Canadian Environmental Protection Act

Priority Substances List
Assessment Report

Mineral Fibres
(Man-Made Vitreous Fibres)

Government of Canada
Environment Canada
Health Canada

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Synopsis

This assessment addresses the subset of mineral fibres known as man-made vitreous fibres (MMVF) for which the database was considered to be sufficient: rock and slag wools, glass wool (excluding glass microfibres), glass microfibres, continuous glass filaments, and aluminosilicate refractory ceramic fibres (RCF). Approximately 250 to 300 kilotonnes of these fibres were produced in Canada in 1991, of which 70% were glass wools, 20% rock and slag wools, 10% continuous glass filament, and less than 1% refractory ceramic fibres. Glass, rock, and slag wools are used mainly for thermal and acoustic insulation, continuous glass filament to reinforce plastics, and refractory ceramic fibres for high-temperature furnace and kiln insulation. Glass microfibres are not known to be produced in Canada, but are probably imported in small amounts in finished products. Releases of man-made vitreous fibres are poorly quantified, but of those that enter the Canadian environment, most are likely emitted into air. Most MMVF are relatively stable and are expected to persist in the ambient environment.

Although MMVF enter the atmosphere in Canada, no data were identified on concentrations in Canadian air, water, sediment, or soil, although some information is available from other countries. Furthermore, no relevant data were found on the effects of MMVF on exposed biota such as terrestrial mammals or birds. Therefore, it is not possible to determine whether Canadian biota are adversely affected by exposure to MMVF.

Airborne MMVF are present as relatively inert solid particles, and, based on limited data from other countries, their concentrations in outdoor air are low, relative to other solid phases. As such, MMVF are not expected to contribute significantly to the formation of ground-level ozone, global warming, or depletion of stratospheric ozone.

Available data on the levels of rock/slag wool to which the general population is exposed are limited. Adverse effects (rock wool only) have been observed in toxicological studies in animal species only at concentrations much greater (by more than 350 times) than the highest concentrations measured in the indoor environment in other countries in living areas during the installation of blown rock wool insulation.

Available data on the levels of glass wool (excluding glass microfibres) to which the general population is exposed are also limited. Only minimal effects (not adverse) have been observed in toxicological studies in animal species at concentrations much greater (i.e., by more than 75 times) than the highest concentrations measured in the indoor environment in other countries in living areas during the installation of glass wool insulation.

Data on the concentrations of glass microfibres to which the general population is exposed in Canada or other countries have not been identified. Since their use in Canada is likely very limited, however, concentrations in the general environment are expected to be very low. Adverse effects have not been observed in limited epidemiological studies of populations exposed to considerably higher concentrations than those likely to be present in the general environment or in animals exposed to much higher concentrations in toxicological studies.

Adverse effects of continuous glass filament have not been observed in epidemiological studies of populations exposed occupationally to considerably higher concentrations than those likely to be present in the general environment (though quantitative data on the latter are lacking). Few respirable fibres are generated in the production and use of continuous filament and therefore it is likely that concentrations in the general environment are extremely small.

On the basis principally of the increased incidence of pulmonary tumours in rats and increases in mesotheliomas in rats and hamsters observed in inhalation bioassays, and supporting data, refractory ceramic fibre has been classified as “probably carcinogenic to humans”, i.e., as a substance for which there is believed to be some chance of adverse health effects at any level of exposure. For such substances, estimated exposure is compared to quantitative estimates of cancer potency to characterize risk and provide guidance for further action (i.e., analysis of options to reduce exposure); however, owing to their use principally in high-temperature industrial applications, with the exception possibly of areas in the vicinity of industrial sources for which relevant Canadian data were not identified, exposure of the general population and resulting exposure potency index (EPI) [and hence priority for further action under CEPA] are expected to be very low.

Based on these considerations, it has been concluded that available information is insufficient to determine whether these substances are entering the environment in quantities or under conditions that may be harmful to the environment. It has been concluded that man-made vitreous fibres are not entering the environment in quantities or under conditions that may constitute a danger to the environment on which human life depends. Rock/slag wool, glass wool (excluding glass microfibres), glass microfibres, and continuous glass filament are not entering the environment in quantities or under conditions that may constitute a danger in Canada to human life or health. It has been concluded that refractory ceramic fibre may enter the environment in quantities or under conditions that may constitute a danger in Canada to human life or health.

1.0 Introduction

The *Canadian Environmental Protection Act* (CEPA) requires the federal Ministers of the Environment and of Health to prepare and publish a Priority Substances List that identifies substances, including chemicals, groups of chemicals, effluents, and wastes, that may be harmful to the environment or constitute a danger to human health. The Act also requires both Ministers to assess these substances and to determine whether they are “toxic” as interpreted in section 11 of the Act, which states:

> “. . .a substance is toxic if it is entering or may enter the environment in a quantity or concentration or under conditions
>
> > (*a*) having or that may have an immediate or long-term harmful effect on the environment;
> >
> > (*b*) constituting or that may constitute a danger to the environment on which human life depends; or
> >
> > (*c*) constituting or that may constitute a danger in Canada to human life or health."

Substances assessed as “toxic” under section 11 may be placed on Schedule I of the Act. Consideration can then be given to developing regulations, guidelines, or codes of practice to control any aspect of these substances’ life cycle, from the research and development stage through manufacture, use, storage, transport, and ultimate disposal.

The mineral fibre “asbestos” is a Toxic Substance that is included on Schedule I of CEPA. In attempting to delineate the scope of this assessment, therefore, a search of on-line databases was conducted for the following other subgroups of “mineral fibres” (the substance specified on the Priority Substances List):

Name	Chemical Abstracts Service (CAS) Registry Number (where applicable)
Wollastonite	13983–17–0
Attapulgite	12174–11–7
Sepiolite	15501–74–3; 18307–28–8
Erionite	66733–21–9
Corundum	1302–74–5
Rock wool	
Ceramic fibre	1302–76–7
Refractory ceramic fibre	
Fibrous glass	
Mineral wool	

Based on preliminary assessment of the results of this search, it was determined that sufficient data might be available to permit assessment of "toxic" for man-made vitreous fibres (MMVF) only, including rock/slag and glass wool (excluding microfibres), glass microfibres, continuous glass filament, and refractory ceramic fibre.

The assessment of whether each subgroup of the priority substance MMVF is "toxic", as defined in CEPA, was based on the determination of whether it **enters** or is likely to enter the Canadian environment in a concentration or quantities or under conditions that could lead to **exposure** of humans or other biota at levels that could cause adverse **effects**.

Information on the effects of MMVF on environmental organisms has not been identified. This assessment focuses, therefore, upon possible effects on human health in the general environment and excludes possible irritation of the skin and eyes by MMVF (effects more commonly associated with exposure in the occupational environment).

Information on the physical and chemical properties of MMVF and their fate and concentrations in the environment was obtained from reviews published by the World Health Organization (WHO, 1988; IARC, 1988). Information on concentrations in the environment and effects of exposure on aquatic organisms was also sought by on-line searches of AQUAREF (1970–1992); ASFA (1978–1992); BIOSIS (1969–1992); CAB Abstracts (1972–1992); Dissertation Abstracts (1961–1992); ENVIRO ENERGYLINE PLUS (1971–1992); Life Sciences Collection (1978–1992); MICROLOG (1980–1992); NTIS (1964–1992); Pollution Abstracts (1970–1992); Water Resources Abstracts (1968–1992); WATERNET (1971–1992); and Zoological Record (1978–1992). In addition, representatives of manufacturing industries, including S. Lethbridge (Owens-Corning Fiberglas Canada Inc.) and G. Bates (Manville Canada Inc.) and officials of Ministries of the Environment in Ontario, Alberta, and British Columbia were contacted concerning releases and concentrations of MMVF in Canada. Information in these areas obtained after June 1993 was not considered in this review.

The assessment of whether MMVF are "toxic" to human health under CEPA is based principally upon documentation prepared by staff of Health Canada (HC) for the International Programme on Chemical Safety (IPCS). Between 1985 and 1987, original data relevant to the assessment of risks to health associated with exposure to MMVF were reviewed by staff of HC in the preparation of a draft IPCS Environmental Health Criteria (EHC) document. This information was further updated in review articles prepared by staff of HC (Meek, 1991a, 1991b). The current assessment has been updated and expanded to emphasize recent data and those most relevant to the assessment of the risks associated with exposure of the population to MMVF in the general environment in Canada.

In preparation of the WHO-IPCS document and the more recent review articles, a wide range of scientific databases was searched; additional information was identified during peer review of the draft EHC by IPCS focal points and a task group of experts, which met in September 1987. More recently, in November 1991, to identify toxicological data relevant to the assessment of effects upon human health, searches were conducted on the following on-line databases: Hazardous Substances Data Bank (HSDB, U.S. National Library of Medicine); Registry of Toxic Effects of Chemical Substances (RTECS, U.S. National Institute for Occupational Safety and Health); TOXLINE (1981 to present; U.S. National Library of Medicine); the TOXLINE backfile (1965 to 1980); TOXLIT (1981 to the present, U.S. National Library of Medicine); and MULTILIS (on-line catalog of Health Protection Branch libraries). Information published in the period since these searches were conducted was identified through a Selective Dissemination of Information (SDI) profile. Additional relevant information was obtained from A.R. Wells, Fiberglas Canada, the Thermal Insulation Manufacturers Association (TIMA), the Refractory Ceramic Fiber Coalition, and J.M. Hughes, Tulane University School of Medicine. Data relevant to assessment of whether MMVF are “toxic” to human health obtained after the period of external peer review (i.e., May 1993) were not considered for inclusion.

To identify data relevant to the estimation of exposure of the general population to MMVF, searches were conducted on the following on-line databases: Environmental Bibliography (1973 to present, Environmental Studies Institute, California); ENVIROLINE (1971 to present, R.R. Bowker, New York); Pollution Abstracts (1970 to present, Cambridge Scientific Abstracts, Maryland); ELIAS (Environment Canada’s Departmental Library network and collection from Fisheries and Oceans Canada); and CISTIMON (monographs catalog of Canada Institute for Scientific and Technical Information). Information on exposure is also included in some of the previously mentioned sources, especially HSDB, TOXLINE, and MULTILIS.

Although review articles were consulted where considered appropriate, all original studies that form the basis for the determination of “toxic” under CEPA have been critically evaluated by staff of Environment Canada (effects on the environment) and Health Canada (effects on human health). The following officials contributed to the preparation of this report:

P. Doyle (Environment Canada)
G. Long (Health Canada)
M.E. Meek (Health Canada)
L. Shutt (Environment Canada)

As part of the review and approvals process established by Environment Canada, technical information relating to the assessment of effects to the environment was reviewed by W.J. Breitsman (Refractory Ceramic Fibre Coalition), A. Bowick

(Thermal Insulation Association of Canada), D. Friesen (Canadian Association of Man-Made Vitreous Fibre Manufacturers), S. Lethbridge (Owens-Corning Fiberglas Canada Inc.), G. Bates (Manville Canada Inc.), and J. Breed (Morgan Crucible Canada Inc.). Following circulation and external peer review of the draft health-related sections by Drs. P. Enterline and G. Marsh (University of Pittsburgh), Dr. A. Wells (Fiberglas Canada; Supporting Documentation only), Dr. D. Bernstein (consultant, Geneva, Switzerland), Dr. T. Hesterberg (Schuller International; Supporting Documentation only), Dr. V. Vu (Office of Prevention, Pesticides and Toxic Substances, U.S. Environmental Protection Agency), and Dr. R. Mast (Dow Corning Corporation, Michigan; Supporting Documentation only), they were approved by the Standards and Guidelines Rulings Committee of the Bureau of Chemical Hazards of Health Canada. The final Assessment Report was reviewed and approved by the Environment Canada/Health Canada CEPA Management Committee.

In this report, a synopsis that will appear in the *Canada Gazette* is presented. Section 2 is an extended summary of the technical information critical to the assessment. The assessment of whether MMVF are “toxic” under CEPA is presented in Section 3. Supporting Documentation, in which the technical information is presented in greater detail, has also been prepared.

Copies of this Assessment Report and the unpublished Supporting Documentation are available upon request from the:

Environmental Health Centre
Health Canada
Room 104
Tunney’s Pasture
Ottawa, Ontario, Canada
K1A 0L2

Commercial Chemicals
Branch
Environment Canada
14th Floor
Place Vincent Massey
351 Saint-Joseph Boulevard
Hull, Quebec, Canada
K1A 0H3

2.0 Summary of Information Critical to Assessment of "Toxic"

2.1 Identity, Properties, Production and Uses

In this report a "fibre" is considered to be an elongated particle with a length/width or aspect ratio of at least 3:1. Several types of manufactured inorganic fibres are distinguished based upon their use, physical properties, and chemical composition (TIMA, 1991). Some synonyms and trade names for MMVF considered in this report (insulation "wools", i.e., glass, rock and slag wools; special-purpose fibres, i.e., glass microfibres; textile fibres, i.e., continuous glass filaments; and aluminosilicate refractory ceramic fibres) are presented in Table 1.

Table 1
Some Synonyms and Trade Names for Man-made Vitreous Fibre Products[a]

Category	Synonym/Trade Name
Glass Wool	TEL fibreglass insulation Fiberglas® (trade name) mineral wool (in Europe and Asia)
Rock Wool	Rockwool® (trade name) basalt wool mineral wool
Slag Wool	mineral wool
Refractory Ceramic Fibres	refractory fibres ceramic fibres (some types only) Fiberfrax® bulk (trade name) Cerwool Kaowool
Glass Microfibres	Micro-Fiber® (trade name) fine fibres ultrafine fibres AAAA diameter fibres AAA diameter fibres AA diameter fibres A diameter fibres B diameter fibres

a. Principal sources: IARC (1988); WHO (1988).

Data on physical and chemical properties of MMVF are presented in Table 2. By definition, MMVF have an amorphous structure, i.e., their constituent atoms are not arranged in a regular lattice as in crystalline materials. Diameters of fibres in MMVF products vary depending upon their method of production. Average diameters are 3 to 10 μm for glass wool, 2 to 6 μm for rock and slag wools, 3 to 25 μm for textile fibres, 0.2 to 4 μm for special purpose fibres, and 1.2 to 3.5 μm for refractory ceramic fibres (RCF) [WHO, 1988; TIMA, 1991]. The variability of fibre diameters, measured as the coefficient of variation, can range from less than 10% for textile fibres to 50% or more for insulation wools (TIMA, 1991). Consequently, a significant proportion of fibres in insulation wool, as well as RCF and special-purpose fibre products, can have diameters of less than 3 μm (the upper limit for respirability). Most fibres in textile products, however, have diameters of more than 3 μm. Because of the processes used in their production, rock and slag wool, and refractory ceramic fibre products can contain large quantities (20 to 60% by weight) of rounded particulate material ("shot"), with diameters of 60 μm or more (Miller, 1982; TIMA, 1991).

Table 2
Physical and Chemical Properties of Some Man-made Vitreous Fibres[a]

Properties	Continuous Glass Filament	Glass Wool	Rock and Slag Wool	Refractory Ceramic Fibres	Glass Microfibres
Typical diameters[b] (μm)	3–25	3–10	2–6	1.2–3.5[c]	0.2–4
Length[d] (cm)	continuous	most > 3	–	–	–
Softening point (°C)[e]	680–860	650–700	–	1 740–1 800	650–850
Non-fibre particulate or shot (weight %)	none	traces	20–50	40–60	none
Time for total fibre dissolution[f] (years)	–	0.4	1.2–2.0	4.9–5.0	1.0–6.5

– No data available.
a. Data obtained from TIMA (1991), unless noted otherwise.
b. Average length-weighted values, except median length-weighted value for refractory ceramic fibres.
c Data from WHO (1988).
d. Values represent fibre lengths in commercial products and not ambient air.
e. Defined as the temperature at which viscosity of the fibres reaches $10^{7.6}$ poise.
f. Data from Scholze and Conradt (1987); measured *in vitro* based on loss of silicon from fibres of 1 μm diameter in flow-through experiments using simulated extracellular fluid (modified Gamble's solution) at a temperature of 37°C.

Data on the length of fibres in MMVF products are limited. Textile fibres are produced in continuous strands and it has been reported that most fibres taken from glass insulation wools were several centimetres long (TIMA, 1991). Because of their amorphous character, during handling (e.g., installation of insulation wools) MMVF tend to fracture across their length and become shorter (TIMA, 1991).

Many glass microfibres have been assigned a code used by the Manville Corporation (formerly Johns-Manville, or J-M). These JM codes refer only to the size of the fibres, particularly the diameter, and not to glass composition. Some products with a particular JM code have been manufactured from only one glass composition, while others have been made from several different compositions (TIMA, 1991).

SiO_2 is the principal constituent (comprising 40 to 70%) of most MMVF (TIMA, 1991). Lesser amounts of "intermediate oxides" (or stabilizers), such as Al_2O_3, TiO_2, and ZrO_2 and "modifiers" (or fluxes) such as MgO, Li_2O, BaO, CaO, Na_2O and K_2O, are also present. Compositions can vary considerably, depending in part upon the characteristics required in the final product. Stabilizers increase the chemical and heat resistance of fibres, whereas "modifiers" decrease fibre durability (TIMA, 1991). Glass wools and most special-purpose fibres contain relatively small amounts of stabilizers (0 to 7%; mostly Al_2O_3), and large quantities of fluxes (18 to 42%; mostly Na_2O and CaO). Refractory ceramic fibres, on the other hand, contain large amounts of stabilizers (45 to 55%; mostly Al_2O_3), but very little flux (< 1%).

MMVF are relatively stable in distilled water at 20°C (Forster, 1984), but dissolve in acidic or basic solutions (e.g., 2 N HCl, 2 N NaOH), and biological fluids (Spurny *et al.*, 1983). Because of their amorphous structure, dissolution rates for MMVF are typically 2 to 4 orders of magnitude greater than those for natural crystalline fibres such as asbestos (Scholze and Conradt, 1987; Law *et al.*, 1990).

Scholze and Conradt (1987) estimated that the time required for glass, rock and slag wools with diameters of 1 μm to dissolve completely in *in vitro* tests in simulated extracelluar fluid (modified Gamble's solution) at 37°C was 0.4 and 1.2 to 2.0 years, respectively (Table 2). Lifetimes for refractory fibres were predicted to be 4.9 to 5.0 years; those for special-purpose fibres were typically less than 2 years, although the estimated lifetime for one variety (E-glass containing 14.1% Al_2O_3) was 6.5 years. These data are generally consistent with results of earlier *in vitro* tests conducted by Forster (1984), Klingholz and Steinkopf (1984), and Leineweber (1984). Results of *in vitro* tests reported recently by Potter and Mattson (1991) indicate, however, that lifetimes of glass wool fibres with diameters of 1 μm can be as short as 0.04 years.

Because of their larger surface area, fine fibres tend to dissolve more quickly than coarser ones of the same composition (Spurny *et al.*, 1983; Scholze and Conradt, 1987). According to Scholze (1988) other factors that can affect the durability of fibres include their rate of cooling during formation, conditions and duration of storing, and the presence of binders or other coatings.

Binders are applied to the surface of most MMVF to hold fibres together; oils are used for dust suppression (WHO, 1988). Textile fibres may contain a sizing agent for lubrication. According to TIMA (1991), binders currently used are based mainly on phenol formaldehyde resins. During curing at elevated temperatures, binders are converted to an insoluble polymer containing very little formaldehyde. The binder content of insulation wool products is normally less than 5% by weight (IARC, 1988), but can be as high as 10% (TIMA, 1991).

For analysis, fibres are collected from ambient air on filters that are normally mounted in holders located in the breathing zones of potentially exposed subjects (WHO/EURO, 1985; Chatfield, 1983). Fibres can be separated from biological tissues by digestion or by ashing (Davies *et al.*, 1986); however, substantial losses of MMVF can occur during both storage (Law *et al.*, 1991) and digestion (Johnson *et al.*, 1984a) of tissues.

Concentrations of airborne MMVF can be measured on a total-mass basis, by comparing weight of filters before and after sampling; however, MMVF in ambient air are normally identified and counted using phase contrast optical microscopy (PCOM), scanning electron microscopy (SEM) or transmission electron microscopy (TEM) [Chatfield, 1983; WHO/EURO, 1985; IARC, 1988].

Limits of visibility that have been reported to be achievable in routine operation are 0.25 μm (WHO, 1988) to 1.6 μm (Balzer *et al.*, 1971) for PCOM, 0.05 μm (WHO, 1988) to 0.2 μm (TIMA, 1992) for SEM, and 0.005 μm (WHO, 1988; TIMA, 1992) for TEM. Application of PCOM is limited by its relatively low resolution and its consequent inability to detect fine (i.e., small-diameter) fibres (IARC, 1988). Interpretation of results of TEM analysis is complicated by lack of standardized sample preparation procedures, which can result in very large differences in results reported by different laboratories (Chatfield, 1983; Toft and Meek, 1986; WHO, 1988).

MMVF are produced from liquid melts at temperatures of 1 000 to 1 500°C (WHO, 1988). Glass filaments and glass wools can be produced from scrap glass or mixtures of raw materials such as sand, soda ash, borax, dolomite, and limestone (Ohberg, 1987; IARC, 1988). Rock wool plants use basalt, as well as limestone, clay, and feldspar, as raw materials (TIMA, 1991). Mine tailings are the source material for some slag wools produced in Canada (Camford Information Services Inc., 1993b). RCF are generally made by melting kaolin clay or a 50:50 mixture of Al_2O_3 and SiO_2,

but other oxides such as ZrO_2 are sometimes added to change the fibre properties. Fibres are typically made by rapid cooling of molten materials (to prevent crystallization) and one of the following fibre-forming processes: mechanical drawing (textile fibres only); flame attenuation; blowing; wheel centrifuging; rotary spinning; or the Downey (rotary disk) process (Ohberg, 1987; TIMA, 1991; Young, 1991).

In 1991 there were 14 Canadian plants producing insulation wools (glass, rock, and slag), one producing textile fibres (continuous glass filament), and one producing RCF (Camford Information Services Inc., 1993a, 1993b, 1993c, 1993d). Total production of MMVF in Canada in 1991 was estimated to be between 250 and 300 kilotonnes, down from a maximum of about 400 kilotonnes in the late 1980s (Camford Information Services Inc., 1993a,1993b, 1993c, 1993d). Glass wool accounted for about 70% of MMVF production in 1991, rock and slag wool 20%, textile (continuous filament) fibres 10%, and RCF less than 1%. Since there is little stockpiling of MMVF in Canada, and since cross-border trade is estimated to be either small or approximately offsetting (Camford Information Services Inc., 1993a, 1993b, 1993c, 1993d; TIMA, 1992), amounts of MMVF used annually in Canada are generally similar to those produced. Although glass microfibres are not known to be produced domestically, they are likely imported in small amounts in finished products such as high-efficiency filters.

According to Camford Information Services Inc. (1993c), nearly 90% of textile fibres (continuous glass filament) consumed in Canada are used to produce fibreglass-reinforced plastic composites. Continuous filament can also be used to reinforce cement, automotive tires, and roofing materials, and can be woven into protective apparel and industrial fabrics (Roberts, 1982; TIMA, 1991). Glass, rock, and slag wools are used mostly for thermal insulation. About 15% of the rock and slag wool produced in Canada is used for acoustic ceiling tile manufacturing (Camford Information Services Inc., 1993b). Because of their thermal resistance (Table 2), refractory ceramic fibres are used mainly for high-temperature furnace and kiln insulation, but other high-temperature applications include insulation for catalytic converters in automobiles, filtration, and gaskets and seals for expansion joints (WHO, 1988; IARC, 1988; TIMA, 1991). Glass microfibres are used in battery-separator media, for high-efficiency filtration, and as thermal and acoustical insulation in aircraft and space vehicles (TIMA, 1991).

2.2 Entry into the Environment

No information was identified on releases of MMVF in Canada, and data elsewhere were limited to emissions in stack gases from facilities manufacturing insulation wool and refractory ceramic fibres. MMVF are also released to ambient air during product handling, use (Marconi *et al.*, 1987), and disposal (TIMA, 1992), but no quantitative estimates of emissions resulting from these activities are available. Discharges in

liquid effluent from manufacturing plants are expected to be small because process waters exposed to fibres are typically recycled (Lethbridge, 1993; Folkard, 1993; Van Asseldonk, 1993; Eckert, 1993).

Concentrations of "respirable" fibres (length > 5 μm, diameter < 3 μm, length/width ratio ≥ 5/1) of up to 2.7 fibres/mL were determined recently by phase contrast optical microscopy in stack gases at several older glass, rock, and slag wool plants in the United States (TIMA/MIMA, 1990; Switala, 1993a, 1993b). Concentrations of total fibres in stack gases measured in 1991 using transmission electron microscopy at 4 RCF production plants and 3 RCF processing facilities ranged up to 14.1 fibres/mL (TIMA, 1992). Although higher concentrations (up to 850 fibres/mL) were reported at a fifth RCF manufacturing plant, emission-control systems at this facility have recently been upgraded (Maxim, 1993). Much lower concentrations of total fibres (up to 0.046 fibres/mL; measured by scanning electron microscopy) were reported by Tiesler (1983) in emissions from glass and rock/slag wool manufacturing plants in the Federal Republic of Germany in the late 1970s.

Tiesler (1983) estimated that an average of 0.0056 kg of fibres of all sizes, and 0.00025 kg of "respirable" fibres (length > 10 μm, diameter < 1 μm; measured by scanning electron microscopy), were released per tonne of insulation wool produced in Germany in the late 1970s. Limited data on emissions of glass fibres per unit weight manufactured in the United States indicated that about 0.00015 g of "respirable" (length > 5 μm, diameter < 3 μm, length/width ratio ≥ 5/1; measured by phase contrast optical microscopy) fibres are released per tonne of glass wool produced (Switala, 1993a). Based upon estimates of amounts of insulation wools manufactured in Canada, and an average emission factor of 0.0002 kg "respirable" fibres/tonne of wool produced (Tiesler, 1983; Switala, 1993a), emissions of "respirable" fibres in 1991 from Canadian glass and rock/slag wool plants were calculated to be 36 to 40 kg and 10 to 12 kg, respectively.

An average amount of approximately 0.018 kg of fibres of all sizes (measured by transmission electron microscopy) was released in stack gases per tonne of RCF manufactured in the United States in 1990 (TIMA, 1992). Based on the 500 to 2 000 tonnes of RCF produced in Canada in 1991 (Camford Information Services Inc., 1993d), it was estimated that 2 to 36 kg of fibres of all sizes were released from the one RCF manufacturing plant in Canada in 1991. No data were identified that would permit quantification of atmospheric releases from the one textile fibre (continuous filament) manufacturing plant operating in Canada.

2.3 Exposure-related Information

2.3.1 Fate

There is very little empirical information on the environmental fate of MMVF; however, based on their physical and chemical properties, most MMVF are expected to be relatively stable and to persist in the ambient environment.

After release in stack gases or during product handling, most MMVF are likely removed from air by gravitational settling. Finer, smaller-diameter particles will remain airborne longer, and be carried further from the source (Marconi *et al.*, 1987).

Gravitational settling and dissolution are expected to be the principal mechanisms of removal of MMVF from water (WHO, 1988). Dissolution will be faster in acidic than in neutral water, and the finest and least chemically resistant MMVF will be most affected. Settling fibres will accumulate in bottom sediment. Because of their amorphous structure, abrasion of MMVF during transport in air or water will normally result in breakage into successively shorter fragments (TIMA, 1991).

2.3.2 Concentrations

Identified data on concentrations of MMVF in environmental media are limited to several studies of outdoor and indoor air in Europe and the United States. Glass fibres have also been detected (but not quantified) in municipal-sewage sludge from 5 large cities in the United States (Bishop *et al.*, 1985).

In the identified studies of concentrations of MMVF in ambient air (Balzer *et al.*, 1971; Balzer, 1976; Hohr, 1985; Gaudichet *et al.*, 1989), the methods of sampling and analysis have varied considerably. Concentrations of glass fibres determined by analytical transmission electron microscopy ranged from 4×10^{-5} fibres/mL at one rural location to 1.7×10^{-3} fibres/mL in 1 out of 3 cities in the Federal Republic of Germany (Hohr, 1985). These levels were greater than concentrations measured by polarizing light microscopy at outdoor locations in Paris (2 to 4 fibres/m^3; 2×10^{-6} to 4×10^{-6} fibres/mL) [Gaudichet *et al.*, 1989] and near a large glass wool insulation plant in Newark, Ohio on 7 consecutive days in both June and December 1988 (generally less than 2×10^{-5} fibres/mL; maximum 1.4×10^{-4} fibres/mL) [Switala, 1993a, 1993b). Data from an earlier study in the San Francisco Bay area indicated that MMVF comprise less than 1% of the total mass of suspended particulate material in ambient air (Balzar *et al.*, 1971). Hohr (1985) estimated that glass fibres comprised only 0.3 to 5.0% of the total inorganic fibre content (measured by transmission electron microscopy) of outdoor air in Germany.

Transmission electron microscopy was also used to measure concentrations of RCF fibres of all sizes in ambient air near the boundaries of several manufacturing and processing plants, and a sanitary landfill operation in the United States in 1991 (TIMA, 1992). Arithmetic mean concentrations of RCF (based on 8 to 20 samples) ranged from 0.0013 to 0.0150 fibres/mL. The highest individual value reported was 0.0479 fibres/mL, measured near a manufacturing plant. Diameters of measured fibres were typically ® 0.5 μm (all were < 3 μm); lengths were typically about 10 μm (maximum was 75 μm).

In indoor air in 17 homes in the United Kingdom, airborne concentrations of fibres determined by transmission electron microscopy in living areas during disturbance of, or insulation with, MMVF-containing materials of various types were generally less than 0.01 fibres/mL, but ranged up to 0.04 fibres/mL on 2 occasions — when blown rock wool insulation was used to insulate a loft, and when one brand of glass fibre blanket insulation was being laid (Jaffrey *et al.*, 1989). Concentrations of airborne fibres determined by transmission electron microscopy in the living areas of 8 homes in the Netherlands during insulation with blown glass or rock wool were 50×10^{-3} to 400×10^{-3} fibres/mL. Levels of respirable fibres determined by phase contrast optical microscopy were 5×10^{-3} to 25×10^{-3} fibres/mL, with peaks up to 65×10^{-3} fibres/mL (van der Wal *et al.*, 1987). Concentrations greater than those in ambient air were still present the following day in some of the homes.

At 79 locations in Paris in buildings with sprayed MMVF-containing insulation, surfacing materials, or wall panels, mean concentrations of respirable fibres determined by phase contrast optical microscopy ranged from 63 to 225 fibres/m^3 (63×10^{-6} to 225×10^{-6} fibres/mL) [Gaudichet *et al.*, 1989]. In several studies conducted in Denmark, mean concentrations of respirable fibres in the air of randomly sampled buildings with various types of MMVF-containing materials determined by phase contrast optical microscopy ranged from 0.04×10^{-3} fibres/mL to 0.25×10^{-3} fibres/mL (Rindel *et al.*, 1987; Nielsen, 1987; Schneider and Lundqvist, 1986; Schneider, 1986). Schneider *et al.* (1990) measured dusts in representative public buildings and reported average concentrations of respirable MMVF ranging from 17 to 210 fibres/m^3.

2.4 Toxicokinetics

Factors that determine the deposition, retention, and clearance of respirable fibres in biological systems have been considered recently by a WHO-IPCS Task Group (WHO, 1993). The potential respiratory health effects of fibrous aerosols are a function of the internal dose to the target tissue, which is determined by airborne concentrations,

pattern and amount of exposure, fibre shape, diameter, length and electrostatic charge (all of which affect lung deposition and clearance), and biopersistence, which is a function largely of physical and chemical properties of the fibres[1].

Because much of the data on effects of MMVF has been obtained in studies in rodents, it is important to consider differences between rats and humans in the deposition of fibrous aerosols. The relative distribution between the tracheobronchial and pulmonary regions of the lung in rodents follows a pattern similar to human regional deposition during nose breathing for insoluble particles with mass median aerodynamic diameter[2] of less than 3 μm; however, while the deposition efficiencies of particles of 5 μm aerodynamic diameter or greater may be significant in humans, they will be extremely small in rodents. It is important, therefore, that a high proportion of fibres be respirable for the rodent in inhalation studies with rodents.

In the nasopharyngeal and tracheobronchial regions, fibres are generally cleared fairly rapidly via mucociliary clearance, whereas fibres deposited in the alveolar space appear to be cleared more slowly, primarily by phagocytosis and to a lesser extent via translocation and, possibly, by dissolution. Translocation refers to the movement of the intact fibre after initial deposition at foci in the alveolar ducts, and on the ciliated epithelium at the terminal bronchioles. These fibres may be translocated via ciliated mucous movement up the bronchial tree and removed from the lung or may be moved through the epithelium with subsequent migration to interstitial storage sites or along lymphatic drainage pathways or transport to pleural regions. Fibres short enough to be fully ingested are thought to be removed mainly by phagocytosis by macrophages, whereas longer fibres may be partly cleared at a slower rate, either by translocation to interstitial sites, breakage, or dissolution. A higher proportion of longer fibres is, therefore, retained in the lung. Indeed, negative results in positive controls exposed to various forms of asbestos in early inhalation bioassays for MMVF may have been attributable to the majority of fibres being less than 5 μ**m in length.**

1. The term biopersistence refers to the ability of a fibre to stay in the biological environment where it was introduced. The term is of particular use in inhalation and intratracheal installation studies, because a large percentage of the fibres that reach the lung are removed by pulmonary clearance and relatively few are retained (persist). The length of time that fibres persist in the tissue is also a function of their durability, which is directly related to their chemical composition and physical characteristics. The term solubility, as used here, relates to the behaviour of fibres in various fluids. In general, the term solubility is more appropriate for use in *in vitro* than in *in vivo* studies, because, in tissue, the degradation of fibres is a function of phenomena other than just their solubility. While the concept of biopersistence is important, quantitative procedures for evaluation of this parameter have not been established.

2. The ratio of fibre diameter to aerodynamic diameter is approximately 1:3.

Dissolution of inhaled MMVF depends both on chemical composition and fibre length. The results of studies of biopersistence in lung tissue *in vivo*, and solubility in physiological fluids *in vitro*, have varied widely for different MMVF and within each of the types of MMVF. (Additional discussion of the solubility of MMVF is included in Section 2.1.) It is difficult, therefore, to draw overall conclusions concerning the persistence of the various types of MMVF in biological tissues, although in *in vivo* studies, the order of biopersistence has generally been refractory ceramic fibre > rock wool > slag wool > glass fibres (Johnson *et al.*, 1984b; Morgan and Holmes, 1984a, 1984b; Hammad, 1984; Bellmann *et al.*, 1987). Results of recent studies indicate that biological response may correlate well with biopersistence in the lung (McClellan *et al.*, 1992).

2.5 Effects-related Information

2.5.1 Experimental Animals and In Vitro

The toxicological studies considered most relevant to this assessment are those in which animals have been exposed by inhalation and for which there has been adequate and well-documented exposure of the lungs to fibres to which humans may be exposed, in animals observed for sufficient periods; these studies are emphasized in the following sections. Results of studies in which fibrous materials have been administered intratracheally (by passing natural defence mechanisms of the lung), or through introduction into body cavities, and *in vitro* investigations, are considered primarily as supporting data (for additional discussion, see Supporting Documentation).

Fibrogenicity

With the exception of one study in which interstitial fibrosis was observed in the lungs of rats exposed to ceramic fibre (Davis *et al*., 1984), in the majority of the early inhalation studies in animal species there has been little or no evidence of fibrosis of the lungs in a range of animal species exposed to various types of MMVF at concentrations up to 100 mg/m^3 for periods ranging from 2 days to 24 months (McConnell *et al*., 1984; Wagner *et al*., 1984; Smith *et al*., 1984; Goldstein *et al*., 1984; Mitchell *et al*., 1986; Muhle *et al*., 1987; Smith *et al*., 1987; Morisset *et al*., 1979; Morrison *et al*., 1981; Lee *et al*., 1981; Johnson and Wagner, 1980; Gross *et al*., 1970; Miller, 1980; Pickrell *et al*., 1983). In most studies, the tissue response was confined to accumulation of pulmonary macrophages, many of which contained the fibres. In all cases, the severity of the tissue reaction was much less than that in animals exposed to equal masses (but higher airborne-fibre concentrations) of chrysotile or crocidolite asbestos.

In the more recently conducted TIMA multi-dose studies, in which well-characterized size selected fibres were delivered directly to the breathing zone of the animals, after 3 months of exposure to 3, 16, or 30 mg/m^3 rock wool[3] there was a dose-dependent increase in cellularity and fibrosis in 1 of 6 rats in the high-dose group; progression was minimal at 6 months, with fibrosis being present in 2 of the 6 animals in the high-dose group (Bunn *et al.*, 1993; TIMA, 1993). There was no progression at 12 months; however, after 18 and 24 months of exposure, there was minimal fibrosis in the lungs of animals in the mid- and high-dose groups. Fibre concentrations in the positive control group and lung-tissue fibre burdens in any of the exposed groups were not reported. Fibrosis has also been reported in a limited study in which hamsters were exposed intratracheally to "rock wool used as a spraying material in insulation" (Adachi *et al.*, 1991).

After 3 months of exposure to slag wool[3], there was a dose-dependent increase in cellularity that progressed minimally at 6 months at the 2 higher doses and for which there was little change at 12, 18, and 24 months (Bunn *et al.*, 1993; TIMA, 1993). In comparison, irreversible fibrotic changes were observed as early as 3 months in the crocidolite-exposed positive controls. Fibre concentrations in the positive control group and lung tissue fibre burdens in any of the exposed groups were not reported.

In rats exposed to fibres of glass wool (Manville 901) or CertainTeed B size selected to be largely rat respirable processed from commercial insulation, there was minimal non-neoplastic pulmonary response. After 3 months of exposure, there was a dose-dependent increase in reversible cellularity in the mid- and high-dose groups with minimal progression at 6 and 24 months. There was some indication of regression of the cellular changes between termination of exposure (24 months) and the terminal sacrifice; this reversibility was more apparent in animals in a recovery protocol that were exposed to 30 mg/m^3 (equivalent to the high-dose in the multi-dose protocol) of fibrous glass for 52 weeks and held without further exposure for 52 weeks (Hesterberg *et al.*, 1993; Bunn *et al.*, 1993). In animals exposed to the 2 forms of glass wool, the lung-fibre burden ranged from 0.24×10^5 in the low-dose group to 5.03×10^5 fibres/mg (dry lung weight) in the high-dose group. The lung-fibre burden in chrysotile-exposed controls was 28.1×10^5 fibres/mg dry lung.

In most intratracheal studies conducted to date (Pott *et al.*, 1984a, 1987; Feron *et al.*, 1985) but not all (Pickrell *et al.*, 1983; Wright and Kuschner, 1977; Smith *et al.*, 1987; Renne *et al.*, 1985), glass wool and glass microfibres have not induced fibrosis.

In the TIMA studies, groups of rats were also exposed to 4 different types of RCF (kaolin, zirconia, high purity kaolin, and after service, a kaolin-based ceramic fibre containing 27% crystalline silica that had been previously exposed to high

3. Final results for 24-month sacrifices available only.

temperature); hamsters were exposed to kaolin RCF fibres. There was pulmonary fibrosis in both the hamsters and rats exposed to all varieties of RCF beginning at 9 months. In an additional multi-dose study in rats with kaolin RCF fibres (Mast *et al*., 1993; Bunn *et al*., 1993), though there was a dose-dependent increase in cellularity only at 3 months, this had progressed to minimal fibrosis at 6 months in the high-dose group. At 12 and 18 months, animals in both the mid- and high-dose groups had fibrosis, with additional progression at 24 months. Lung burdens were increased in a dose-related manner, and after 24 months ranged from 6 to 28 × 10^4 fibres/mg dry lung. Based on pooling of these data with the results from the single-dose study in which rats were exposed to 30 mg/m^3, there was a clear relationship between dose and fibrotic lung disease in rats with no fibrosis at the low dose (3 mg/m^3) and fibrosis at the mid and high doses (9, 16, and 30 mg/m^3).

One month following intratracheal administration of “Fiberfrax” (an aluminum silicate RCF) to rats, there were significant granulomatous reactions and early fibrosis. The degree of pulmonary reactivity for this material was considered to be less than that for UICC chrysotile B but greater than that for short chrysotile (Lemaire *et al*., 1989).

Carcinogenicity

Rock Wool

In inhalation studies reported to date, investigations of the carcinogenicity of rock wool have been limited to earlier separate investigations in 2 strains of rats exposed to single concentrations (Le Bouffant *et al*., 1987; Wagner *et al*., 1984); preliminary results[4] are also available for the more recent multiple-dose study in rats, conducted by TIMA (Bunn *et al*., 1993; TIMA, 1993).

Significant increases in pulmonary tumour incidence were not observed in the earlier studies conducted by Le Bouffant *et al*. (1987) and Wagner *et al*. (1984). In the more recent TIMA studies, Fischer 344 rats were exposed to 3 concentrations of rock wool for 2 years (Bunn *et al*., 1993; TIMA, 1993). The incidence[5] of pulmonary tumours at 24 months (all adenomas) was 1/45, 0/42, and 3/45, in animals exposed to 3 mg/m^3, 16 mg/m^3, and 30 mg/m^3, respectively, compared to 2/44 in animals exposed to filtered air. There were, however, few tumours in the positive control group exposed to 10 mg/m^3 of crocidolite at 24 months[5] (2/31: 1 adenoma, 1 carcinoma). Fibre concentrations in the positive control group and lung-tissue fibre burdens in any of the exposed groups were not reported.

4. Final results for 24-month sacrifices and preliminary results only for terminal sacrifice.

5. Based on preliminary results from the terminal sacrifice, tumor incidence was 3 pulmonary adenomas in 128 air exposed controls, 4 pulmonary adenomas in 119 animals in the low-dose group, 3 pulmonary adenomas and 1 carcinoma in 119 animals in the mid-dose group, and 5 pulmonary adenomas in 118 animals in the high-dose group. In 103 crocidolite-exposed controls (exposed for 44 weeks), there were 11 pulmonary adenomas, 8 carcinomas and 1 mesothelioma (Kamstrup, 1993).

There were no lung tumors in Syrian hamsters receiving 2 mg "rock wool used as spraying material in construction" intratracheally, once per week for 5 weeks and examined at 2 years in a limited study; however, the mean diameter of the administered fibres was very large (6.13 μm) [Adachi *et al*., 1991]. Increases in tumour incidence have been observed following intrapleural or intraperitoneal administration of rock wool (Wagner *et al*., 1984; Maltoni and Minardi, 1989; Pott *et al*., 1984b, 1987).

Slag Wool

For slag wool, there has been one long-term inhalation single-dose study in both rats and hamsters (Smith *et al*., 1987), and, more recently, a multiple-dose study in rats conducted by TIMA, for which only preliminary results are available[4] (TIMA, 1993; Bunn *et al*., 1993).

There were no increases in pulmonary tumors in Osborne-Mendel rats or Syrian hamsters in the earlier study reported by Smith *et al*. (1987); notably, however, there were few or no tumours in the positive control groups exposed to crocidolite, for which 95% of the fibres were ® 5 μm in length.

In the TIMA studies, in Fischer 344 rats exposed to slag wool for 2 years, the incidence[6] of pulmonary adenomas at 24 months was 1/44, 0/41, and 3/46 in groups exposed to 3 mg/m^3, 16 mg/m^3, and 30 mg/m^3, respectively, compared to 2/44 in the control group receiving filtered air (Bunn *et al*., 1993; TIMA, 1993). There were, however, few tumours in the positive control group exposed to 10 mg/m^3 of crocidolite (2/31: 1 adenoma, 1 carcinoma)[6]. Fibre concentrations in the positive control group and lung-tissue fibre burdens in any of the exposed groups were not reported.

Small increases in tumour incidence have been observed following intrapleural or intraperitoneal administration of slag wool (Pott *et al*., 1984b, 1987).

Glass Wool

In available studies, 2 strains of rats have been exposed to glass wool, both with (Wagner *et al*., 1984) and without resin (Le Bouffant *et al*., 1987; Wagner *et al*., 1984). Rats and hamsters have also been exposed to blowing-insulation glass wool with silicone lubricant and to building-insulation glass wool with phenol-formaldehyde

6. Based upon preliminary results from the terminal sacrifices, tumor incidence was 3 pulmonary adenomas in 128 air exposed controls, 1 pulmonary adenoma and 1 carcinoma in 122 animals in the low-dose group, 0 pulmonary tumors in 121 animals in the mid-dose group and 5 adenomas in 120 animals in the high-dose group. In 103 crocidolite-exposed controls (exposed for 44 weeks), there were 11 pulmonary adenomas, 8 carcinomas and 1 mesothelioma (Kamstrup, 1993).

binder (Smith *et al*., 1987); in all but one of these investigations, animals have been exposed to single concentrations only (Smith *et al*., 1987). In an additional study, rats and monkeys were exposed to several poorly characterized varieties of glass wool insulation (Mitchell *et al*., 1986). More recently, in the studies conducted for TIMA, rats have been exposed to multiple doses of size-selected subsets of both Manville 901 and CertainTeed B glass wool fibre (Bunn *et al*., 1993; Hesterberg *et al*., 1993).

There were no significant increases in pulmonary tumour incidence in exposed animals in the earlier studies conducted by Le Bouffant *et al*. (1987), Wagner *et al*. (1984), and Smith *et al*. (1987), although it should be noted that in the latter study, results were also negative in the positive control group exposed to crocidolite, a large proportion of which contained only short fibres. In the more recent TIMA studies, in Fischer 344 rats exposed to size-selected subsets of Manville 901 glass wool fibre, lung tumour incidence was 0% (no tumours), 0.8% (1 adenoma) and 5.9% (6 adenomas and 1 carcinoma) in groups exposed to 3 mg/m^3, 16 mg/m^3 and 30 mg/m^3, respectively, compared to 3.3% (3 adenomas and 1 carcinoma) in controls exposed to filtered air (Bunn *et al*., 1993; Hesterberg *et al*., 1993). In the positive control group exposed to 10 mg/m^3 (fibre number concentration not specified) of chrysotile asbestos, the incidence of pulmonary tumours was 17.4% (6 adenomas and 6 carcinomas; 1 mesothelioma). In exposed animals, the lung fibre burden ranged from 0.24×10^5 in the low-dose group to 2.88×10^5 fibres/mg (dry lung weight) in the high-dose group. The lung fibre burden in chrysotile-exposed controls was 28.1 ⎫10^5 fibres/mg dry lung.

In the same strain of rats exposed to similar concentrations of size-selected subsets of CertainTeed B glass wool fibres in the TIMA studies, the incidences of pulmonary tumours were 3.4% (3 adenomas, 1 carcinoma), 7.5% (6 adenomas, 3 carcinomas), and 2.7% (3 adenomas), compared to 3.3% (3 adenomas and 1 carcinoma) in controls exposed to filtered air. In the positive control group exposed to 10 mg/m^3 (fibre number concentration not specified) of chrysotile asbestos, the incidence of pulmonary tumours was 17.4% (6 adenomas and 6 carcinomas; 1 mesothelioma). In animals exposed to glass wool, the lung fibre burden ranged from 0.48×10^5 in the low-dose group to 5.03×10^5 fibres/mg (dry lung weight) in the high-dose group. The lung fibre burden in chrysotile controls was 28.1×10^5 fibres/mg dry lung (Bunn *et al*., 1993; Hesterberg *et al*., 1993). For both of the glass wool fibres, there were no statistically significant differences in tumour incidence in any of the exposure groups when compared to the air controls.

A low incidence of mesotheliomas has been induced by glass wool in a few studies involving intrapleural or intrathoracic administration (Stanton *et al*., 1977, 1981; Wagner *et al*., 1984); such results have not been confirmed in other investigations (Wagner *et al*., 1973, 1976).

Glass Microfibres

There have been numerous inhalation studies in which animals have been exposed to small-diameter glass fibres (described by most investigators as “glass microfibres”). These include studies in 3 strains of rats and in Syrian hamsters exposed to JM 100 glass microfibres (Le Bouffant *et al*., 1987; McConnell *et al*., 1984; Wagner *et al*., 1984; Smith *et al*., 1984), and one investigation in one strain of rats exposed to JM 104 glass microfibres (Muhle *et al*., 1987). In a limited study, baboons were also exposed to a mixture of JM 102 and 104 glass microfibres (Goldstein *et al*., 1984). With the exception of the study by Smith *et al*. (1984), animals were exposed to a single-dose level in all cases.

There have been no significant increases in pulmonary tumour incidence in animals exposed by inhalation to glass microfibres in studies conducted to date. It should be noted, however, that in the study by Smith *et al*. (1987), results were also negative in the positive control group exposed to crocidolite, a large proportion of which contained only short fibres. Moreover, there were few or no tumours in positive control groups exposed in the investigation of Muhle *et al*. (1987) to crocidolite or chrysotile.

Similar to the results obtained in inhalation studies, there have been no statistically significant increases in lung tumour incidence following intratracheal administration of glass microfibre in most studies conducted to date (Smith *et al*., 1987; Renne *et al*., 1985; Feron *et al*., 1985; Adachi *et al*., 1991); however, there have been some contradictory observations from one laboratory (Pott *et al*., 1984a).

Following intrapleural or intraperitoneal administration of glass microfibres, there have been increases in tumour incidence, which have been a function largely of fibre size distribution and durability. Long, thin fibres — i.e., those with diameters < 1.5 μm and lengths > 4 μm — are the most potent (Wagner *et al*., 1984; Muhle *et al*., 1987; Smith *et al*., 1987; Pott *et al*., 1984b, 1987, 1989).

In *in vitro* studies, a variety of fibrous materials delayed mitosis in human fibroblasts and CHO-K_1 cells, with the order of potency in CHO-K_1 cells being chrysotile > fine glass (JM 100) > crocidolite > coarse glass (JM 110). JM 100 glass microfibres have also induced chromosomal breaks, rearrangements, and polyploidy in CHO-K_1 cells, while JM 110 glass fibres had no effect (Sincock *et al*., 1982). In addition, cell transformation in Syrian hamster embryo cells (SHE) has also been induced by Code 100 glass microfibres (Mikalsen *et al*., 1988; Oshimura *et al*., 1984), as have cytogenetic abnormalities (Oshimura *et al*., 1984).

Continuous Filament

The carcinogenic potential of continuous filament glass fibres has been investigated in only one study following intraperitoneal administration (Pott *et al*., 1987). Although no increases in tumour incidence were observed, the diameters of these fibres were well above the normal limits for use in this assay.

Refractory Ceramic Fibres

The carcinogenicity of RCF has been investigated in 2 inhalation studies in 2 strains of rats and in hamsters (Davis *et al*., 1984; Smith *et al*., 1987). Preliminary results of investigations conducted for TIMA of the effects of RCF on hamsters (1 RCF type) and rats (4 RCF types) and the results of a multiple-dose study in rats have also been reported (Glass *et al*., 1992; Mast *et al*., 1993; Bunn *et al*., 1993).

In Wistar rats exposed for 12 months to 10 mg/m^3 ceramic (aluminum silicate) fibres, Davis *et al*. (1984) reported “relatively large numbers of pulmonary neoplasms”, with lung tumours developing in 8/48 animals. In 4 of the animals, however, the tumours were malignant histiocytomas (in addition to 1 adenoma and 3 adenocarcinomas), which have not generally been associated with exposure to asbestos. There was also one peritoneal mesothelioma in another animal in the exposed group. (It should be noted that the non-fibrous content of the exposure aerosol in this investigation was relatively large.)

In an additional inhalation study, in 70 hamsters exposed to ceramic aluminum silicate fibre (Smith *et al*., 1987), there was one malignant mesothelioma; however, there were no other primary lung tumours in hamsters surviving the exposure period or in similarly exposed rats in this study. The results for the positive controls exposed to crocidolite containing a large proportion of short fibres in this investigation were essentially negative, however. The lung tissue fibre burden in the ceramic fibre-exposed animals was 2.18×10^4 fibres/mg (dry weight) in rats and 0.86×10^4 in hamsters, compared to 3.87×10^5 and 7.31×10^5 fibres/mg in rats and hamsters, respectively.

In the TIMA studies, groups of Fischer 344 rats were exposed to 4 different types of RCF (kaolin, zirconia, high purity kaolin, and after service, a kaolin-based ceramic fibre containing 27% crystalline silica that had been previously exposed to high temperature) [Glass *et al*., 1992; Hart *et al*., 1992; Bunn *et al*., 1993]; Syrian hamsters were exposed to kaolin RCF fibres (Hesterberg *et al*., 1991; Mast *et al*., 1992). Hamsters exposed to 30 mg/m^3 kaolin-based RCF (30 mg/m^3) for 18 months developed malignant mesotheliomas in 43 of 102 animals, but no pulmonary tumours, compared to no lung tumours or mesotheliomas in air-exposed controls (Hesterberg *et al*., 1991; Mast *et al*., 1992). It should be noted that the results in the positive control group in this study exposed to a somewhat lower mass concentration (10 mg/m^3) of

chrysotile were negative; no tumours were observed. Lung fibre burdens in RCF-exposed hamsters were not reported, but were 2.4×10^5 fibres/mg dry lung in chrysotile-exposed animals (Mast, 1993).

In rats exposed to 30 mg/m^3 (the maximum tolerated dose) kaolin-based RCF, there was a significant increase in pulmonary tumours compared to air controls, with 13.0% incidence (8 adenomas and 8 carcinomas; 2 mesotheliomas). For animals exposed to the same concentration of the zirconia-based and high-purity, kaolin-based RCFs, the increase in pulmonary tumours was also significant (7.4% incidence of pulmonary tumours: 4 adenomas and 5 carcinomas; 3 mesotheliomas for the zirconia-based fibre; 15.7%: 10 adenomas and 9 carcinomas; 2 mesotheliomas for the high-purity, kaolin-based fibre). In rats exposed to "after service" kaolin-based RCF, the lung tumour incidence was 3.4% (2 adenomas and 2 carcinomas; 1 mesothelioma). In air-exposed controls, the lung tumour incidence was 1.5% (2 adenomas); in the positive control group exposed to 10 mg/m^3 chrysotile (fibre number concentration not specified), the lung tumour incidence was 18.5% (7 adenomas and 6 carcinomas). The lung fibre burden in rats exposed to the kaolin-based RCF was 3.7×10^5, compared to 189×10^5 fibres/mg dry lung in the positive control group.

A multi-dose study was also conducted, with rats exposed for 2 years to 3, 9, or 16 mg/m^3 of the kaolin-based RCF (Mast *et al*., 1993; Bunn *et al*., 1993). Based on "preliminary" assessment, the lung tumour incidence at 3 mg/m^3 was 1.6% (2 adenomas); at 9 mg/m^3, it was 3.9% (4 adenomas and 1 carcinoma). At 16 mg/m^3, pulmonary tumour incidence was 1.6% (1 adenoma and 1 carcinoma). The incidence of pulmonary tumours in positive controls exposed to chrysotile was 13/69 (7 adenomas and 6 carcinomas; 1 mesothelioma) [Hesterberg *et al*., 1993]; in air-exposed animals, it was 0.8% (1 adenoma). Lung burdens were increased in a dose-related manner, and after 24 months ranged from 6 to 28×10^4 fibers/mg dry lung. Based on pooling of these data with the results from the single-dose study in which rats were exposed to 30 mg/m^3, there was a clear dose response, with the incidences of lung cancer and mesothelioma being significant at the highest (MTD) concentration (Bunn *et al*., 1993).

Following intratracheal administration of 2 mg of aluminum silicate ceramic fibre once a week for 5 weeks, the mean lifespan of hamsters was significantly reduced (Smith *et al*., 1987); however, there were no pulmonary tumours in the hamsters or in rats receiving aluminum silicate ceramic fibre on a similar schedule. Eight percent of rats and 74% of hamsters similarly exposed to crocidolite developed pulmonary tumours.

Vu (1992) reported "preliminary results" of a TIMA study in which 2 mg of each of 4 types of RCF was intratracheally instilled in rats. All 4 RCF (kaolin, high purity, zirconia, after service) induced lung tumors (3.7 to 6.5%), and pulmonary and pleural

fibrosis. There was a pleural mesothelioma in 1 of 107 rats exposed to zirconia-based RCF. Positive controls exposed to 0.66 mg chrysotile asbestos also developed lung tumors (14.5%) but there were no mesotheliomas. None of the 118 negative controls had any respiratory tumors. No other information was provided in the secondary account of this study.

The induction of tumours by RCF has been examined in at least 5 investigations involving intrapleural or intraperitoneal administration (Davis *et al*., 1984; Smith *et al*., 1987; Pott *et al*., 1989; Wagner *et al*., 1973; Pigott and Ishmael, 1992). In general, chrysotile and crocidolite have been more potent than equal masses of RCF in inducing tumours following intrapleural or intraperitoneal administration, with the exception that in one study (Smith *et al*., 1987), abdominal mesotheliomas were observed in 83% of rats receiving a single intraperitoneal dose of 25 mg of RCF (mean diameter = 1.8 μm), compared to 80% in rats exposed in a similar fashion to the same mass of crocidolite. For similar fibre numbers, however, preliminary results of a relevant investigation indicate that the potency of chrysotile and ceramic fibre may be similar (Pott *et al*., 1989). Tumour incidence in rats administered 202×10^6 (0.25 mg) UICC Canadian chrysotile fibres (> 5 μm in length, < 0.3 μm in diameter with aspect ratio > 5:1) was 68%, compared to 70% in animals administered a similar dose on a fibre number basis of ceramic wool (Fiberfrax) [173×10^6 fibres, 0.45 mg].

Hart *et al*. (1992) have reported the effects of RCF upon inhibition of cell proliferation, colony-forming efficiency, and the induction of micronuclei and polynuclei in Chinese hamster ovary cells, using the same 4 size-selected RCF to which animals were exposed in the TIMA studies (i.e., kaolin, zirconia, high-purity kaolin, and after service). Positive controls included both crocidolite and chrysotile. The relative toxicities for the RCF were consistent in the 3 *in vitro* assays based on concentration in $\mu g/cm^2$; in each case, the after service fibre was the least toxic, the zirconia fibre was intermediate, and the kaolin and high-purity kaolin fibres were the most toxic. In all 3 assays, crocidolite was more toxic than the RCF. In the inhibition of cell proliferation and micronuclei/polynuclei assays, chrysotile was more toxic then crocidolite. Chrysotile was not included in the colony-forming efficiency assay.

When the concentration of RCF was expressed as number of fibres per cm^2, relative toxicities were similar, although the variation between the kaolin and high-purity kaolin was increased. The authors also reported a good correlation between the results of these *in vitro* studies and those *in vivo* in the TIMA inhalation studies.

2.5.2 Humans

Non Malignant Respiratory Disease

The respiratory effects of rock or slag wool have been investigated in a limited number of cross-sectional studies (Carpenter and Spolyar, 1945; Stahuljak-Beritic *et al*., 1982; Malmberg *et al*., 1984; Petersen and Sabroe, 1991; Cavalleri *et al*., 1992; Hughes *et al*., 1993). By far, the majority of such studies have been conducted in populations exposed to glass wool (Wright, 1968; Nasr *et al*., 1971; Utidjian and Cooper, 1976; Hill *et al*., 1973, 1984; Moulin *et al*., 1987; Lockey, 1987; Saracci and Simonato, 1982; Sixt *et al*., 1983; Kilburn *et al*., 1992; Hughes *et al*., 1993; Clausen *et al*., 1993). In several additional studies, workers have been exposed to unspecified MMVF (Engholm and Von Schmalensee, 1982; Ernst *et al*., 1987) and there is one investigation each of workers involved in the production of continuous filament (Finnegan *et al*., 1985) and ceramic fibre (Lemasters *et al*., 1991).

For most MMVF, there has been little convincing evidence of non-malignant respiratory disease (NMRD) in MMVF production workers. In the most extensive cross-sectional study of workers in 2 mineral and 5 fibrous-glass plants, there was an increase in the prevalence of small opacities in exposed workers (23/1 435; 1.6%) compared to unexposed referent workers (2/305; 0.7%) [Hughes *et al*., 1993]. Although 93% of the exposed workers with small opacities worked at the 2 plants with the highest exposures to fine fibres, on a second reading the prevalence of opacities was lower and not significantly different than that in pre-employment films; there was also no relation between opacities and exposure indices. The authors concluded that there were “no adverse clinical, functional or radiographic signs of effects of exposure” to the MMVF-exposed workers. Although Kilburn *et al*. (1992) reported “evidence of pneumoconioses” (fine irregular opacities, pleural plaques, or both) on chest radiographs in workers exposed to fibrous glass (in appliance-manufacturing workers with more than 20 years employment), these conclusions are not supported by the information presented in the published account of the study and have not been confirmed in more extensive and better-documented studies (e.g., Hughes *et al*., 1993).

Lemasters *et al*. (1991) reported preliminary results of an industry-wide study, in which the respiratory health of 1 030 workers manufacturing RCF has been examined. Of the 23 of 1 030 workers with pleural changes, 21 had pleural plaques. Of 70 employees with more than “20 years since first [RCF] production job”, 8 had pleural changes. Of 29 workers with more than 20 years duration in RCF production, 6 had pleural changes. Based on regression modelling, pleural changes were significantly related to “time since first [RCF] production job”, as well as to time since first exposure to asbestos and duration of exposure to asbestos. When 3 cases and 5 non-cases with significant asbestos exposure were omitted in the analyses, there was still a

significant relationship between the time since first RCF production job and pleural changes. A case-control study to further investigate the relationship between exposure to asbestos and RCF and pleural changes is underway.

There has been little evidence of NMRD in MMVF production workers in analytical epidemiological investigations (i.e., cohort and case-control) conducted to date, including 2 large cohort studies in 16 661 workers in 17 rock/slag wool, glass wool, and continuous glass filament production plants in the United States (Marsh *et al*., 1990) and in 21 967 workers in 13 such facilities in 7 European countries (Simonato *et al*., 1987). Although there was a significant increase in NMRD for workers with > 20 years since first employment in one mineral wool production plant in the U.S. study (SMR = 189.0, based on 14 observed deaths), there was no excess overall in this sector (SMR = 135 for workers with > 20 years since first employment, based on 32 observed deaths) [Marsh *et al*., 1990]. In 135 026 construction workers exposed intermittently to various types of MMVF in Sweden (Engholm *et al*., 1987) and in smaller studies of distinct cohorts of 2 557 workers in a glass wool production facility in Ontario (Shannon *et al*., 1987), 1 465 glass filament workers in Ontario (Shannon *et al*., 1990), and 2 807 Swedish workers exposed to MMVF in the prefabricated-housing industry (Gustavsson *et al*., 1992), there were no significant increases in NMRD.

With the exclusion of isolated case reports of respiratory symptoms and dermatitis associated with exposure to MMVF in the home and office environments, and 2 limited cross-sectional studies of ocular and respiratory effects in offices and schools, adverse effects on the general population have not been reported. For example, Newball and Brahim (1976) attributed respiratory symptoms in members of a family to fibrous glass exposure from a residential air-conditioning system. Dermatitis has been observed in individuals exposed to disturbed MMVF insulation in office buildings (Verbeck *et al*., 1981; Farkas, 1983) and to clothing contaminated during laundering with MMVF-containing materials (Lucas, 1976).

Carcinogenicity

The most informative results for assessing the potential carcinogenicity of MMVF are those derived from the large U.S.[7] and European cohort studies mentioned above (Marsh *et al*., 1990; Simonato *et al*., 1987) and to a lesser extent from smaller cohort studies of glass wool (Shannon *et al*., 1987) and glass filament (Shannon *et al*., 1990)

7. Results of Poisson regression modelling of data for the large U.S. cohort indicated that although the overall SMR for respiratory cancer was significantly elevated in the total cohort, there was no significant pattern of risk associated with any indicator of exposure, including process, plant, or duration of exposure.

production workers in Canada. The relevant results of these studies are presented by fibre type in Table 3 and are restricted to SMRs calculated on the basis of comparison with local rates (with the exception of the Canadian studies, for which provincial rates were used).

In the U.S. study, there was a statistically significant increase in deaths from respiratory cancer in workers in the 6 plants that produced slag wool or rock wool/slag wool (Marsh *et al*., 1990). The SMR was 135.6, based upon 73 observed deaths from this cause. There was no clear trend in respiratory cancer deaths with time since first exposure nor with duration of employment or estimated cumulative exposure.

Marsh *et al*. (1990) noted that statistically significant inter-plant differences in SMRs for mineral wool workers might be related to the use of slag versus rock in the production of fibres, although they indicated that the exposure to fibres was no higher in slag versus rock wool plants[8]. The slag was predominantly from a copper smelter, a lead smelter, steel mills and iron foundries, and could potentially contain many carcinogenic contaminants, including arsenic and various metals. The authors concluded: “Thus, the cancer excesses could be in part due to exposure to these contaminants in the plants.”

The results of several additional studies are relevant to assessment of the possible role of confounding exposures in the increase in respiratory cancer observed in mineral wool workers in the U.S. study. In a case-control study of workers in a previous update of the large U.S. cohort (Enterline and Marsh, 1984) who had died of lung cancer between January 1950 and December 1982 and a 4% random sample of workers stratified by plant and year of birth, there was a significant relationship between estimated cumulative exposure and respiratory cancer in mineral wool, but not for fibrous glass workers after control for smoking, based on telephone interviews of workers or their families (Enterline *et al*., 1987). In a case-control study of 55 lung cancer cases (total = 61) in 4 841 men with greater than 1 year of employment in 9 slag wool plants (4 of which were included in the large U.S. cohort) and 98 individually matched controls (for plant, potential for exposure, race, and age), there were no significant differences between cases and controls in duration of or cumulative exposure (Wong *et al*., 1991). Smoking was considered to be responsible for the increase in mortality from lung cancer, which increased with increasing pack-years. Based on analyses of lung-tissue burdens, McDonald *et al*. (1990) reported that the amosite content of the lungs was high in 4 of 6 workers from one of the mineral wool plants in the large U.S. cohort (plant no. 17).

8. Of the 6 mineral wool plants in the large U.S. study, 4 used slag exclusively and the remaining 2 had used both rock and slag.

Table 3
Lung Cancer Mortality–Epidemiological Studies of Man-made Vitreous Fibre Production Workers (Adapted from WHO [1988])

		Fibre type		
Feature	**Study**	**Glass filament**	**Glass wool[c, d]**	**Rock/slag wool**
Number of lung cancer deaths	USA[a]	84	340	73
	Europe[b]	15	93	81
		Standardized mortality ratios compared to local rates[e]		
Lung cancer mortality	USA[a]	98	112 ($p < 0.05$)	136 ($p < 0.05$)
	Europe[b]	97	103	124
Time (years) since first exposure (<10/10–19/20–29/30 +)	USA[a]	103 47 122 99	92 108 111 115	89 156 137 132
	Europe[b]	176 76 0 0	68 113 100 138	104 122 124 185
Duration (years) of employment (< 10/10–19/ 20–29/30 +)	USA[a]	113 61 121 54	121 98 109 97 ($p < 0.05$)	143 146 118 118 ($p < 0.05$)
(< 20/20 + years)/ (> 20 years since first exposure)	Europe[b]	0/0	118/60	143/141
Technological phase:	Europe[b]			
– early/intermediate/late			92 / 111 / 77	257 ($p < 0.05$) / 141 / 111
– by time since first exposure (early phase)			108 70 80 121	0 0 317 295
Small-diameter fibres by time (years) since first exposure (< 10 /10–19/20–29/30 +)	USA[a]		61 125 104 112	
Estimated concentrations of respirable fibres	USA[a]	lower	intermediate (highest in small-diameter fibre production facilities)	higher

a. Marsh *et al*. (1990).
b. Saracci *et al*. (1984); Simonato *et al*. (1987).
c. Data for “fibrous glass-both” and “fibrous glass-wool” plants in the U.S. study combined.
d. In the only additional relevant study of a much smaller cohort of glass wool production workers, there was a statistically significant excess of lung cancer mortality compared to provincial rates (O = 19, SMR = 199) which was not related to time from first exposure (< 10 yrs, SMR = 241; 10+ yrs, SMR = 195) or duration of employment (< 5 yrs, SMR = 291; > 5 yrs, SMR = 174) [Shannon *et al*., 1987]. There was a small increase in deaths due to lung cancer (O = 11; SMR = 136; not significant) in a cohort of 1 465 workers exposed to glass filament in Ontario (Shannon *et al*., 1990).
e. p values related to SMRs themselves where only one or two are shown; otherwise the statistical tests examined for linear trends.

In the European study, there was a statistically non-significant excess in lung cancer deaths among workers in the 7 rock/slag wool production plants[9] (SMR = 124, based on 81 observed deaths) [Simonato *et al*., 1987]. There was a statistically non-significant relationship of lung cancer mortality with time since first exposure but no relationship with duration of employment. The excess was concentrated among workers employed in the early technological phase (with a very large, statistically significant SMR of 257), the period in which airborne fibre levels were estimated to have been higher than in other phases.

Where it was possible to take exposure to compounds such as arsenic in slag, polycyclic aromatic hydrocarbons in furnace fumes due to poor ventilation, bitumen or formaldehyde used in binders, or the use of asbestos in rock wool production plants in the large European study, these potential confounders did not explain the observed excess (Simonato *et al*., 1987). Based on analysis of lung cancer mortality in relation to information on the years in which slag, bitumen or pitch, asbestos or formaldehyde were used in various factories in the European study, there was a significant excess in lung cancer mortality associated with the use of slag 20 years since first exposure, only. This observation is difficult to interpret, however, due to the wide overlap between the period of the use of slag and the early technological phase.

In the U.S. study, the standardized mortality ratio for respiratory cancer mortality in workers in the 6 glass wool production plants[10] was 106.7 (statistically non-significant), based upon 99 observed deaths from this cause (Marsh *et al*., 1990). The previously reported (non-significant) increase in respiratory cancer deaths with time since first exposure (Enterline *et al*., 1987) was not confirmed in the 1990 update, due principally to a reduction in the SMR for workers with 30 or more years since first employment (Marsh *et al*., 1990). There was no relationship between respiratory cancer and either duration of employment or estimated cumulative exposure.

In a nested case-control study of 144 lung cancer cases at one of the plants in the large U.S. study (plant no. 9, in which workers were potentially exposed to small diameter fibres, fibrous glass wool, and fibrous glass filament), 102 cases of NMRD and 299 and 201 controls, respectively, matched for birthplace, education, income, marital state, and smoking (age at first start and duration), only the odds ratio for lung cancer and smoking was significant (Chiazze *et al*., 1992).

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9. In the large European study, slag had been used in 5 of the 7 plants. Three of the plants had periods in which either slag wool or mixed wool/slag wool was produced. The remaining 2 plants used slag as an additive to rock wool in some short-term experiments.

10. Based upon 6 plants in which only glass wool was produced. The SMR (112) based on 8 plants (including 2 that produced both continuous filament and glass wool) was significant at the 5% level; however, there was no relationship with time since first exposure, duration of employment, or estimated cumulative exposure.

In the European study, there was also no significant increase in lung cancer mortality in workers in 4 glass wool production plants (SMR = 103, based on 93 deaths from this cause) [Simonato *et al*., 1987]. There was, however, a statistically non-significant relationship of lung cancer deaths with time from first exposure but not with duration of employment. No excess was discernable among workers employed in the early technological phase, for which it was estimated that levels of respirable fibres were similar to those in later phases. In the smaller Canadian study of glass wool production workers, there was a statistically significant excess of mortality due to lung cancer (SMR = 199, based on 19 observed deaths from this cause compared with those expected on the basis of provincial rates) [Shannon *et al*., 1987]. The lung cancer excess was not related to time from first exposure nor to duration of employment. Indeed, 4 out of the 19 lung cancer deaths observed in this study occurred in workers with less than 1 year of employment.

There were no significant increases in respiratory cancer mortality in 1 015 workers potentially exposed to small-diameter glass fibres in 4 plants in the U.S. study (Marsh *et al*., 1990). The respiratory cancer SMRs in workers “ever exposed” to small-diameter glass fibres with time since onset of exposure were 60.6 (1 observed death), 124.6 (7 observed deaths), 103.8 (10 observed deaths), and 111.8 (7 observed deaths) for < 10 years, 10 to 19 years, 20 to 29 years, and 30 + years, respectively. The authors attributed the lack of confirmation of the non-significant increase in lung cancer mortality with time since first exposure observed in the earlier follow up of the cohort (Enterline *et al*., 1987) to a decrease in SMR for workers with 30 years or more from first exposure, relative to the earlier update. It should be noted, however, that the data available on historical exposure of workers exposed in the production of small-diameter glass fibres were extremely limited. Workers were assigned to this sector simply on the basis that they were ever employed in departments which at one time made small fibres (Marsh, 1993).

In the plants examined in both the U.S. and European studies, there was no excess of respiratory or lung cancer mortality, respectively, in the continuous glass filament production sector (SMRs were 98 and 97, respectively, based on 84 observed deaths from respiratory cancer and 15 observed deaths from lung cancer) [Marsh *et al*., 1990; Simonato *et al*., 1987]. There were no relationships of lung cancer mortality with time from first exposure or with duration of employment; however, the average length of follow-up of the continuous filament workers in the European study was less than that in other production sectors, i.e., 16 years, and the number of observed deaths was small. In the smaller Canadian study of glass filament workers, there were 11 deaths from lung cancer (SMR = 136; not significant), but no relationship with time since first exposure or duration of employment. In this study, only 37% of the person-years were for workers with more than 15 years from first exposure (Shannon *et al*., 1990).

A total of 5 mesotheliomas was reported in the large U.S. and European investigations (Marsh *et al*., 1990; Simonato *et al*., 1987). None of the rates in any of the production sectors was excessive and there is no epidemiological evidence, therefore, that mesotheliomas are associated with exposure in MMVF production (Enterline, 1991).

There has been some evidence of excesses of cancers at sites other than the respiratory system in workers exposed in the production of MMVF, including a statistically significant excess incidence of cancer of the buccal cavity and pharynx and of bladder cancer mortality in rock/slag wool production workers in the large European study (Simonato *et al*., 1987). A non-significant excess of mortality due to laryngeal cancer in an Italian subcohort of glass wool production workers in the European study has also been reported (Bertazzi *et al*., 1986). Although a statistically significant excess incidence of cancers of the buccal cavity in the distinct cohort of French glass wool production workers was reported by Moulin *et al*. (1986), in a brief secondary account of the results of an additional follow-up, the observed increase was not confirmed (Brown *et al*., 1991). Moreover, in general, observed excesses were small, were not observed consistently, or may have been attributable to other factors.

Investigations of cancer incidence or mortality in the general population exposed to MMVF have not been identified.

2.5.3 Ecotoxicology

Other than results of studies on laboratory mammals presented in Section 2.5.1, no data were identified on the effects of exposure to MMVF on aquatic or terrestrial organisms.

3.0 Assessment of "Toxic" under CEPA

3.1 CEPA 11(*a*): Environment

Approximately 250 to 300 kilotonnes of MMVF were produced and used in Canada in 1991, of which 70% were glass wools, 20% rock and slag wools, 10% textile fibres, and less than 1% refractory ceramic fibres. Releases resulting from production and use of MMVF products are poorly quantified, but most MMVF that enter the Canadian environment are likely emitted into air. Although there is little information on the environmental fate of MMVF, most are expected to be relatively stable and persist in the ambient environment.

Although MMVF enter the atmosphere in Canada, no data were identified on concentrations in Canadian air, water, sediment, or soil. Furthermore, no relevant data were found on the effects of MMVF to exposed biota, such as terrestrial mammals or birds. It is not possible, therefore, to determine whether Canadian biota are adversely affected by exposure to MMVF.

Therefore, it has been concluded that the available information is insufficient to determine whether man-made vitreous fibres (MMVF) are entering the environment in quantities or under conditions that may be harmful to the environment.

3.2 CEPA 11(*b*): Environment on Which Human Life Depends

Because MMVF are relatively inert solid particles, they do not contribute to global warming, or to depletion of stratospheric ozone.

Therefore, it has been concluded that MMVF are not entering the environment in quantities or under conditions that may constitute a danger to the environment on which human life depends.

3.3 CEPA 11(*c*): Human Life or Health

Distinction of effects (and hence risk) for various types of MMVF is limited largely by the available database. For example, although it is possible to assess the risks of rock and slag wool separately on the basis of toxicological studies in animal species, it is difficult to make such a distinction on the basis of the results of epidemiological studies of production workers, owing to manufacture commonly of both rock and slag

wool in the same facilities[11]. To the extent possible, this assessment addresses the following MMVF, largely on the basis of availability of relevant data, although it is fully recognized that there are substantial differences in the physical and chemical properties, even within each of these classes of MMVF:

rock/slag wool
glass wool (excluding glass microfibres)
special purpose glass microfibres
continuous glass filament (textile fibres)
refractory ceramic fibres

The following assessment addresses associations between non-malignant respiratory disease and respiratory cancer and exposure to various forms of MMVF. In the 2 most extensive epidemiological studies conducted to date (Marsh *et al*., 1990; Simonato *et al*., 1987), there has been no evidence that mesotheliomas are associated with exposure in any sector of MMVF production; in the discussion that follows, this effect is not addressed further.

Rock/Slag Wool

On the basis of the observed excess in respiratory and lung cancer observed among workers in the production of rock/slag wool in epidemiological studies conducted to date, rock/slag wool has been classified in Group III (possibly carcinogenic to humans) of the classification scheme for carcinogenicity developed for the assessment of "toxic" under paragraph 11(*c*) of CEPA (EHD, 1992)[12]. Although concomitant exposure to other substances may have contributed to the observed effect, currently available data are consistent with the hypothesis that the fibres themselves are the

11. In the published account of the study of the large U.S. cohort, data on standardized mortality ratios for respiratory cancer for individual plants were reported (Marsh *et al*., 1990); however, in only 2 of the 6 mineral wool production facilities were workers exposed in the production of rock wool. In both of these plants, slag wool had also been produced. In the large European cohort, slag had been used in 5 of the 7 plants included in rock wool/slag wool production (Simonato *et al*., 1987). Three of the plants had periods in which either slag wool or mixed rock wool/slag wool was produced. The remaining 2 plants used slag as an additive to rock wool in some short-term experiments.

12. Available data are considered insufficient to quantify the possible cancer risk associated with exposure to rock/slag wool on the basis of epidemiological studies. Based on the environmental survey conducted in the large European epidemiological study, airborne-fibre levels in the early phase of the rock/slag wool production industry were estimated to be about 1 to 2 fibres/mL, with concentrations up to 10 fibres/mL for the dustiest work (Dodgson *et al*., 1987a, 1987b). In the large U.S. study, concentrations in mineral wool production were estimated to be 1.5 fibres/mL prior to 1945, 0.3 fibres/mL for 1945–1960, and 0.03 fibres/mL since then (Enterline *et al*., 1987). Concentrations present in the general environment (e.g., indoor air immediately following installation of blown rock wool insulation) determined by T.E.M. and PCOM are 0.04 to 0.065 fibres/mL or 15.4 to 50 times less than mean concentrations in the early phase of production.

principal determinants of risk. In the large European cohort, excess cancer was observed in the early phase of production when airborne fibre concentrations were higher (though this overlapped with the period of exposure to slag); there was also a non-significant relationship with time since first exposure. Although increases in cancer incidence have not been observed in animal species exposed to rock/slag wool in inhalation studies conducted to date, it should be noted that only preliminary results are available for the most extensive investigation (Bunn *et al*., 1993; TIMA, 1993); moreover, the results of studies involving intracavitary administration are consistent with the hypothesis that it is the rock/slag wool fibres that are the principal determinants of excess risk in the epidemiological studies conducted to date (Wagner *et al*., 1984; Maltoni and Minardi, 1989; Pott *et al*., 1984b, 1987).

For substances classified in Group III, effect levels or tolerable daily intakes (TDIs) are compared to exposure in the general environment. For rock/slag wool, the only sufficiently well-documented adverse effect observed in either epidemiological or toxicological studies conducted to date by relevant routes of administration was a dose-related increase in minimal fibrosis following exposure of rats for 24 months to 16 and 30 mg/m^3 rock wool (145 and 247 fibres/mL, respectively), based on preliminary results of the TIMA studies. Dose-related increases in cellularity only were observed in animals similarly exposed to slag wool (Bunn *et al*., 1993; TIMA, 1993).

Available data on the levels of rock/slag wool to which the general population is exposed are limited. In a study conducted in the United Kingdom, concentrations of airborne fibres determined by transmission electron microscopy (T.E.M.) in living areas of homes ranged up to 0.04 fibres/mL on 2 occasions (including one when blown rock wool insulation was used to insulate a loft) [Jaffrey *et al*., 1989]. Concentrations of airborne fibres determined by T.E.M. in the living areas of homes in the Netherlands during insulation with blown glass or rock wool were 50×10^{-3} to 400×10^{-3} fibres/mL; levels of respirable fibres determined by phase contrast optical microscopy were 5×10^{-3} fibres/mL to 25×10^{-3} fibres/cm^3 with peaks up to 65×10^{-3} fibres/mL (van der Wal *et al*., 1987). Adverse effects (rock wool only) have been observed, therefore, in toxicological studies in animal species only at concentrations much greater (i.e., by more than 350 times) than the highest concentrations measured in the general environment under worst-case conditions (i.e., in living areas during the installation of blown rock wool insulation).

Therefore, it has been concluded that rock/slag wool are not entering the environment in quantities or under conditions that may constitute a danger in Canada to human life or health.

Glass Wool (excluding glass microfibres)

On the basis of the lack of observed excesses of cancer in glass wool production workers in the most extensive epidemiological studies conducted to date for which the power to detect such increases was relatively good[13] (Simonato *et al*., 1987; Marsh *et al*., 1990), and the lack of observation of significant increases in tumour incidence in animals exposed by inhalation and inconclusive evidence concerning their potential to induce tumours following intrapleural or intraperitoneal administration, glass wool (excluding glass microfibres) has been classified in Group IV (unlikely to be carcinogenic to humans) of the classification scheme for carcinogenicity developed for the assessment of "toxic" under paragraph 11(*c*) of CEPA (EHD, 1992). It should be noted, however, that classification in Group III (possibly carcinogenic to humans) might also be appropriate, since small increases in cancer incidence or mortality would not have been detected in the available epidemiological studies, and because of variations in fibre size distributions to which humans and rats are exposed.

For substances classified in Group IV, effect levels or TDIs are compared to exposure in the general environment. For glass wool, the only effect documented in epidemiological or toxicological studies by relevant routes of administration conducted to date was a dose-dependent increase in pulmonary cellularity with minimal progression, which regressed upon termination of exposure in rats exposed to 3, 16, and 30 mg/m^3 of size-selected subsets of Manville 901 and CertainTeed B (~ 30 to 240 fibres/mL) [Bunn *et al*., 1993].

Available data on the levels of glass wool to which the general population is exposed are limited. In a study conducted in the U.K., concentrations of airborne fibres determined by transmission electron microscopy (T.E.M.) in living areas of homes ranged up to 0.04 fibres/mL on 2 occasions (including one when one brand of glass fibre blanket insulation was being laid) [Jaffrey *et al*., 1989]. Concentrations of airborne fibres determined by T.E.M. in the living areas of homes in the Netherlands during insulation with blown glass or rock wool were 50×10^{-3} to 400×10^{-3} fibres/cm^3; levels of respirable fibres determined by phase contrast optical microscopy were 5×10^{-3} to 25×10^{-3} fibres/cm^3, with peaks up to 65×10^{-3} fibres/cm^3 (van der Wal *et al*., 1987). Therefore, only minimal effects (not adverse) have been observed in toxicological studies in animal species at concentrations much greater (i.e., by more than 75 times) than the highest concentrations measured in the general environment under worst-case conditions (i.e., in living areas during the installation of glass wool insulation).

13. The power to detect a 1.5 and 2.0 fold increase in respiratory cancer (one-tailed test; p = 0.05) in the glass wool production sector in the large U.S. study was 1 (Marsh, 1993).

Therefore, it has been concluded that glass wool (excluding glass microfibres) is not entering the environment in quantities or under conditions that may constitute a danger in Canada to human life or health.

Glass Microfibres

Although results concerning the potential carcinogenicity of glass microfibres in epidemiological studies and toxicological studies in animals conducted by routes of administration most relevant for risk assessment (i.e., inhalation) have been negative, owing principally to the limitations of these data and based upon positive results in studies involving intracavitary administration and supporting *in vitro* results, glass microfibres have been classified in Group III (possibly carcinogenic to humans) of the classification scheme for carcinogenicity developed for the assessment of "toxic" under paragraph 11(*c*) of CEPA (EHD, 1992).

For substances classified in Group III, effect levels or TDIs are compared to exposure in the general environment. Data on the concentrations of glass microfibres to which the general population are exposed in Canada or other countries have not been identified; however, although a high proportion of these fibres is respirable owing to their relatively small nominal diameters (range of diameters: 0.75 to 2.0 μm [WHO, 1988]), and since glass microfibres are not known to be produced in Canada and are used principally in specialty applications such as high-efficiency filter sheets and insulation for aircraft and space vehicles, concentrations in the general environment are expected to be very low. Adverse effects have not been observed in limited epidemiological studies of populations exposed to considerably higher concentrations than those likely to be present in the general environment (although quantitative data on the latter are lacking) or in animals exposed to much higher concentrations in toxicological studies.

Therefore, it has been concluded that glass microfibres are not entering the environment in quantities or under conditions that may constitute a danger in Canada to human life or health.

Continuous Glass Filament

The lack of observed effects in both man and animals exposed to continuous glass filament (although the database for the latter is extremely limited) in studies conducted to date is consistent with the small number of airborne respirable fibres likely to be associated with a material with a relatively large nominal diameter. In view of the limited power of some of the epidemiological studies conducted to date to detect

increases in cancer mortality in continuous filament production workers[14] and the lack of adequate data on carcinogenicity in animal species, however, it has been classified in Group VI (unclassifiable with respect to carcinogenicity in humans) of the classification scheme for carcinogenicity developed for the assessment of "toxic" under paragraph 11(*c*) of CEPA (EHD, 1992).

For substances classified in Group VI, effect levels or TDIs are compared to exposure in the general environment. Adverse effects have not been observed in epidemiological studies (although they are limited) of populations exposed occupationally to considerably higher concentrations than those likely to be present in the general environment (although quantitative data on the latter are lacking).

Based principally on the likelihood that few respirable fibres are generated in the production and use of continuous filament and that concentrations in the general environment should be extremely small, it has been concluded that continuous glass filament is not entering the environment in quantities or under conditions that may constitute a danger in Canada to human life or health.

Refractory Ceramic Fibre

On the basis principally of the increased incidence of pulmonary tumours (dose-related in the only study in which rats were exposed to multiple concentrations) in rats and increases in mesotheliomas in rats (non-significant) and hamsters observed in the most extensive inhalation study (Mast *et al*., 1992, 1993; Hesterberg *et al*., 1991; Glass *et al*., 1992; Bunn *et al*., 1993) and supporting data from earlier inhalation bioassays (Davis *et al*., 1984) and those involving intratracheal, intracavitary, and *in vitro* administration, refractory ceramic fibre has been classified in Group II (probably carcinogenic to humans) of the classification scheme for carcinogenicity developed for the assessment of "toxic" under paragraph 11(*c*) of CEPA (EHD, 1992).

For such substances, estimated total daily intake or concentrations to which the general population is exposed are compared to quantitative estimates of cancer potency (Exposure Potency Index or EPI) to characterize risk and provide guidance in establishing priorities for further action (i.e., analysis of options to reduce exposure) under CEPA. Identified data on the concentrations of RCF in the general environment are restricted to those in the vicinity of a point source in the United States; however, owing to their use principally in high temperature industrial applications, and with the

14. The power to detect a 1.5 and 2.0 fold increase in respiratory cancer in the continuous filament sector in the large U.S. study (one tailed test; p = 0.05) was 0.99 and 1.0, respectively (March, 1993).

exception possibly of areas in the vicinity of industrial sources for which Canadian data were not identified, exposure of the general population and resulting EPIs (and hence priority for further action under CEPA) are expected to be very low.

On the basis of available data, refractory ceramic fibre has been classified as "probably carcinogenic to humans", and therefore, it has been concluded that this substance may enter the environment in quantities or under conditions that may constitute a danger in Canada to human life or health.

This approach is consistent with the objective that exposure to such compounds (i.e., those for which the critical effect is considered not to have a threshold) should be reduced wherever possible and obviates the need to establish an arbitrary *de minimis* level of risk for the determination of "toxic" under CEPA.

4.0 Recommendations

Acquisition of additional information in the following areas would permit a more complete assessment of the potential risks to health associated with exposure to man-made vitreous fibres:

1. data on the concentrations of MMVF in Canadian air near point sources, especially production facilities;
2. additional characterization of the potential role of concomitant exposures to other substances in the excess cancer risk observed in workers exposed to rock/slag wool in the large U.S. and European cohort studies;
3. additional epidemiological investigations of workers exposed to glass microfibres. A multiple-dose inhalation study for glass microfibres with protocol similar to those conducted recently for other materials by TIMA is also desirable;
4. analytical epidemiological investigations of non-malignant and malignant respiratory disease in populations of workers exposed to refractory ceramic fibre following sufficient latency periods;
5. additional investigation of the role and characterization of biopersistence in the pathogenesis of disease associated with exposure to fibrous dusts; and
6. development of a more sensitive scale for scoring of fibrosis in experimental animals associated with inhalation of fibrous dusts.

In light of other priorities, it is also recommended that the assessment for rock and slag wool be reconsidered when the TIMA studies on the carcinogenicity of these materials are completed.

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