cohort.

Cause of death	SMR	
	National rates	Local rates
Simonato et al. 1986:		
All malignant neoplasms	1.11*	No data
Trachea, bronchus and lung	1.25*	1.10
Buccal cavity and pharynx	1.23	No data
Boffetta et al. 1997:		
All malignant neoplasms	1.13*	No data
Trachea, bronchus and lung	1.32*	No data
Buccal cavity and pharynx	1.49	No data

* $p<0.05$

When the exposed workers were divided into groups of exposure to stone/slag wool or glass wool, the SMR for lung cancer and for cancer of the buccal cavity and pharynx was similar in the two groups. See Table 3.20 for more details.

Table 3.21. SIR (based on national rates) for selected malignant neoplasms in exposed workers in the European cohort. Data from Simonato et al. (1986).

Cause of death	SIR		
	Total cohort	Stone/slag wool	Glass wool
All malignant neoplasms	1.01	No data	No data
Trachea, bronchus and lung	1.16	1.28*	0.80
Buccal cavity and pharynx	1.64*	1.97*	0.83

* p<0.05

Table 3.22. SMR (based on national and local rates) for selected malignant neoplasms for stone/slag wool and glass wool workers in the European cohort.

Cause of death	Stone/slag wool		Glass wool	
	National rates	Local rates	National rates	Local rates
Simonato et al. 1986:				
All malignant neoplasms		No data		
Trachea, bronchus and lung	1.24	1.24	1.27*	1.03
Buccal cavity and pharynx		No data		
Boffetta et al. 1997:				
All malignant neoplasms	1.08	No data	1.11*	No data
Trachea, bronchus and lung	1.34*	No data	1.27*	No data
Buccal cavity and pharynx	1.33	No data	1.47	No data

* p<0.05

In the second follow-up (Simonato et al. 1986) the SMR and SIR for lung cancer for both stone/slag wool workers and glass wool workers showed a pattern of increasing mortality with time since first exposure but not with duration of employment. The SMR and SIR for lung cancer for stone/slag wool workers but not glass wool workers decreased from the early to the late technological phase. In the updating of neoplastic mortality (Boffetta et al. 1997) the relative risk of lung cancer among stone/slag wool workers increased with time-since-first-employment and duration of employment but the trend in lung cancer mortality according to technologic phase at first employment was less marked than in the second follow-up.

One study estimated the individual cumulative exposure to stone/slag wool fibres in 159 stone/slag wool workers who had died from lung cancer. No trend in relative risk for lung cancer was seen with cumulative exposure among workers employed for one year or more. (Consonni et al. 1998 - quoted from IARC 2002).

In a nested case-control study that included detailed information on exposure to stone/slag wool fibres, individual smoking habits and potential occupational confounders, no increased risk of lung cancer with increasing fibre exposure was reported (Kjaerheim et al. 2002 - quoted from IARC 2002). In another nested case-control study, there was no evidence of a relationship between lung cancer in glass wool workers and fibre diameter, duration of exposure or time since first employment (Gardner et al. 1988 - quoted from IARC 2002).

3.7.1.2 US cohort

In the expanded US cohort a statistically significant excess in mortality from respiratory system cancer (mainly trachea, bronchus and lung) was observed in fibreglass workers when compared to US rates but when compared to local county rates the excess was no longer statistically significant. See Table 3.23 for more details.
For the 5 factories that mainly produced glass wool (1, 4, 6, 11, and 14), the SMR (compared to local county rates) for respiratory system cancer was statistically significantly elevated for all workers but not for long-term workers (employed for more than 5 years). No statistically significant excess in mortality from respiratory system cancer compared to local rates was observed at the individual factories.
Among the total fibreglass cohort, the SMR for respiratory system cancer increased with calendar time and with time since first employment but these increases were less pronounced among long-term workers. No evidence of an increased mortality risk for respiratory system cancer by duration of employment was observed.
For stone/slag wool workers, a statistically significant excess in mortality from cancer of the trachea, bronchus and lung was observed when compared to US rates but when compared to local county rates the excess was no longer statistically significant. See Table 3.23 for more details.
The excess in mortality from respiratory system cancer for stone/slag wool workers was due to excesses in factories 7 and 13 and a statistically significant excess in factory 12. For stone/slag wool workers, relative risk regression modelling of internal cohort rates for respiratory system cancer revealed no consistent evidence of an association with any of the respirable fibre measures considered with or without adjustment for potential confounding factors.
The cohort was not expanded for workers from stone/slag wool factory no. 17 but nevertheless a follow-up was conducted for these workers. A statistically significant excess in mortality from cancer of the trachea, bronchus and lung occurred when compared to national (SMR: 1.95) and local county rates (SMR: 1.53).
The SMR was not statistically significantly elevated for other types of malignant neoplasms including buccal cavity and pharynx. (Marsh et al. 1996 and 2001c).

All statistically significantly elevated SMRs for respiratory system cancer in fibreglass as well as stone/slag wool workers were reduced to not statistically significant levels when adjusted for cigarette smoking (Marsh et al. 2001a).

Table 3.23. SMR (based on US and local county rates) for selected malignant neoplasms in exposed stone/slag wool and fibreglass workers in the expanded US cohort (data from Marsh et al. 1996 and 2001c).

Cause of death	Stone/slag wool		Fibreglass	
	US rates	Local county rates	US rates	Local county rates
All malignant neoplasms	1.14	1.13	0.98	0.94**
Buccal cavity and pharynx	No data		1.07	1.11
Respiratory system	1.24	1.17	1.16**	1.06
Larynx	No data		1.04	1.01
Trachea, bronchus and lung	1.29*	1.22	1.17**	1.07
All other	No data		0.80	0.85

* $p < 0.05$; ** $p < 0.01$

In nested case-control studies no statistically significant association was observed between SMRs for respiratory system cancer and increasing exposure to respirable

fibreglass or stone/slag wool when adjusted for smoking. In the study with fibreglass workers, some evidence was provided of increased risk for respiratory system cancer among workers at the higher observed levels of average intensity of exposure to formaldehyde and/or silica. (Marsh et al. 2001c, Stone et al. 2001, Youk et al. 2001).

The pattern of findings for respiratory system cancer mortality in the expanded cohort was generally consistent with those observed in previous follow-ups based on the original cohort data. In all three follow-ups with the original cohort, the SMR for respiratory system cancer was elevated for all workers in the cohort when compared to US rates and local county rates. A greater excess mortality from respiratory system cancer was observed among stone/slag wool workers than among fibreglass workers. (Enterline et al. 1983, 1987, Marsh et al. 1990).

A total of 10 deaths possible due to malignant mesothelioma were identified in the US cohort (8 in fibreglass and 2 in stone/slag wool workers) based on any mention of the word "mesothelioma" on the death certificate. A subsequent review of medical records and pathology specimens for 3 of the 10 workers deemed two deaths as definitely not due to mesothelioma and one as having a 50% chance of being caused by mesothelioma. Two other deaths, for which only medical records were available, were given a less than 50% chance of being due to mesothelioma. Eight of the 10 decedents had potential occupational asbestos exposure inside or outside the MMVF industry. According to the authors the overall mortality risk from malignant mesothelioma did not seem to be elevated in the US cohort. (Marsh et al. 2001b).

3.7.2 Oral intake

No data were found.

3.7.3 Dermal contact

No data were found.

3.7.4 IARC evaluation on human carcinogenicity

Cited from IARC (2002)

3.7.4.1 Glass wool

"The findings of the United States cohort study provided no evidence of excess mortality from all causes combined or from all cancers combined, using local rates. A statistically significant 6% excess in respiratory cancer (primarily trachea, bronchus and lung) mortality was observed. When analysis was restricted to long-term workers, the excess was reduced and was no longer statistically significant. Adjustment for smoking based on a random sample of workers suggests that smoking may account for the excesses in respiratory cancer observed in the male glass fibre cohort (glass wool and continuous glass filament combined). The standardized mortality ratios for respiratory cancer were related neither to duration of employment among the total cohort or among long-term workers nor to duration of exposure, cumulative exposure or average intensity of exposure to respirable glass fibre (glass wool and continuous glass filament combined). Analysis by product group showed a statistically significant excess of respiratory

cancer for all workers from plants grouped as 'mostly glass wool', but this excess risk for the 'mostly-glass-wool' product group was reduced and no longer statistically significant when the cohort was limited to long-term workers (≥ 5 years of employment). There was no evidence of an excess of mesothelioma or non-respiratory cancers.

The case-control study of respiratory cancer nested within the United States cohort enabled control of plant co-exposure and a more detailed control for confounding by smoking. Duration of exposure, cumulative exposure, average intensity of exposure and the time since first exposure to respirable glass fibre were not associated with an increased risk for respiratory cancer. These results were not altered by using different characterizations of categorized respirable fibre exposure or by alternative models for continuous exposure data.

The European cohort study of glass wool workers demonstrated an increased mortality from lung cancer (trachea, bronchus and lung) but no trend with time since first hire or duration of employment. One death from mesothelioma was observed in this cohort. This study did not estimate fibre exposure, but used surrogate measures such as 'technological phase at first employment. No information was available either on co-exposure or on smoking habits."

"There is inadequate evidence in humans for the carcinogenicity of glass wool."

3.7.4.2 Stone and slag wool

"The present evaluation relies mainly on cohort and nested case-control studies, in which exposure to stone wool and exposure to slag wool were not considered separately.

The extended follow-up of the rock (stone)/slag wool cohort from the USA indicated an overall risk of respiratory cancer when either national or local comparison rates were used. However, no association was found with duration of exposure or with time since first exposure. Standardised mortality ratios were no longer elevated when indirect adjustment for smoking was made. The nested case-control study showed no association between respiratory cancer and estimated cumulative exposure to respirable fibres, with or without adjustment for possible confounding by smoking and other sources of occupational exposure. Another nested case-control study partially overlapping with the study in the USA showed no increased risk for respiratory cancer in association with exposure to slag wool.

The extended follow-up of the European cohort study indicated an overall elevated risk for lung cancer when national comparison rates were used. This study showed an increasing risk with years since first exposure. The highest standardised mortality ratio was found among workers with the longest time since first employment and among those first employed during the 'early technological phase', i.e. before the introduction of oil and binders and use of the batch-processing method. However, in a case-control study that included detailed information on exposure to fibres, individual smoking habits and potential occupational confounders, no increased risk of lung cancer with increasing fibre exposure was reported.

The results from these studies provide no evidence of an increased risk for pleural mesotheliomas or any other tumours."

"There is inadequate evidence in humans for the carcinogenicity of rock (stone) wool/slag wool."

3.7.4.3 HT fibres

No data are available.

3.7.4.4 Conclusion on human carcinogenicity

"Results from the most recent cohort and nested case-control studies of United States workers exposed to glass wool and continuous glass filament and of European workers exposed to rock (stone) and slag wool have not provided consistent evidence of an association between exposure to fibres and risk for lung cancer or mesothelioma.

These studies, like all epidemiological investigations, have limitations that must be born in mind when interpreting their results. Although the exposure assessment methods used in these studies are far better than in most epidemiological studies, there is still the potential for exposure misclassification. Notable these studies were not able to examine fully the risks to workers exposed to more durable fibres. Information on smoking and on the other potential confounders that were adjusted for in these studies are also subject to measurement error, which may have influenced the validity of the adjustments made for these factors. Under ascertainment and misclassification of mesothelioma may also be a concern in these studies, which primarily relied upon death certificate information. Finally, although these studies are very large by epidemiological standards, their sensitivity may be limited by the fact that fibre exposure levels were low for a large proportion of the study population.

Of some concern are risks for workers in industries that use or remove these products (e.g. construction), who may have experienced higher, but perhaps more intermittent, exposure to man-made vitreous fibres. The data available to evaluate cancer risks from exposure to man-made vitreous fibres in these populations are very limited."

4 Animal toxicity

4.1 Single dose toxicity

4.1.1 Intratracheal instillation

Three types of insulation glass fibre (median diameters 2.3 – 4.1 μm), a fine (median diameter 0.1 μm) and a thicker (median diameter 0.2 μm) type of glass micro fibre was instilled intra-tracheally to groups of 20 hamsters. The dose was 7 mg of the glass micro fibre. No report on weight dose for the other fibre types or fibre concentration for any group was reported. None of the glass wool treated hamsters died, while 3/20 of the thicker micro fibre treated hamsters and all hamsters treated with the fine micro fibre died within 30 days. The dead animals had haemorrhagic and oedematous lungs. (Smith et al. 1987 – quoted from IARC 1988).

4.2 Irritation

Rubbing of the shaved skin of guinea pigs with a tampon of glass wool produced erythema and ,rarely, puncitorm haemorrhages. Pellerat & Condert 1946 – quoted from IARC 1988).

4.3 Sensitisation

No data were found.

4.4 Repeated dose toxicity

4.4.1 Inhalation

Accumulation of macrophages occurred in a number of inhalation studies conducted in the mouse, rat, guinea-pig and hamster exposed to concentrations of glass fibres of up to 100 mg/m^3 for periods ranging from 2 days to 24 months. No evidence of fibrosis of the lung was observed in most of the studies. The tissue reaction is weaker with glass and stone wool than with special purpose glass fibres and much less severe than with asbestos. (Schepers & Delahunt 1955; Gross et al. 1970; Lee et al. 1979 and 1981; Morriset et al. 1979; Lee et al. 1981; Pickrell et al 1983; Smith et al. 1984 – quoted from WHO 1988).

Alveolar lipoproteinosis was reported in a 90 day-study where rats, guinea pigs and hamsters were exposed to relatively high concentrations of glass fibres (420 mg/m^3; 0.73 x 10^9/m^3 fibres between 5 and 10 μm long and around 1.2 μm in diameter) 6 h/day, 5 d/week. The effect regressed one year after the end of exposure. (Lee et al. 1979 – quoted from WHO 1988 and IARC 1988).

Groups of 52-61 rats and 47-60 hamsters were treated by nose-only inhalation 6 h/day, 5 days/week for 24 months to dust clouds of four types of glass fibres, stone wool, refractory ceramic fibres or asbestos with mean diameters ranging from 0.45-

6.1 μm at dose levels of up to 3000 fibres/cm^3 (3 x 10^9 fibres/m^3). For glass fibres with a diameter of 4.5 μm (possibly glass wool), concentrations of 300 or 3000 fibres/cm^3 (3 x 10^8 - 3 x 10^9 fibres/m^3) were used. Stone wool (diameter of 2.7 μm) in a concentration of 200 fibres/cm^3 (2 x 10^8 fibres/m^3) was used. In some of the groups (not specified), very slight peri-bronchial fibrosis was observed (Smith et al. 1984; 1987 – quoted from IARC 1988).

Alveolar macrophagic reaction and slight septal fibrosis was observed in rats exposed whole body for up to 2 years to 5 mg/m^3 glass or stone wool. For glass wool, the weight concentration corresponded to 70 f/ml (7.0 x 10^7 f/m^3) respirable glass fibres of which 68.7 % had a diameter < 1 μm, and 88.3 % had a diameter < 3 μm. For the stone wool, the concentration of respirable fibres was 13 f /ml (1.3 x 10^7 f/m^3), 22.7 % with diameters < 1 μm and 69.4 % with diameters < 3 μm. (Le Bouffant et al. 1987).

4.4.2 Intratracheal instillation

Rats exposed intra-tracheally to US glass wool (diameter 0.1- 0.6 μm, no report of the dose) for 6 months showed 5-10% lymphocytes and many multinucleated giant cells (10-20%) (Miller 1980 – quoted from IARC 1988).

4.4.3 Oral intake

No data were found.

4.4.4 Dermal contact

No data were found.

4.5 Toxicity to reproduction

No data were found.

4.6 Mutagenic and genotoxic effects

4.6.1 *In vitro* studies

A number of studies have shown that glass fibres can cause effects in genotoxicity tests in non-human mammalian cells. The fibres have shown to cause DNA damage, micronucleus and bi- and multinucleated cell formation. It appears that the potential for inducing cell transformation and chromosomal aberrations is related to the dimensions of the fibres, long fibres being more active than shorter fibres. (IARC 2002).

A few studies of the genotoxic effects of stone wool fibres have been performed, showing a potential to induce mutations in bacterial test systems as well as DNA damage and chromosomal and nuclear aberrations in cultured cells. (IARC 2002).

4.6.2 *In vivo* studies

No data were found.

4.7 Carcinogenic effects

4.7.1 Inhalation

4.7.1.1 Insulation glass wool

Six studies in rats and 3 studies in hamsters with different types of glass fibres including glass wools were available. The data from these studies relevant for evaluation of the carcinogenic potential of glass wools are summarised in Table 4.1.

4.7.1.2 Stone(rock) wool

Three long-term inhalation studies in rats with different types of stone wool were available. The studies are summarised in Table 4.2.

4.7.1.3 HT-fibre

A group of 140 Fischer 344 rats was exposed by nose-only inhalation 6 h/day, 5d/weeks for 104 weeks to 30 mg/m^3 HT-fibre. A control group was kept in air. The animals were kept for a treatment free period until 20% survival of the control rats. The fibre concentration was at least 250 x 10^6 WHO fibres/m^3. The geometric mean diameter was 0.87 μm and the geometric mean length 10.8 μm. The retained lung burden after 24 months was 60.2 x 10^6 WHO fibres. There was no effect on survival in the HT-fibre treated group when compared to controls. No fibrosis, no carcinomas and 5 adenomas in 107 HT-fibre exposed rats were observed. The air control group had no fibrosis, one carcinoma and three adenomas in 107 rats. (Kamstrup et al. 1998; 2001 – quoted from IARC 2002).

4.7.2 Intratracheal

4.7.2.1 Glass wool

No data were found.

4.7.2.2 Stone (rock) wool

Groups of 40-59 Wistar rats were treated by intra-tracheal instillation with a total dose of 5 mg or 10 mg of a stone wool suspension within a week and observed for 131 weeks. The low dose group received 4x10^6 fibres, the high dose group 8x10^6 fibres (> 5μm long, < 2μm in diameter, ratio 5:1). No primary lung tumours (adenoma, adenocarcinoma, squamous cell tumour and cystic keratinising squamous cell tumours) were seen in the 59 low dose rats or the 40 high dose rats, while 5/59 low dose rats and 4/40 high dose rats developed other lung tumours (fibrosarcoma, lymphosarcoma, mesothelioma or metastases from other sites). The tumour incidences were not significantly elevated. The saline control group had no primary lung tumours and 2/40 other lung tumours. Incidences of primary lung

Table 4.1. Chronic inhalation studies with insulation glass wools in rodents (referenced from IARC 2002).

Fibre type	Number and dimension of fibres in aerosol	Positive control Nos. and dimensions of fibres	Animals: number / group, strain, species. (Number at risk)	Exposure type, time + Post exposure observation period	Lung burden	Glass wool : No. of thoracic tumours/no. of animals Other findings	Controls: No. of thoracic tumours/no. of animals Comments	Reference
Glass fibres	168 WHO-fibres/cm^3; 700 fibres >5μm/cm^3	Amosite asbestos 1178 WHO-fibres/cm^3	46 Sprague-Dawley rats	Whole body, 5h/d, 5d/wk, 3mths + up to 21 mths	Not determined	2/11 adenomas	Amosite: 1/11 adenoma 2/11 carcinomas Untreated: 0/13 tumours Low number of animals at risk	Lee et al. 1981 – quoted from IARC 2002
Glass fibre with and without resin	10 mg/m^3 (>5μm long) With resin ≈ 240 WHO fibres/cm^3 Without resin ≈ 323 WHO fibres/cm^3	Chrysotile asbestos 3800 WHO-fibres/cm^3	56 SPF Fischer rats	Whole body, 7h/d, 5d/wk, 12 mths + lifetime	With resin: 1.9 mg fibres at 12 mths; 0.5 mg fibres at 21 mths. Without resin: 0.9 mg fibres at 12 mths; 0.2 mg fibres at 21 mths.	With resin 1/48 adenomas; Without resin 1/47 adenomas.	Chrysotile: 1/48 adenomas and 11/48 adenocarcinomas Type of glass fibres not specified.	Wagner et al. 1984 - quoted from IARC 2002
Glass wool	5 mg/m^3 48 WHO-fibres/cm^3 70 total f/ml > 5 μm long	Chrysotile asbestos 5901 WHO-fibres/cm^3	48 Wistar rats IOPS/Han	Whole body, 5h/d, 5d/wk, up to 12 mths + 4-16 mths or 24 mths+4mths	Not determined	1/45 lung carcinomas No fibrosis at 12 mths. Slight fibrosis at 24 mths.	Chrysotile: 9/47 Neg controls: 0/47	Le Bouffant et al. 1984 – quoted from IARC 2002
Insulation glass wool with binder: MMVF10.	MMVF10: 9,9 mg/m^3 30 fibres/cm^3 >10μm long and < 1 μm diam. GMD: 1.1μm	Crocidolite asbestos 90 f/cm^3 >10μm long	52-61 Osborne-Mendel rats	Nose-only, 6h/d, 5d/wk, 24 mths; observed for life	MMVF10: 2x10^3 f/mg dry lung at 3 mths.	MMVF10: 0/57 tumours, no fibrosis	Crocidolite: 3/57 tumours + fibrosis	Smith et al. 1987 - quoted from IARC 2002

Fibre type	Number and dimension of fibres in aerosol	Positive control Nos. and dimensions of fibres	Animals: number / group, strain, species. (Number at risk)	Exposure type, time + Post exposure observation period	Lung burden	Glass wool : No. of thoracic tumours/no. of animals Other findings	Controls: No. of thoracic tumours/no. of animals Comments	Reference
Insulation glass wool without binder: MMVF11. Binder coated insulation glass wool: O-C	MMVF11: 4.4 mg/m^3 25 fibres/cm^3 >10μm long and < 1 μm diam. GMD: 1.2μm O-C: 7.0 mg/m^3 5 fibres/cm^3 >10μm long and < 1 μm diam. GMD: 3μm				MMVF11: 3x10^4 f/mg dry lung at 3 mths. O-C: 600 f/mg dry lung at 3 mths.	MMVF11: 0/52 tumours, no fibrosis O-C: 0/58 tumours no fibrosis		
Binder coated insulation glass wool: O-C	15 mg/m^3. No dimensions specified.	none	500 Fischer 344 rats	Whole-body, 7h/d, 5d/wk, 86 wks	Not determined	0/500, no fibrosis. 22 % mononuclear cell leukaemia (significant compared to air controls, but background incidence is high in aging F 344-rats.)	No concentration of fibres in the aerosol or the lung given. Not positive control.	Moorman et al. 1988 - quoted from IARC 2002
Insulation glass wool: MMVF10	3, 16 or 30 mg/m^3 high conc.: MMVF10: 232 WHO fibres/cm^3	Chrysotile asbestos, 10 mg/m^3; 10.6x10^3 WHO-fibres/cm^3	140 Fischer 344 /N rats (112-120)	Nose-only, 6h/d, 5d/wk, up to 24 mths; observed for life	24 mths, 30 mg/m^3: 5-6x10^6 fibres/lung >20μm long.	MMVF10: 7/119 lung tumours (1 carcinoma) non-significant ; no mesothelioma.	Chrysotile: 13/69 lung tumours, 1/69 mesothelioma Air: 3.3% lung tumours	Hesterberg et al. 1993; 1999; Hesterberg & Hart 2001 quoted from IARC 2002)

Fibre type	Number and dimension of fibres in aerosol	Positive control Nos. and dimensions of fibres	Animals: number / group, strain, species. (Number at risk)	Exposure type, time + Post exposure observation period	Lung burden	Glass wool : No. of thoracic tumours/no. of animals Other findings	Controls: No. of thoracic tumours/no. of animals Comments	Reference
Insulation glass wool: MMVF11	MMVF11: 246 WHO fibres/cm^3					MMVF11: 3/112 lung tumours, non-significant; no mesothelioma. Inflammation during exposure, but no fibrosis after 3 mths recovery period.		
Insulation glass wool with binder: MMVF10. Insulation glass wool without binder: MMVF11. Binder coated insulation glass wool: O-C	MMVF10: 9,9 mg/m^3 30 fibres/cm^3 >10μm long and < 1 μm diam. GMD: 1.1μm MMVF11: 4.4 mg/m^3 25 fibres/cm^3 >10μm long and < 1 μm diam. GMD: 1.2μm O-C: 7.0 mg/m^3 5 fibres/cm^3 >10μm long and < 1 μm diam. GMD: 3μm	Crocidolite asbestos 90 f/cm^3 >10μm long	60-70 Syrian golden hamsters	Nose-only, 6h/d, 5d/wk, 24 mths; observed for life	MMVF10: 1000 f/mg dry lung at 3 mths. MMVF11: $1x10^4$ f/mg dry lung at 3 mths. O-C: 500 f/mg dry lung at 3 mths.	MMVF10: 0//66 tumours, no fibrosis MMVF11: 0/60 tumours, no fibrosis O-C: 0/61 tumours, no fibrosis	Crocidolite no tumours, some fibrosis. Clean air controls: 1/58 carcinoma.	Smith et al. 1987 - quoted from IARC 2002

Fibre type	Number and dimension of fibres in aerosol	Positive control Nos. and dimensions of fibres	Animals: number / group, strain, species. (Number at risk)	Exposure type, time + Post exposure observation period	Lung burden	Glass wool : No. of thoracic tumours/no. of animals Other findings	Controls: No. of thoracic tumours/no. of animals Comments	Reference
Glass fibres	168 WHO-fibres/cm^3; 700 fibres > 5μm/cm^3	Amosite asbestos 1178 WHO-fibres/cm^3	30-35 hamsters	Whole body, 5h/d, 5d/wk, 3mths + up to 21 mths	Not determined	0/9 thoracic tumours	Amosite asbestos: 0/5 tumours	Lee et al. 1981 - quoted from IARC 2002
Insulation glass wool: MMVF10a	30mg/m^3 339 WHO fibres/cm^3 134 fibres >10μm long	Amosite asbestos 36, 165 or 263 WHO fibres/cm^3	125 Syrian golden hamsters (81)	Nose-only, 6h/d, 5d/wk, up to 18mhs weeks + 6-observed for life	MMVF10a: 18 mths: $4.6x10^6$ fibres/lung >20μm long Lung burden reduction in 18 mths + 6 mths group: 66%. Asbestos high dose 18 mths: 144<10^6fibres/lung>20μm long Lung burden reduction in 18 mths + 6 mths asbestos group: 21%	0/81 lung tumours or mesothelioma	Amosite asbestos : 0/85 and 0/87 lung tumours and 22/85 and 17/87mesothelioma for mid and high dose, respectively.	Hesterberg et al. 1999 - quoted from IARC 2002
Insulation glass wool: MMVF 10a MMVF 33: special glass fibre	MMVF 10a: 250-300 WHO fibres/cm^3 MMVF 33: 250-300 f/cm^3	Amosite asbestos 25, 125, 250 and 300 WHO f/cm^3	140 Syrian golden hamsters	Nose-only, 6h/d, 5d/wk, up to 78 wk	-	MMVF 10a: no lung tumour or mesothelioma Inflammation reversible in recovery period, no fibrosis	MMVF 33: 1 mesothelioma. Inflammation and mild, progressing fibrosis from week 26 Asbestos: 3.6; 25.9 and 19.5% had mesotheliomas in the low, mid and high-dose groups, respectively. Inflammation and progressing fibrosis from week 13 in all groups	McConnell et al. 1999 - abstract

Table 4.2. Inhalation studies on carcinogenicity in rats of different types of stone wool. (reproduced from IARC, 2002).

Test substance	Fibre dimensions: length (Ł), diameter (D)	Dosing schedule/ cumulative exposure ($mg/m^3 \times h$)	Duration of exposure	Period of observation	No. of animals examined	No. of animals with tumours[a]	Histo-logical type[b]	Median or average survival time (weeks)
Exposure by inhalation to respirable dust at a concentration of 5 mg/m^3 rock (stone) wool (male and female Wistar rats, 8–9 weeks old) (Le Bouffant et al., 1984)								
French resin-free rock (stone) wool	40% fibres < 10 µm length, 23% < 1 µm diameter	ND	5 h/day, 5 days/week, for 52 or 104 weeks	12–28 months	47	0	–	NG
Canadian chrysotile	6% fibres > 5 µm length	ND	5 h/day, 5 days/week, for 52 or 104 weeks	12–28 months	47	9	9A	NG
Control	–	–	5 h/day, 5 days/week, for 52 or 104 weeks	12–28 months	47	0	–	NG
Exposure by inhalation to respirable dust at a concentration of ~10 mg/m^3 rock (stone) wool (SPF Fischer rats) (Wagner et al., 1984)								
Resin-free rock (stone) wool	71% fibres ≤ 20 µm length, 58% ≤ 1 µm diameter	17495	7 h/day, 5 days/week, for 52 weeks	12 months–lifetime[c]	48	2	2A	NG
UICC Canadian chrysotile	16% fibres ≥ 20 µm length, 29% ≥ 0.5 µm diameter	17499	7 h/day, 5 days/week, for 52 weeks	12 months–lifetime[c]	48	12	11AdCa 1A	NG
Control	–	–	7 h/day, 5 days/week, for 52 weeks	12 months–lifetime[c]	48	0	–	NG

Test substance	Fibre dimensions: length (L), diameter (D)	Dosing schedule/ cumulative exposure ($mg/m^3 \times h$)	Duration of exposure	Period of observation	No. of animals examined	No. of animals with tumours[a]	Histo-logical type[b]	Median or average survival time (weeks)
Exposure by nose-only inhalation to respirable dust at concentrations of 3, 16 and 30 mg/m^3 rock (stone) wool (MMVF21) (male Fischer 344 rats, 8 weeks old) (McConnell et al., 1994)								
Rock (stone) wool (MMVF21)	GML, 13.0 µm GMD, 0.94 µm	9 672	6 h/day, 5 days/week, for 104 weeks	28 months	114	5	4A 1Ca	~104
	GML, 15.4 µm GMD, 0.90 µm	50 232	6 h/day, 5 days/week, for 104 weeks	28 months	115	5	4A 1Ca	~104
	GML, 14 µm GMD, 0.98 µm	94 848	6 h/day, 5 days/week, for 104 weeks	28 months	114	5	4A 1Ca	~104
Crocidolite	GML, 4.1 µm GMD, 0.28 µm	13 000	6 h/day, 5 days/week, for 44 weeks	28 months	106	14	10A 5Ca 1M	~100
Control	–	–	6 h/day, 5 days/week, for 104 weeks	28 months	126	2	2A	~104

NG: not given; GML: geometric mean length; GMD: geometric mean diameter

[a] Tumours of the lung, pleura, thorax or abdominal cavity.

[b] A: adenoma; AdCa: adenocarcinoma; BT, bronchoalveolar tumour; Ca: relatively undifferentiated epidermoid carcinoma; M: mesothelioma.

[c] Lifetime, until survival rate was $\leq 20\%$.

The fibre concentration in the study by Le Bouffant et al. 1984 was 41 total f/ml, with the respirable fraction being 13 f/ml.

tumours were 3/38 and 8/37 (significant) and incidences of other lung tumours were 6/38 (significant) and 4/37 in rats treated with $70x10^6$ and $300x10^6$ tremolite fibres (> 5μm long, < 2μm in diameter, ratio >5:1), respectively. (Pott et al. 1994 – quoted from IARC 2002).

4.7.2.3 HT-fibre

No data were found.

4.7.3 Intrapleural

Only data concerning stone wool were available.

Groups of 48 SPF Sprague-Dawley rats treated with single intrapleural injections of 20 mg Swedish stone wool with resin or without resin coating or chrysotile asbestos developed 3, 2 and 6 mesotheliomas, respectively. No tumour were seen in the saline control group. (Wagner et al. 1984 – quoted from IARC 2002)

4.7.4 Oral

No data were available.

4.7.5 Dermal

No data were available.

4.7.6 Intraperitoneal

4.7.6.1 Insulation glass wool

Wistar rats were treated with German glass wool intraperitoneally with 24, 120 or 1200 x 10^6 fibres > 5 μm in length, using chrysotile asbestos as positive control showed mesotheliomas and spindle-cell sarcomas in 1/34, 4/36 and 23/32 of the low, mid and high dosed, respectively. Survival times were 518, 514 and 301 days. Tumour incidences in chrysotile treated animals ranged from 6/37-25/31 and the survival time from 468-407 days. Control animals, receiving granular dust in saline, had no tumours. (Pott et al. 1976 - quoted from IARC 2002).

Wistar rats were given intraperitoneal injections of 0.4 x 10^9 or 1.0 x 10^9 WHO fibres/rats of MMVF11 insulation glass wool. 12/40 and 16/23 animals developed mesotheliomas, in the low and high dose group, respectively, while the saline treated controls had no tumours. (Pott 1995; Roller et al. 1996 and Roller & Pott 1998 - quoted from IARC 2002).

Wistar rats were given 5-40 weekly intraperitoneal injections of B-01-09 glass wool, summing up to 2.5, 5, 10 x 10^9 fibres >5 μm/rats for females and 10 or 20 x 10^9 fibres > 5 μm/ rats for males showed 3/40, 4/40 and 3/40 mesotheliomas in females and 10/40 and 33/40 mesotheliomas in males, respectively. Saline controls had 1/208 mesothelioma. (Pott 1995; Roller et al, 1996 - quoted from IARC 2002).

Two experimental glass wools, B-09-0.6 and B-09-2.0, caused 3-53% mesothelioma incidence in rats treated with 2-6 x 10^9 WHO-fibres/rat, the longer and thicker fibre B-09-2.0 being the more tumourigenic. No tumours were seen in the saline treated animals. (Roller et al 1996; 1997 - quoted from IARC 2002).

Groups of Wistar rats received an intraperitoneal injection of 973 x 10^9 WHO-fibres/rat standard insulation glass wool (MMVF10) or 410 x 10^6 WHO-fibres/rat amosite asbestos. Incidences of mesotheliomas were 13/22 and 21/24, respectively. (Miller at al. 1999 – quoted from IARC 2002).

No tumours were seen in Syrian golden hamsters dosed intraperitoneally with an unspecified glass wool or chrysotile asbestos. (Pott et al. 1976 - quoted from IARC, 2002).

4.7.6.2 Stone (rock) wool

A number of studies of the carcinogenic potential of various stone wool products following intraperitoneal injections have been performed. The different stone wool fibres were injected intraperitoneally at doses of 5 – 1000 x 10^6 fibres with WHO-fibre dimension (>5 μm long, <1μm in diameter). The animals were observed for 130 weeks. Negative control groups receiving saline or granular dust of carbon or silicone carbide or remaining untreated were used. Positive controls treated with chrysotile, crocidolite, amosite or tremolite asbestos were used. Survival times varied from 38-122 weeks. The studies indicate that injection of stone wool fibres in the abdominal cavity result in an increased incidence of mesothelioma/sarcoma during the observation period of 2 years in average. The tumour incidence was dose-dependent for most of the fibre types, reaching statistical significance in the higher dosage groups. Tumour incidences in asbestos treated animals were higher than for stone wool treated animals. (IARC 2002).

4.7.6.3 HT-fibre

An intraperitoneal study was performed with HT-fibre at a dose of 2.1 x 10^9 WHO fibres in order to compare with a study with the traditional stone wool MMVF21, where 1x10^9 fibres were used. No induction of mesothelioma was seen in the HT-fibre treated group or the concurrent saline control group, while the study with MMVF 21 showed 32/57 mesotheliomas in stone wool treated rats and 0/91 in the control rats of that study. (Kamstrup et al. 2002- quoted from IARC 2002).

4.7.7 IARC evaluation of animal carcinogenicity studies

Cited from IARC (2002):

4.7.7.1 Glass wool

Insulation glass wools were tested in well-designed, long-term inhalation studies in rats and hamsters. No significant increase in lung tumours and no mesotheliomas were observed in rats and no lung tumours or mesotheliomas were observed in hamsters exposed to insulation glass wool. Two different asbestos types used as positive controls produced increases in lung tumours and mesotheliomas.

Two insulation glass wools that produced no increase in tumours when administrated by inhalation did induce mesotheliomas when injected at high doses (approximately 10^9 fibres) into the peritoneal cavity of rats.

There is limited evidence in experimental animals for the carcinogenicity of glass wool.

4.7.7.2 Stone wool

In a well-designed, long-term inhalation study in which rats were exposed to stone wool, no significant increase in lung tumour incidence and no mesotheliomas were observed. Crocidolite asbestos was used as the positive control and led to high lung tumour incidence and one mesothelioma.

After intra-tracheal instillation of stone wool in two studies, no significant increase in the incidence of lung tumours or mesotheliomas was found. Tremolite asbestos was used as a positive control and induced lung tumours.

In several studies of intraperitoneal injection of high doses (approximately 10^9 fibres), stone wool induced a significant increase in mesothelioma incidence. The more biopersistent stone wool fibres produced a higher incidence of tumours than fibres with lower biopersistence.

There is limited evidence in experimental animals for the carcinogenicity of stone wool

4.7.7.3 HT-fibre

The newly developed, less biopersistent fibre (a high-alumina, low-silica wool) has been tested in a well-designed, long-term inhalation study in rats and produced no significant increase in the incidence of lung tumours and no mesotheliomas.

In a study in rats of the HT-fibre administered by intraperitoneal injection at a high dose (approximately 10^9 fibres), no abdominal tumours were observed.

There is inadequate evidence in experimental animals for the carcinogenicity of (certain newly developed, less biopersistent fibres including the alkaline earth silicate (X-607) wool,) the high-alumina, low-silica (HT) wool (and fibres A,C, F and G).

5 Regulations

5.1 Ambient air

Denmark (C-value):	1300 fibres/m^3, Main Group 1 (MST 2002).
WHO :	-
US-EPA:	-

5.2 Drinking water

Denmark:	-
WHO:	-
US-EPA :	-

5.3 Soil

Denmark:	-
The Netherlands:	-

5.4 Occupational Exposure Limits

Denmark:	1 WHO-fibre/cm^3 for glass wool, stone wool and slag wool. (At 2005).
ACGIH:	TLV: 1 fibre/cm^3 for glass, rock(stone), slag wool and special purpose fibres. (ACGIH 2001- quoted from IARC 2002).
Germany:	High temperature glass fibres: 0.5 fibre/cm^3; others 0.25 fibre/cm^3. (MAK 2001- quoted from IARC 2002).

5.5 EU-Classification

Mineral wool (man-made vitreous (silicate) fibres with random orientation with alkaline oxide and alkali earth oxide ($Na_2O+K_2O+CaO+MgO+BaO$) content greater than 18 % by weight) is classified for irritative properties (Xi;R38 - irritating to the skin) and for possible carcinogenic effects (Carc 3;R40 - possible risks of irreversible effects). (OJ 1997, MM 2002).
The classification as a carcinogen need not apply if it can be shown that the substance fulfils one of the following conditions (OJ 1997):
1) a short-term biopersistence test by inhalation has shown that the fibres longer than 20 μm have a weighted half-life less than 10 days, or

2) a short-term biopersistence test by intra-tracheal instillation has shown that the fibres longer than 20 μm have a weighted half-life less than 40 days, or
3) an appropriate intra-peritoneal test has shown no evidence of excess carcinogenicity, or
4) absence of relevant pathogenicity or neoplastic changes in a suitable long-term inhalation study.
Furthermore, the classification as a carcinogen need not apply to fibres with a length weighted geometric mean diameter less two standard errors greater than 6 μm.

5.6 IARC-classification for carcinogenic effect

Insulation glass wool: Group 3.
Stone wool: Group 3.
HT fibre: no overall evaluation performed.
(IARC 2002).

5.7 US-Navy

US-Navy exposure standard for all MMVFs: 1 fibre/cm^3. (National Research Council 2000 – quoted from IARC 2002).

5.8 US-OSHA

1 fibre/cm^3 for respirable MMVF insulation wools agreed by US Health and Safety Partnership Program (between OSHA and producers and users 1999).

6 Summary and evaluation

6.1 Description

Mineral wool designates several types of synthetic, loose, tangled and discontinuous fibres produced from glass, stone, slag or clay. This evaluation describes insulation glass wool, stone wool and a new type of fibre introduced as a replacement for stone wool: the HT-fibre. These fibre types have different composition of silica and other oxides. The physical dimensions are approximately 3-10 μm in diameter and length-width ratio of 3:1. Binders and oils are added during production to hinder dust formation and hold the wool fibres together.

6.2 Environment

Concentration of fibres (special purpose glass fibres, glass wool and stone wool) in ambient air range from 2 fibres/m^3 in measurements in Paris to 1.7 x 10^3 fibres/m^3 in a German Ruhr-district city, while emission from a glass and stone wool plant in Germany was in the order of 10^4 fibres/m^3.
Measurements of indoor concentration showed average levels of less than 1 x 10^2 fibres/m^3.

MMVFs can be removed from the environment by breakage, dissolution, sedimentation or thermal destruction.

6.3 Human exposure

Human exposure to fibres occurs through contaminated air, primarily in occupational settings in production or application areas. Current average exposure levels in workers are generally less than 0.5 x 10^6 respirable fibres/m^3 although higher levels have been measured in e.g. insulation work. The concentration of MMVFs measured in outdoor and indoor air in non-occupational settings have been found to be much lower than in occupational settings.

No direct relation between respirable fibre concentration and non-respirable fibre concentration was found. The concentration and average length of the non-respirable fibres varied with type of fibre and way of application.

6.4 Toxicokinetics

The biopersistence and dissolution of several MMVFs and asbestos has been evaluated. MMVFs had a higher dissolution and cleared much more rapid from the lungs than the asbestos fibres that had a lower dissolution.

Transverse fragmentation of MMVFs has been demonstrated in *in vitro* studies and has been suggested as an explanation for the observation that the number of long fibres decreased more rapidly than the number of short fibres for the less biopersistent fibres in the biopersistence studies.

A case-control study of autopsies from production workers showed no significant difference in retention of MMVFs in the lung between the exposed workers and the controls. The mean duration of exposure was 11 years and the mean time elapsed since the end of exposure was 12 years.

6.5 Human toxicity

6.5.1 Single dose toxicity

No data were found.

6.5.2 Irritation

Several studies have shown that MMVFs may cause irritation of the skin, eye and upper respiratory tract.

The irritative effect on the skin is a mechanical one and results from fibres with a diameter greater than 4-5 μm. The skin irritation potential depends on the fibre diameters: <5 μm slight, if any, 5-7.5 μm moderate and 7.5-10 μm high, but also on other factors e.g. the presence of shots (rounded particles of approximately 60 μm in diameter formed in some wool production processes, see section 1.2.2). The fibres can penetrate the skin and it has been suggested that skin penetration is directly proportional to fibre diameter and inversely proportional to fibre length.

In one study it was shown that 25% of ordinary people exhibited skin reactions when patch tested with stone wool. In workers exposed to glass or stone wool up to 65% had cutaneous lesions and/or symptoms. Workers develop a tolerance to the itching. Data from Finland showed that carpenters, building workers and insulation workers had the highest risk of occupational irritant contact dermatitis from MMVFs. In Danish construction workers a dose-response correlation was found between duration of exposure and rate of irritative symptoms from the skin, the eyes, and the upper respiratory tract. Two thirds of the workers working daily with mineral wool had some of these symptoms once a week or oftener. No exposure levels have been reported for any of these studies.

In Danish kindergartens with visible MMVF ceilings compared to kindergartens without (control institutions), the frequency of eye and nose irritation in adults, skin irritation, common cold and sore throat in adults and children, and otitis media in children was statistically significantly higher. Among adults, the concentrations of airborne respirable and non-respirable MMVFs were positively correlated with eye irritation, and the presence of settled non-respirable MMVFs on surfaces occasionally cleaned was positively correlated with skin and nose irritation. No significant differences were found between the kindergartens with regard to amount of settled fibres on regularly or occasionally cleaned surfaces or with regard to mean concentration of respirable fibres. For non-respirable fibres the mean concentration was 23-40 fibres/m^3 in kindergartens with visible MMVF ceiling. In the control institutions, the level of non-respirable fibres was often lower than the analytical detection limit (40-80 fibres/m^3).
Employees in a German administrative building with sound absorbing mineral fibre boards complained of skin, eye and respiratory irritation. The fibre content in the air was measured to be 100-200 fibres (not stated if total count or concentration) >3 μm in diameter.

6.5.3 Sensitisation

A few cases of allergic contact dermatitis in workers exposed to MMVFs have been described. Upon patch testing, resins used to bind mineral fibres together were shown to be the allergens.

6.5.4 Repeated dose toxicity

6.5.4.1 European cohort

IARC has coordinated a large European cohort study which focused on the mortality and cancer incidence among production workers in a total of 13 MMVF factories in Denmark, Finland, Norway, Sweden, United Kingdom, Germany and Italy. The cohort consisted of 7 stone/slag wool factories, 4 glass wool factories, and 2 continuous filament factories. The population under study was the workforce ever employed in the 13 factories from the year of start of production to 1977 and consisted of 10108 stone/slag wool workers and 8335 glass wool workers.

In Europe most stone/slag wool plants began using stone instead of slag after the mid-1940s and currently most European factories continue to melt stone.

From 1977 to 1980 scientist measured the concentrations and size of airborne fibres in 6 of the 7 stone/slag wool factories and all 4 glass wool factories in the European cohort. For different occupational groups the arithmetic mean respirable fibre concentrations in the 6 stone/slag wool factories was in the range of (0.01 - 0.67) x 10^6 fibres/m^3. For the different factories, the median lengths of stone wool fibres ranged from 10 to 20 μm and the median diameters ranged from 1.2 to 2 μm. For different occupational groups the arithmetic mean respirable fibre concentrations in the 4 glass wool factories was in the range of (0.01 – 1.00) x 10^6 fibres/m^3. For the different factories, the median lengths of glass wool fibres ranged from 8 to15 μm and the median diameters ranged from 0.7 to 1 μm. Compared to the stone wool fibres, glass wool fibres tended to be shorter and thinner.

An historical investigation based on questionnaires has been conducted to reconstruct past conditions of exposure in the European cohort. The investigation resulted in a division of the production into technological phases. For the glass wool factories the airborne fibre concentration was probably similar in the early technological phase to the measurements in the late technological phase. For the stone/slag wool factories, the airborne fibre concentration was higher (about 1 x 10^6 fibres/m^3 and possible as high as 10-25 x 10^6 fibres/m^3) in the early than in the late technological phase.

The historical exposure investigation in the European cohort also provided information on possible exposure to other agents in the factories included in the study. The authors are ending up concluding that the agents that could potentially present a risk for lung cancer in the epidemiological study were the use of asbestos in one factory and the contamination of olivine and exposure to coal-tar pitch volatiles at another factory. Exposure levels of formaldehyde were probably high in the initial period of use since most factories reported that the odour of formaldehyde was frequently detected and occasionally it was reported as causing severe irritation.

No evidence of an increased mortality risk for non-malignant respiratory diseases (acute infections, influenza, pneumonia, and bronchitis, emphysema and asthma)

was found in exposed workers in the European cohort based on calculations of SMR and relative risk according to time since first employment, duration of employment, and technological phase at first employment. Five deaths from pneumoconiosis including one from asbestosis were reported but no statistics was applied.

Mortality from non-malignant renal diseases and ischemic heart disease in stone/slag wool and glass wool workers from the European cohort were not statistically significantly increased. The authors made a suggestion of an increasing risk of death from non-malignant renal diseases among stone/slag wool workers with duration of employment or employment in the early technological phase. No such relation was found in the glass wool sub-cohort. The few deaths, however, limited the power of the analyses so no statistically significant trends were observed. A trend was seen for an increasing risk of ischemic heart disease in stone/slag wool workers with years since first employment and in glass wool workers with technological phase at first employment.

6.5.4.2 US cohort

Since 1975, the University of Pittsburgh has been conducting a large historical cohort study of production and maintenance workers from the 17 of the oldest and largest fibre glass and stone/slag wool factories in the United States. The main objective of their study was to evaluate mortality risks among these workers with a focus on respiratory diseases. The cohort consisted of 6 stone/slag wool factories and 11 fibreglass factories. The original population under study was the male workforce employed for at least 1 year between 1945 and 1963 in the 17 factories. In 1987 the cohort was expanded to include workers employed until 1978, female employees, and workers from additional manufacturing sites. The expanded cohort consisted of 3035 stone/slag wool workers and 10961 workers mainly exposed to glass wool.
In 1979 a cross-sectional investigation was begun with respiratory health assessment of 1028 workers employed in 7 of the factories in the US cohort. This study was followed up until 1986 with 1444 workers using a modified study design including e.g. comparison with blue-collar workers from the local communities.

In the USA, the production of stone wool dominated until the late-1930s when several of the factories converted to the use of slag, which was a cheap waste product from the production of iron.

From 1975 to 1978 scientists measured the concentrations and size of airborne fibres in 16 of the 17 factories in the US cohort. Based on these measurements and on work histories for individual workers, the mean average intensity of exposure to respirable fibres was estimated. Exposure to fibreglass (mean: 0.04×10^6 fibres/m^3) was lower than exposure to stone/slag wool (mean: 0.35×10^6 fibres/m^3). For fibreglass factories past exposures were believed to differ little from current levels, while exposure levels to stone/slag wool were evaluated to be 1.5×10^6 fibres/m^3 prior to 1945, 0.3×10^6 fibres/m^3 for the years 1945-60 and 0.03×10^6 fibres/m^3 after 1960. For the different factories, the nominal diameters of stone/slag wool fibres ranged from 5 to 8 μm and the nominal diameters of glass wool fibres ranged from 3 to 15 μm.

For the studies on respiratory health assessment, the authors derived individual exposure estimates based on the above measurements combined with job histories. The estimated mean concentration of airborne respirable fibres was 0.03×10^6 fibres/m^3.

In 1988, the North American Insulation Manufacturer's Association initiated an environmental project to provide comprehensive data on respirable MMVF exposures and on exposure to other workplace contaminants for the 11 fibreglass factories and five of the six stone/slag wool factories. Exposures were estimated quantitatively for respirable fibres, formaldehyde, and silica, and qualitatively for arsenic, asbestos, asphalt, epoxy, PAHs, phenolics, styrene, urea, and radiation. For respirable fibres the mean average intensity of exposure was in the range of 0.07 – 0.66 x 10^6 fibres/m^3 for stone/slag wool factories and 0.05 – 0.21 x 10^6 fibres/m^3 for mainly glass wool factories. For most of the factories co-exposure to formaldehyde, phenolics and urea dominated over the other co-exposures.

The prevalence of ever smoking and current smoking among male workers in both the fibreglass and stone/slag wool factories was higher than in the US population. Among female workers in the stone/slag wool factories, the prevalence of ever smoking and current smoking was also higher than in the US population but among females in the fibreglass factories, the prevalence was slightly lower than in the US population.

In the expanded US cohort a statistically significant excess in mortality from non-malignant respiratory disease excluding influenza and pneumonia (NMRD excluding IP) was observed in fibreglass workers when compared to US rates but when compared to local county rates a deficit in deaths were observed. No evidence of an increased mortality risk for NMRD excluding IP by duration of employment or time since first employment was observed.
For stone/slag wool workers, an excess in mortality from NMRD excluding IP was observed both when compared to US rates and local rates but none of the numbers were statistically significant.
In one stone/slag wool factory in which co-exposure to asbestos was reported, a statistically significant excess in mortality from NMRD excluding IP occurred when compared to local county rates (SMR: 1.83).
The pattern of findings for NMRD excluding IP mortality in the expanded cohort was generally consistent with those observed in previous follow-ups based on the original cohort data.

For the studies on respiratory health assessment, workers from 7 of the factories in the US cohort were questioned on respiratory symptoms, were tested for pulmonary function by spirometry, and had chest radiographs taken. In both the original study and in the follow-up, respiratory symptoms and the level of pulmonary function were related to cigarette smoking and not to fibre exposure. In the original study, the authors concluded that exposure to MMVF with small diameters may lead to low-level profusion of small opacities in the lungs, even though the authors did not regard the findings as clinically significant. In the follow-up study, the authors concluded that the results indicated no adverse clinical, functional or radiographic signs of effects of exposure to MMVFs in these workers.

In the expanded US cohort no statistically significantly elevated mortality risks were observed among the non-malignant non-respiratory diseases (including nephritis and nephrosis, and all heart diseases) in fibreglass workers. A case-control study of fibreglass workers in the US reported no association between exposure to respirable fibreglass or respirable silica and nephritis or nephrosis. For stone/slag wool workers, the mortality from nephritis and nephrosis was statistically significantly elevated. The excess was observed in all but one of the study factories. The authors are stating that to some extent, these excesses may be

associated with reported long-term exposures to airborne lead, cadmium or arsenic in one of the factories.
In the follow-ups made in the original US cohort, SMRs for non-respiratory diseases were only reported for fibreglass and stone/slag wool workers combined. Mortality from nephritis and nephrosis was elevated in both the 1982 and 1985 follow-up and reached statistical significance in the 1985 follow-up.

6.5.4.3 Respiratory diseases

6.5.4.3.1 Pneumoconiosis

Pneumoconiosis is the condition of permanent deposition of particulate matter in the lungs and by the tissue reaction to its presence. Pneumoconiosis may lead to fibrosis. All of the recent studies found no significant excess of small opacities on chest autoradiographs except two studies, which were considered uninterpretable by the IARC working group.

6.5.4.3.2 Pleural abnormalities

In all of the recent studies no statistically significant excess of pleural abnormalities were observed on thoracic radiography except in the two studies, which were considered uninterpretable by the IARC working group. Moreover, a nested case-control study failed to demonstrate a relationship with exposure to fibres.

6.5.4.3.3 Respiratory symptoms

Respiratory symptoms were assessed by questionnaires. In the production studies from USA and Japan no statistically significant association was found between respiratory symptoms and exposure to fibres. The estimated (based on a survey and individual job histories) mean concentration of airborne respirable fibres was 0.03 x 10^6 fibres/m^3 in the American study.

In one of the French glass fibre production studies odds ratios for cough and phlegm were significantly increased among glass wool workers at one factory that contained 51% of the study population but not among workers in the other four factories. A few percent of the workers in the first factory had co-exposure to resins. In the other French production study a significant excess for dyspnoea and nasal congestion was revealed among exposed workers. In these studies the measured mean concentration of airborne respirable fibres was 0.05 – 0.18 x 10^6 fibres/m^3 in different work areas for some of the factories.

In Danish stone/slag wool production workers the prevalence of reported emphysema was 3.8% in the workers versus 0.9% in the control group, resulting in a relative risk of 4.5 (95% CI: 1.0-20.6). The exposure level was not determined for the study population. The estimated mean concentration of airborne respirable fibres was 0.1 – 0.2 x 10^6 fibres/m^3 in the European stone/slag wool industry in the examined period.

In Swedish construction workers high exposure to insulation wool was associated with statistically significant increased odds ratios for persistent cough of the same magnitude as current smoking. The exposure level was not determined for the study population. The measured mean concentration of airborne respirable fibres

was 0.06 – 0.91 x 10^6 fibres/m^3 for different occupations within the Swedish construction industry 1978-90. Exposure concentrations of up to 5.08 x 10^6 fibres/m^3 were measured for insulators, which generally was exposed to the highest values.

6.5.4.3.4 Pulmonary function

Pulmonary function was measured by spirometry. In the production studies from USA, France and Australia no statistically significant association was found between pulmonary function and exposure to fibres. The estimated (based on a survey and individual job histories) mean concentration of airborne respirable fibres was 0.03 x 10^6 fibres/m^3 in the American study. In the French study the measured mean concentration of airborne respirable fibres was 0.05 – 0.18 x 10^6 fibres/m^3 in different work areas.

In Danish stone/slag wool production workers the FEV_1/FVC ratio was statistically significantly lower than in the control group, indicating obstructive lung disease. Subgroup analysis showed that the elevated risk of airway obstruction was restricted to heavy smokers. The exposure level was not determined for the study population. The estimated mean concentration of airborne respirable fibres was 0.1 – 0.2 x 10^6 fibres/m^3 in the European stone/slag wool industry in the examined period.

In Danish insulators the FEV_1 was statistically significantly lower than in the control group independent of smoking habits. It was reported that 66% of the insulation workers had a FEV_1/FVC ratio of under 70%, whereas only 9% of the control group had such low values, indicating obstructive lung disease in the workers. Comparison with measurements made 6 or 8 years earlier showed a significantly higher decline in FEV_1 (independent of smoking habits) and FVC (only for current smokers) in insulation workers than in the control group. The exposure level was not determined for the study population. The measured usual concentration of airborne fibres was in the range of 0.03 – 1 x 10^6 fibres/m^3 for Danish insulators but concentration up to 10 x 10^6 fibres/m^3 occurred.

In Swedish construction workers there were no significant differences in means of VC and FEV_1 between construction workers exposed to insulation wool and construction workers not exposed to insulation wool. Comparison with measurements made on average 3.9 years later showed no statistically significant difference in yearly change of VC and FEV_1 between exposed and unexposed construction workers. The exposure level was not determined for the study population. The measured mean concentration of airborne respirable fibres was 0.06 – 0.91 x 10^6 fibres/m^3 for different occupations within the Swedish construction industry 1978-90. Exposure concentrations of up to 5.08 x 10^6 fibres/m^3 were measured for insulators, which generally was exposed to the highest values.

6.5.5 Toxicity to reproduction

No data have been found.

6.5.6 Mutagenic and genotoxic effects

No data have been found.

6.5.7 Carcinogenic effects

Two large cohorts of man made mineral fibre workers, one in the US and one in Europe have been studied over several decades with respect to carcinogenicity of the fibres. No data were available on the HT-fibres.

6.5.7.1 European cohort

In the European cohort, the SMR for lung cancer in exposed stone/slag wool and glass wool workers was elevated compared to national (statistically significant) and local reference populations (statistically non-significant). The risk of lung cancer among stone/slag wool workers increased with time-since-first-employment and decreased from the early to the late technological phase. In nested case-control studies no increased risk of lung cancer with increasing fibre exposure was reported.

The SMR for cancer of the buccal cavity and pharynx was statistically significantly elevated in the last updating. The SMR was not statistically significantly elevated for other types of malignant neoplasms. Five mesothelioma deaths occurred in the exposed workers.

6.5.7.2 US cohort

In the US cohort a statistically significant excess in mortality from respiratory system cancer was observed in fibreglass as well as stone/slag wool workers when compared to US rates but when compared to local county rates the excess was no longer statistically significant. A greater excess mortality from respiratory system cancer was observed among stone/slag wool workers than among fibreglass workers. Among the total fibreglass cohort, the SMR for respiratory system cancer increased with calendar time and with time since first employment but these increases were less pronounced among long-term workers. For the factories that mainly produced glass wool, the SMR for respiratory system cancer was statistically significantly elevated for all workers but not for long-term workers. All statistically significantly elevated SMRs for respiratory system cancer in fibreglass as well as stone/slag wool workers were reduced to not statistically significant levels when adjusted for cigarette smoking. In nested case-control studies no statistically significant association was observed between SMRs for respiratory system cancer and increasing exposure to respirable fibreglass or stone/slag wool when adjusted for smoking.

The SMR was not statistically significantly elevated for other types of malignant neoplasms including buccal cavity and pharynx. Overall mortality risk from malignant mesothelioma did not seem to be elevated in the US cohort.

6.5.7.3 IARC evaluation on human carcinogenicity

IARC concluded that there was inadequate evidence in humans for the carcinogenicity of glass wool and stone/slag wool.

Results from the most recent cohorts and nested case-control studies of workers exposed to glass wool and to stone/slag wool did not provide consistent evidence of an association between exposure to fibres and risk for lung cancer or mesothelioma.

Of some concern are risks for e.g. construction workers, who may have experienced higher, but perhaps more intermittent, exposure to man-made vitreous fibres.

6.6 Animal toxicity

6.6.1 Single dose toxicity

No data have been found.

6.6.2 Irritation

No data have been found.

6.6.3 Sensitisation

No data have been found.

6.6.4 Repeated dose toxicity

Macrophage accumulation was seen in a number of inhalation studies in rodents with exposure for up to 2 years to different MMVFs (unspecified). Levels of exposure were generally reported in mg/m^3 and not as fibre concentration. Exposure levels up to 100 mg/m^3 were used.

Exposure by inhalation (7.3×10^8 $fibres/m^3$) glass fibres (5-10 μm long and 1.2 μm in diameter for 90 days caused alveolar lipoproteinosis in rats, guinea pigs and hamsters.

Rats and hamsters exposed to glass wool at concentrations of $3 \times 10^8 – 3 \times 10^9$ $fibres/m^3$ or to stone wool concentrations of 2×10^8 $fibres/m^3$ for 2 years showed very slight peri-bronchial fibrosis.

Rats exposed by inhalation to 4.8×10^7 f/m^3 respirable glass wool or to 1.1×10^7 f/m^3 respirable stone wool for up to 2 years showed alveolar macrophagic reaction and slight septal fibrosis.

6.6.5 Toxicity to reproduction

No data have been found.

6.6.6 Mutagenic and genotoxic effects

Glass and stone wool have shown a potential for inducing DNA-damage and cell transformation in vitro. The activity is related to the dimensions of the fibres, long and thick fibres being more potent than short and thin fibres.

6.6.7 Carcinogenic effects

6.6.7.1 Insulation glass wool

Six inhalation studies in rats and 3 studies in hamsters with different types of glass wool were available at exposure levels ranging from 2.5 x 10^7 – 7.0 x 10^8 f/m^3, most of the studies using 2.3-3.4 x 10^7 f/m^3. There was no increase in lung tumour incidence in one rat study, while two rat studies showed a slight increase in the number of rats with tumours in the lung after inhalation exposure for 3-24 months. Incidences of tumours were lower than for asbestos treated control rats. No lung tumour was seen in any of the glass wool treated hamsters. No mesothelioma was seen in any glass wool treated animal.

Five intraperitoneal studies in rats and one in hamsters were conducted with different types of glass wool fibres at exposure levels of 2.4 x 10^7 – 9.7 x 10^9 f/m^3. Results from the rat studies showed that glass wool has a potential for causing mesothelioma in the abdominal cavity. However, the incidence of tumours was lower than in the asbestos treated control animals. It appears that the hamster is a less sensitive species to this effect, as no mesothelioma was seen from glass wool or from asbestos fibre injection in the abdomen.

IARC concluded that "*limited evidence in animals for the carcinogenicity of glass wool".*

6.6.7.2 Stone wool

Three long-term inhalation studies in rats exposed to stone wool were available. The studies used different asbestos types as positive controls. Stone wool concentrations were reported in weight per volume except for one study using 1.3 x 10^7 respirable fibres/m^3. A low number of adenomas was seen in the stone wool treated groups, and no mesothelioma were reported in any stone wool treated animal. In contrast, the asbestos treated animals showed several lung tumours and mesotheliomas.

There was no significant increase in lung tumours in an intra-tracheal test conducted with stone wool in rats with doses up to 8 x 10^6 f/rat.

A non-significant increase in mesotheliomas was seen in an intrapleural test in rats using 20 mg stone wool. No measurement of the fibre concentration was given.

Several studies of intraperitoneal injection in rats of stone wool of approximately 10^6-10^9 fibres/animal were available showing a significant increase in the incidence of mesothelioma.

IARC concluded that there is *limited evidence in animals for the carcinogenicity of stone wool.*

6.6.7.3 HT-fibre

No carcinoma and 5 adenomas were seen in a long-term inhalation study using 107 rats/group with the HT-fibre at 2.5 x 10^8 f/m^3. The air control group had 1 carcinoma and 3 adenomas.

An intraperitoneal study with HT fibres at a dose of 10^9 fibres/rat did not show any abdominal tumours.

IARC concluded that there is *inadequate evidence* in experimental animals for the carcinogenicity of the HT-fibre.

6.7 Evaluation

MMVFs have been on the market for over 60 years and a large number of human and animal studies are available. Despite the apparently large toxicological database on the fibres, the evaluation of the risk of adverse health effects of MMVFs presents a number of overall and more study-specific difficulties, which are discussed below.

In the animal studies, the fibres (types, dimensions) are not always transparently described as product names are used. Also, the levels are often expressed in weight/volume and not in fibre concentration. The animal models are difficult to use because of differences in anatomy and physiology of the respiratory tract and possibly also different sensitivity to the fibres between animals and humans. Inhalation studies have been supplemented by intra-tracheal, intrapleural and intraperitoneal studies in rodents. The results of such tests can be used to indicate the potential of the fibres to create an effect, but no quantitative risk assessment is possible on the basis of these results.

The epidemiological data are most extensively described for two large cohorts of MMVF production workers in the US and in Europe. These cohorts focused on the standardised mortality ratio especially for lung cancer and non-malignant respiratory diseases. Within the US cohort a cross-sectional investigation was conducted with respiratory health assessment. Several other epidemiological studies in production workers and end-users also evaluated the respiratory health.

Comparison of fibre exposure levels of the workers in these different epidemiological studies is complicated by several factors. In many of the studies, exposure to several kinds of MMVFs occurred and it is not always clear from the articles exactly what fibres the workers have been exposed to. In e.g. the stone/slag wool factories in the US cohort different articles disagrees on whether it is stone or slag wool that is produced at a specific factory, and at factories where mainly glass wool is produced exposure to other kinds of glass fibres might also have occurred. Exposure measurements may be performed at personal level or in the room by different techniques and the results have been reported in many different ways. For some of the studies the exposure measurements have been combined with knowledge of past exposure and personal job histories to obtain individual exposure estimates. In several of the epidemiological studies, exposure measurements were not performed as a part of the studies but reference was made to measurements or estimates made by others.

Co-exposure to other fibres or chemicals has been documented in several of the studies. In e.g. the European cohort, factories with more than an occasional processing of asbestos were excluded from the study but it is known that exposure to asbestos may have occurred at all of these factories as well as at the factories in the US cohort. In most of the studies with end-users some exposure to asbestos has been reported and generally adjusted for. Where not reported a possible exposure to asbestos must be born in mind. Smoking is another confounder, the role of which and possible interaction with fibres should be born in mind. In e.g. the US

cohort it was shown that the number of smokers were higher among the workers than in the general population.

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

A statistically significant increased mortality risk for nephritis and nephrosis was seen in stone/slag wool workers in the US cohort. In the European cohort this risk was not increased for stone/slag wool workers but the authors made a suggestion of an increasing risk of death from non-malignant renal diseases with duration of employment or employment in the early technological phase. The nephritis and nephrosis is not likely to be caused by the stone/slag wool fibres because the fibres will predominately be retained in the respiratory tract rather than being absorbed.

Glass fibres and stone wool have shown effects in genotoxicity studies in non-human mammalian cells. Longer fibres seem to be more active than shorter fibres. Genotoxic effects are not expected to occur systemically following inhalation exposure because the fibres will predominately 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, *in vitro* cellular tests do not take into account some important parameters of fibre toxicity *in vivo* e.g. the clearance from the lungs.

Because of their similarity with asbestos-fibres, MMVF have been considered carcinogenic. However, compared to asbestos fibres MMVFs are of lower biopersistence. They are cleared more rapidly from the lungs due to dissolution and transverse breakage of the fibres. In the European and US cohorts statistically significantly elevated SMRs were found for respiratory system cancer in glass as well as stone/slag wool workers compared to national rates. No significant excess risk was found for any other cancers. In nested case-control studies adjusting for smoking and co-exposures no increased risk of respiratory cancer with increasing fibre exposure was reported. IARC are concluding that results from the most recent studies in the US and European cohort have not provided consistent evidence of an association between exposure to fibres and risk of lung cancer. Although they are evaluating that there is *inadequate evidence* in humans for the carcinogenicity of glass and stone/slag wool they are stating: *Of some concern are risks for workers in industries that use or remove these products (e.g. construction), who may have experienced higher, but perhaps more intermittent, exposure to MMVFs.* On this background, a carcinogenic potential of glass and stone/slag wool cannot be fully excluded but the potential is considered to be low.

Other effects of concern are the toxicological effects in the lung after repeated exposure to fibres. In the European and US cohorts no increased mortality from non-malignant respiratory diseases (acute infections, influenza, pneumonia, and bronchitis, emphysema and asthma) were found. For non-malignant respiratory diseases it might be more relevant to look at the prevalence or incidence than at the mortality since a worker with e.g. pneumoconiosis might not necessarily die from his disease. Several studies evaluated the respiratory health of production workers and end-users based on thoracic radiography, spirometry and questionnaires. No convincing evidence was found of pneumoconiosis and pleural abnormalities in the recent studies including the cross-sectional study in the US cohort.
Glass and stone/slag wool fibres seem to be able to cause obstructive lung disease as indicated by spirometric measurements and some of the respiratory symptoms

assessed by the questionnaires. In most of the studies with production workers no statistically significant association was found between pulmonary function and exposure to fibres including the cross-sectional study in the US cohort in which the mean concentration of airborne respirable fibres was estimated to be 0.03 x 10^6 fibres/m^3 based on exposure measurements combined with job histories. In Danish stone/slag wool production workers the FEV_1/FVC ratio was statistically significantly lower than in the control group, indicating obstructive lung disease. This observation was supported by a higher prevalence of emphysema in the workers than in the control group. Subgroup analysis showed that the elevated risk of airway obstruction was restricted to heavy smokers. The exposure level was not determined for the study population. The estimated mean concentration of airborne respirable fibres was 0.1 – 0.2 x 10^6 fibres/m^3 in the European stone/slag wool industry in the examined period.
In Swedish construction workers spirometry gave no evidence of obstructive lung disease. However, high exposure to insulation wool was associated with statistically significant increased odds ratios for persistent cough of the same magnitude as current smoking. Comparison with measurements made on average 3.9 years later showed no statistically significant difference in yearly change of VC and FEV_1 between exposed and unexposed construction workers. The exposure level was not determined for the study population. The measured mean concentration of airborne respirable fibres was 0.06 – 0.91 x 10^6 fibres/m^3 for different occupations within the Swedish construction industry 1978-90. Values up to 5.08 x 10^6 fibres/m^3 were measured in insulators, which generally was exposed to the highest values.
In Danish insulators an increased prevalence of obstructive lung disease was indicated in the workers. In addition comparison with measurements made 6 or 8 years earlier showed a significantly higher decline in FEV_1 and FVC in insulation workers than in the control group. The exposure level was not determined for the study population. The measured usual concentration of airborne fibres was in the range of 0.03 – 1 x 10^6 fibres/m^3 for Danish insulators but concentration up to 10 x 10^6 fibres/m^3 occurred.
Since the exposure level was not determined for the last 3 studies a likely explanation for the observed differences could be differences in the exposure. Insulators are the group of workers, which are generally exposed to the highest values making it reasonable that obstructive lung disease is observed among them but not among construction workers that also include other groups of workers with less exposure to glass and stone wool.

Other effects of concern are the acute irritancy of the fibres to the skin, eyes and the respiratory tract, which has been documented in several human studies. The irritation is not caused by respirable fibres but by fibres with a diameter greater than 4-5 μm. The fibre concentrations at which these irritative effects occur are not well reported and cannot be used as a basis for calculation of a quality criterion. Furthermore it is not clear whether the irritation stems mainly from fibres in the air or from direct exposure to settled fibres. However, the exposure level that might cause irritation seems to be lower than the level that might cause obstructive lung disease.

The overall available information on the HT-fibre (2 studies in rats) indicates a low toxicity. Thus, it is evaluated that the quality criteria, which will be defined for glass wool and stone wool, will ensure protection from adverse effects of HT-fibres as well.

6.7.1 Critical effect and NOAEL

The critical effect following inhalation exposure to glass and stone wool is considered to be effects in the respiratory tract (irritation and obstructive lung disease) observed in humans. The respiratory tract irritation is mainly caused by the non-respirable fibres whereas the obstructive lung disease is caused by the respirable fibres reaching the lungs.

The fibre concentrations at which the irritative effect occurs are not well reported and thus, a health-based quality criterion in ambient air for non-respirable glass and stone wool fibres cannot be set based on the available data.

In the cross-sectional study in the US cohort with production workers (Hughes et al. 1993), no evidence of decreased pulmonary function (as well as of pneumoconiosis and pleural abnormalities) was observed. The mean concentration of airborne respirable fibres was estimated to be 0.03×10^6 fibres/m^3 based on exposure measurements combined with job histories

In the study with Danish insulators (Clausen et a. 1993), obstructive lung disease was indicated. The exposure level was not determined but it seemed likely to be higher than the level reported above because insulators generally are the group of workers exposed to the highest values of fibres.

For the purpose of establishing a health-based quality criterion in ambient air, the mean concentration of airborne respirable fibres estimated to be 0.03×10^6 fibres/m^3 in the cross-sectional study in the US cohort with production workers (Hughes et al. 1993) (see Table 3.13) could be considered as a NOAEL for effects observed in the respiratory tract of humans. However, there remains some uncertainty regarding the interpretation of the exposure assessments performed in this study. Furthermore, it could also be questioned whether these US exposure assessments are relevant for the situation in Denmark today. It is therefore, considered that a health-based quality criterion in ambient air for respirable glass and stone wool fibres cannot be set based on the available data.

The available information on the HT-fibre indicates a low toxicity. However, a health-based quality criterion in ambient air for HT fibres cannot be set based on the available data.

In conclusion, health-based quality criteria in ambient air for glass wool, stone wool and HT fibres cannot be set based on the available data.

7 Quality criteria in air

Health-based quality criteria in ambient air for glass wool, stone/slag wool and HT fibres, which are the types of mineral wool produced in Denmark, cannot be set based on the available data.

The C-value at present for mineral wool is 1300 fibres/m^3 and mineral wool is placed in Main Group 1 (MST 2002).
Due to the available data there are no obvious reasons for changing the C-value for glass wool and stone/slag wool fibres.
Although that a carcinogenic potential to humans cannot be fully excluded based on the available data, the carcinogenic potential is considered to be low as glass wool and stone/slag wool seem to be cleared relatively rapidly from the lungs due to dissolution and transverse breakage of the fibres and consequently, to be of relatively low biopersistence. A placing in Main Group 2 instead of Main Group 1 is thus justified.

The C-value for the HT-fibres is proposed to be the same as the value for glass wool and stone/slag wool until human data become available for this fibre type and a revision is deemed necessary. A placing in Main Group 2 is justified because of the low carcinogenic potential considered due to the relatively low biopersistency of the HT fibres.

7.1.1 C-value

1300 fibres/m^3 as respirable fibres, Main Group 2.

8 References

Albin M, G Engholm, N Hallin, L Hagmar (1998). Impact of exposure to insulation wool on lung function and cough in Swedish construction workers. Occup Environ Med **55**, 661-667.

Andersen A and F Langmark (1986). Incidence of cancer in the mineral-wool producing industry in Norway. Scand J Work Environ Health **12**, suppl 1, 72-77.

At (2005). Grænseværdier for stoffer og materialer. AT-vejledning C.0.1, april 2005.

Bertazzi PA, C Zocchetti, L Riboldi, A Pesatori, L Radice and R Latocca (1986). Cancer mortality of an Italian cohort of workers in man-made glass-fiber production. Scand J Work Environ Health **12**, suppl 1, 65-71.

Björnberg A (1985). Glass fiber dermatitis. Am J Ind Med **8**, 395-400.

Björnberg A and G-B Löwhagen (1977). Patch testing with mineral wool (Rockwool®). Acta Dermatovener (Stockholm) **57**, 257-260.

Bofetta P, R Saracci, A Andersen, PA Bertazzi, J Chang-Claude, J Cherrie, G Ferro, R Fretzel-Beyme, J Hansen, J Olsen, N Plato, L Teppo, P Westerholm, P Winter, C Zocchetti (1997). Cancer Mortality among Man-Made Vitreous Fiber Production Workers. Epidemiology, **8**, no 3, 259-268.

Buchanich JM, GM Marsh and Youk AO (2001). Historical cohort study of US man-made vitreous fiber production workers: V. Tobacco-smoking habits. J Occup Environ Med **43**, 793-802.

CEPA (2001). Mineral Fibres (Man-Made Vitreous Fibres). Priority Substances List Assessment Report, Canadian Environmental Protection Act.

Cherrie J and J Dodgson (1986). Past exposures to airborne fibers and other potential risk factors in the European man-made mineral fiber production industry. Scand J Work Environ Health **12**, suppl 1, 26-33.

Cherrie J, J Dodgson, S Grat and W Maclaren (1986). Environmental surveys in the European man-made mineral fiber production industry. Scand J Work Environ Health **12**, suppl 1, 18-25.

Chiazze L, DK Watkins; C Fryar, W Fayerweather, JR Bender and M Chiazze (1999). Mortality from nephritis and nephrosis in the fibreglass manufacturing industry. Occup Environ Med **56**, 164-166.

Claude J and R Frentzel-Beyme (1986). Mortality of workers in German rock-wool factory – A second look with extended follow-up. Scand J Work Environ Health **12**, suppl 1, 53-60.

Clausen J, B Netterstrøm and C Wolff (1993). Lung function in insulation workers. Br J Ind Med **50**, 252-256.

Conde-Salazar L, D Guimaraens, LV Romero, A Harto and M Gonzalez (1985). Contact Derm **13**, 195-196.

Davis JMG (1986). A review of experimental evidence for the carcinogenicity of man-made vitreous fibers. Scand J Work Environ Health **12**, suppl 1, 12-17.

Dorland (1988). Dorland's Illustrated Medical Dictionary, 27th ed., Saunders 1988.

Enterline PE, GM Marsh and NA Esmen (1983). Respiratory disease among workers exposed to man-made mineral fibers. Am Rev Respir Dis **128**, 1-7.

Enterline PE, GM Marsh, V Henderson and C Callahan (1987). Mortality update of a cohort of US man-made mineral fibre workers. Ann Occup Hyg **31**, 625-656.

Esmen N, M Corn, Y Hammad, D Whittier and N Kotsko (1979). Summary of measurements of employee exposure to airborne dust and fiber in sixteen facilities producing man-made mineral fibers. Am Ind Hyg Assoc J, **40**, 108-117.

Gardner MJ, PD Winter, B Pannett, MJC Simpson, C Hamilton and ED Acheson (1986). Mortality of workers in the man-made mineral fiber production industry in the United Kingdom. Scand J Work Environ Health **12**, suppl 1, 85-93.

Gaudichet A, P Petit, MA Billon-Galland and G Dufour (1989). Levels of atmospheric pollution by man-made mineral fibres in buildings. In: Non-occupational exposure to mineral fibres. IARC Scientific Publications, **90**, Lyon, 1989.

Hansen EJ, FV Rasmussen; F Hardt and O Kamstrup (1999). Lung Function and Respiratory Health of Long-term Fiber-exposed Stonewool Factory Workers. Am J Respir Crit Care Med **160**, 466-472.

Höhr D (1985). Transmissionselektronenemikroskopische Untersuchung: Faserförmige Stäube in der Ausseluft. Staub – Reinhalt Luft **45**, nr 4, 171-174.

Hughes JM, RN Jones, HW Glindmeyer, YY Hammad and H Weill (1993). Follow up study of workers exposed to man made mineral fibres. Br J Ind Med **50**, 658-667.

IARC (1988). Man-made Mineral Fibres and Radon. In: IARC Monographs on the Evaluation of the Carcinogenic Risk to Humans, Vol. **43**, Lyon, 1988.

IARC (2002). Man-made Vitreous fibres. In: IARC Monographs on the Evaluation of the Carcinogenic Risk to Humans, Vol. **81**, Lyon, 2002.

Jolanki R, I Mäkinen, K Suuronen, K Alanko and T Estlander (2002). Occupational irritant contact dermatitis from synthetic mineral fibres according to Finnish statistics. Contact Derm **47**, 329-333.

Kaufer E, JC Vigneron and S Veissière (1987). Enquête épidémiologique dans deux usines productrices de fibres minerals artificielles. I. Mesure des niveaux d'empoussièrement. Arch Mal Prof **48**, 1-6.

Kilburn KH and Warshaw RH (1991). Difficulties of attribution of effect in workers exposed to fibreglass and asbestos. Am J Ind Med **20**, 745-751.

Kilburn KH, D Powers, RH Warshaw (1992) Pulmonary effects of exposure to fine fiberglass: irregular opacities and small airways obstruction. Br J Ind Med **49**, 714-720.

Le Bouffant L, H Daniel, JP Henin, JC Martin, C Normand, G Tichoux and F Trolard (1987). Experimental study on long-term effects of inhaled MMMF on the lung of rats. Ann Occup Hyg **31**, 765-790.

Lockey JE and CS Ross (1994). Radon and man-made vitreous fibers. J Allergy Clin Immunol **94**, 310-317.

Marsh G, A Youk, M Quinn, L Schall, R Stone, T Smith, V Henderson, L Wayne and K Lee (1996). Mortality among United States rock wool and slag wool workers: 1989 update. J Occup Health Safety Aust NZ **12**, 297-312.

Marsh GM, AO Youk, RA Stone, JM Buchanich, MJ Gula, TJ Smith and MM Quinn (2001c). Historical cohort study of US man-made vitreous fiber production workers: I. Fiberglass cohort follow-up: Initial findings. J Occup Environ Med **43**, 741-756.

Marsh GM, JM Buchanich and Youk AO (2001a). Historical cohort study of US man-made vitreous fiber production workers: VI. Respiratory system cancer standardized mortality ratios adjusted for the confounding effect of cigarette smoking. J Occup Environ Med **43**, 803-808.

Marsh GM, MJ Gula, AO Youk, JM Buchanich, A Churg and TV Colby (2001b). Historical cohort study of US man-made vitreous fiber production workers: II. Mortality from mesothelioma. J Occup Environ Med **43**, 757-766.

Marsh GM, PE Enterline, RA Stone and VL Henderson (1990). Mortality among a cohort of US man-made mineral fiber workers: 1985 follow-up. J Occup Med **32**, 594-604.

McConnell EE, C Axten, TW Hesterberg, J Chevalier. WC Miiller, J Everitt, G Oberdorster, G R Chase, P Thevenaz and P Kotin (1999). Studies on the inhalation toxicology of two fibreglasses and amosite asbestos in the Syrian golden hamster. Part II. Results of chronic exposure. Inhal Toxicol **11**, 785-835.

Moulin JJ, P Wild, JM Mur, JF Caillard, N Massin, C Meyer-Bisch, JP Toamain, P Hanser, S Liet MN Du Roscoat and A Segala (1988). Respiratory health assessment by questionnaire of 2024 workers involved in man-made mineral fiber production. Int Arch Occup Environ Health **61**, 171-178.

MM (2002). The Statutory Order from the Ministry of the Environment no. 439 of June 3, 2002, on the List of Chemical Substances.

MST (2002). B-værdivejledningen. Vejledning Nr. 2 2002. Miljøstyrelsen, Miljøministeriet.

OJ (1997). Commission directive 97/69 EC of 5 December 1997 adapting to technical progress for the 23rd time Council Directive 67/548/EEC on the approximation of the laws, regulations and administrative provisions relating to the classification, packaging and labelling of dangerous substances. Official Journal of the European Communities, **L343**, 19-24.

Olsen JH, OM Jensen and O Kampstrup (1986). Influence of smoking habits and place of residence on the risk of lung cancer among workers in one rock-wool producing plant in Denmark. Scand J Work Environ Health **12**, suppl 1, 48-52.

Petersen R and S Sabroe (1991). Irritative symptoms and exposure to mineral wool. Am J Ind Med **20**, 113-122.

Quinn MM, Smith TJ, AO Youk, GM Marsh, RA Stone, JM Buchanich and MJ Gula (2001). Historical cohort study of US man-made vitreous fiber production workers: VIII. Exposure-specific job analysis. J Occup Environ Med **43**, 824-834.

Rindel A, C Hugod, E Bach and NO Breum (1989). Effect on health of man-made mineral fibres in kindergarten ceilings. In: Non-occupational exposure to mineral fibres. IARC Scientific Publications, **90**, Lyon, 1989, 449-453.

Sali D, P Bofetta, A Andersen, JW Cherrie, J Chang Claude, J Hansen, JH Olsen, AC Pesatori, N Plato, L Teppo, P Westerholm, P Winther and R Saracci (1999). Non-neoplastic mortality of European workers who produce man made vitreous fibres. Occup Environ Med **56**, 612-617.

Saracci R (1986). Ten years of epidemiologic investigations on man-made mineral fibers and health. Scand J Work Environ Health **12**, suppl 1, 5-11.

Schneider T (1979). Exposures to man-made mineral fibres in user industries in Scandinavia. Ann Occup Hyg **22**, 153-162.

Simonato L, AC Fletcher, J Cherrie, A Andersen, PA Bertazzi, N Charnay, J Claude, J Dodgson, J Estève, R Frentzel-Beyme, MJ Gardner, OM Jensen, JH Olsen, R Saracci, L Teppo, R Winkelmann, P Westerholm, PD Winter and C Zocchetti (1986). The man-made mineral fiber European historical cohort study. Extension of the follow-up. Scand J Work Environ Health **12**, suppl 1, 34-47.

Simonato L, AC Fletcher, JW Cherrie, A Andersen, P Bertazzi, N Charnay, J Claude, J Dodgson, J Esteve, R Frentzel-Beyme, MJ Gardner, O Jensen, J Olsen, L Teppo, R Winkelmann, P Westerholm, PD Winter, C Zocchetti and R Saracci, (1987). The international agency for research on cancer historical cohort study of MMMF production workers in seven European countries: Extension of the follow-up. Ann Occup Hyg **31**, 603-623.

Smith TJ, MM Quinn, GM Marsh, AO Youk, RA Stone, JM Buchanich and MJ Gula (2001). Historical cohort study of US man-made vitreous fiber production workers: VII. Overview of the exposure assessment. J Occup Environ Med **43**, 809-823.

Stam-Westerveld EB, PJ Coenraads, PGM van der Valk, MCJM de Jong and V Fidler (1994). Rubbing test responses of the skin to man-made mineral fibres of different diameters. Contact Derm **31**, 1-4.

Stone RA, Youk AO, GM Marsh, JM Buchanich, MB McHenry and TJ Smith (2001). Historical cohort study of US man-made vitreous fiber production workers: IV. Quantitative exsposure-response analysis of the nested case-control study of respiratory system cancer. J Occup Environ Med **43**, 779-792.

Teppo L and E Kojonen (1986). Mortality and cancer risk among workeres exposed to man-made mineral fibers in Finland. Scand J Work Environ Health **12**, suppl 1, 61-64.

Thriene B, A Sobottka, H Willer and J Weidhase (1996). Man-made mineral fibre boards in buildings health risks caused by quality deficiencies. Toxicology letters **88**, 299-303.

Weill H, Hughes JM, YY Hammad, HW Glindmeyer, G Sharon and R Jones (1983). Respiratory health in workers exposed to man-made vitreous fibers. Am Rev Respir Dis **128**, 104-112.

Westerholm P and A-M Bolander (1986). Mortality and cancer incidence in the man-made mineral fiber industry in Sweden. Scand J Work Environ Health **12**, suppl 1, 78-84.

WHO (1988): Man-made mineral fibres. Environmental Health Criteria **77**, World Health Organisation, International Programme on Chemical Safety, Geneva.

Youk AO, GM Marsh, RA Stone, JM Buchanich and TJ Smith (2001). Historical cohort study of US man-made vitreous fiber production workers: III. Analysis of exposure-weighted measures of respirable fibers and formaldehyde in the nested case-control study of respiratory system cancer. J Occup Environ Med **43**, 767-778.

Evaluation of health hazards by exposure to Mineral wools (glass, stone/slag, HT) 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 mineral wools (glass, stone/slag, HT (high-alumina, low-silica wool used for insulation)). This resulted in 2010 in the present report which includes a health-based quality criterion for the substances in ambient air.

Danish Ministry of the Environment
Environmental Protection Agency

Strandgade 29
1401 Copenhagen K, Denmark
Tel.: (+45) 72 54 40 00

www.mst.dk