NOHSC
National Occupational Health & Safety Commission

NOHSC REPORT

Chrysotile Asbestos Health Assessment of Alternatives

MARCH 2001

Chrysotile Asbestos

HEALTH ASSESSMENT OF ALTERNATIVE MATERIALS
IN THE EVENT OF A PHASE-OUT OF USES OF
CHRYSOTILE ASBESTOS IN AUSTRALIA

March 2001

A report prepared for the
National Occupational Health and Safety Commission
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Foreword

In seeking to achieve Australian workplaces free from injury and disease NOHSC works to lead and coordinate national efforts to prevent workplace death, injury and disease. We seek to achieve our mission through the quality and relevance of information we provide and to influence the activities of all parties with roles in improving Australia's OHS performance.

NOHSC has five strategic objectives:

- Improving national data systems and analysis,
- Improving national access to OHS information,
- Improving national components of the OHS and related regulatory framework,
- Facilitating and coordinating national OHS research efforts, and
- Monitoring progress against the National OHS Improvement /framework.

This publication is a contribution to achieving those objectives.

Contents

Summary

1. This report on the health aspects of the alternative materials to asbestos, identified in the NICNAS Full Public Report on Priority *Existing Chemical No. 9* Chrysotile asbestos, February 1999 (PEC 9), has been prepared at the request of the National Occupational Health and Safety Commission. The materials have, as far as practicable, been reviewed as separate entities as follows:

(i) **synthetic vitreous (mineral) fibres:** (a) insulation wools (glass, rock and slag wool, and new bio-soluble insulation wool); (b) special purpose glass fibres; (c) refractory ceramic fibres (RCF); (d) refractory fibres other than RCF; (e) high temperature calcium magnesium silicate (CMS) wools; and (f) continuous filament glass fibres;

(ii) **natural mineral fibres:** (a) attapulgite (palygorskite); and (b) wollastonite;

(iii) **synthetic organic fibres**: (a) aramid; and (b) carbon and graphite fibres; and

(iv) **natural organic fibres:** cellulose.

2. Each type of material has been reviewed and presented as a stand-alone chapter with its own references and evaluation of the health effects. The reviews assessed the data provided in previous reviews of these materials carried out by agencies including the International Agency for Research on Cancer (IARC), the World Health Organisation (WHO), the International Programme on Chemical Safety (IPCS), and the International Labour Organisation (ILO), and also assessed data published since those major reviews. Evaluations have been based on the model adopted by the IARC in its monograph series, but modified to include non-cancer effects. An explanation of the evaluation system used is as follows:

sufficient evidence means that the studies have demonstrated the toxicity and/or carcinogenicity, or the non-toxicity and/or non-carcinogenicity of the material;

limited evidence means there are some data available, but the data do not clearly establish the presence or absence of toxicity or carcinogenicity;

inadequate data means that any studies done on the material were not appropriate for testing toxicity and/or carcinogenicity; and

no data means that there had not been any studies done.

3. A summary of all the evaluations is provided in the following tables 1 to 7. In all tables:

yes = sufficient evidence for the effect
no = sufficient evidence for lack of the effect;
\+ = limited evidence for the effect;
-- = inadequate or no data.

4. Chrysotile asbestos has been included in Table 7 below for comparison with the alternative materials reviewed in this report. In all respects, chrysotile is more hazardous than any of the alternative materials.

5. Summary of the evidence for health effects of synthetic vitreous fibres

Table 1.

Health Effects	Fibre			
	Glass wool	**Rock wool**	**Slag wool**	**New 'bio-soluble' insulation wools**
Non-inhalation animal studies:				
intraperitoneal or intrapleural cancer	yes	yes	--	no
intratracheal cancer	no	no	no	--
Animal inhalation studies:				
relative solubility	high	moderate	high	very high
fibrosis	no	yes	no	--
cancer	no	no	no	--
mesothelioma	no	no	no	--
Human studies:				
skin itch, and/or eye, respiratory discomfort	yes	yes	yes	yes
asthma	no	no	no	--
abnormal lung function	no	no	no	--
cancer	no	no	no	--
mesothelioma	no	no	no	--

Table 2.

Health Effects	Fibre			
	Refractory ceramic fibres (RCF)	**High temperature (CMS) wools**	**Special purpose glass fibres**	**Continuous filament glass fibres**
Non-inhalation animal studies:				
intraperitoneal or intrapleural cancer	yes	--	yes	no
intratracheal cancer	yes	--	yes	--
Animal inhalation studies:				
relative solubility	low	very high	low	low
fibrosis	yes	no	yes	--
cancer	yes	no	no	--
mesothelioma	yes	no	yes	--
Human studies:				
skin itch, and/or eye, respiratory discomfort	yes	--	--	yes
asthma	--	--	no	yes
abnormal lung function	--	--	no	--
cancer	--	--	no	no
mesothelioma	--	--	no	no

Table 3.

Health Effects	Fibre			
	Titanates	**Silicon carbide**	**Aluminium oxide**	**Saffil®**
Non-inhalation animal studies:				
intraperitoneal or intrapleural cancer	yes	yes	±	no
intratracheal cancer	--	--	--	--
Animal inhalation studies:				
relative solubility	low	low	low	low
fibrosis	±	yes	--	no
cancer	±	yes	--	no
mesothelioma	--	yes	--	no
Human studies:				
skin itch, and/or eye, respiratory discomfort	--	--	--	--
asthma	--	--	--	--
abnormal lung function	--	--	--	--
cancer	--	±	--	--
mesothelioma	--	--	--	--

6. Summary of the evidence for health effects of natural mineral fibres

Table 4.

Health Effects	Fibre		
	Attapulgite		**Wollastonite**
	short fibres	**long fibres**	
Non-inhalation animal studies:			
intraperitoneal or intrapleural cancer	no	yes	no
intratracheal cancer	--	--	no
Animal inhalation studies:			
relative solubility	low	low	high
fibrosis	no	yes	no
cancer	no	yes	no
mesothelioma	no	yes	no
Human studies:			
skin itch, and/or eye, respiratory discomfort	--	--	--
asthma	--	--	--
abnormal lung function	--	--	±
cancer	--	--	--
mesothelioma	--	--	--

7. Summary of the evidence for health effects of synthetic organic fibres

Table 5.

Health Effects	Fibre	
	Aramid (Kevlar)	Carbon/graphite
Non-inhalation animal studies:		
intraperitoneal or intrapleural cancer	±	±
intratracheal cancer	--	--
Animal inhalation studies:		
relative solubility	low	low
fibrosis	yes	--
cancer	no	--
mesothelioma	no	--
Human studies:		
skin itch, and/or eye, respiratory discomfort	--	--
asthma	--	--
abnormal lung function	--	--
cancer	--	--
mesothelioma	--	--

8. Summary of the evidence for health effects of natural organic fibres

Table 6.

Health effects	Fibre
	Cellulose
Non-inhalation animal studies:	
intraperitoneal or intrapleural cancer	±
intratracheal cancer	--
Animal inhalation studies:	
relative solubility	low
fibrosis	yes
cancer	--
mesothelioma	--
Human studies:	
skin itch, and/or eye, respiratory discomfort	yes
asthma	--
abnormal lung function	--
cancer	--
mesothelioma	--

9. Summary of the evidence for health effects of alternative materials

Table 7.

Health effects	Fibre																		
	Chry-sotile	Glass	Rock	Slag	Bio Sol wools	RCF	CMS wool	SP glass	Cont fil glass	Tita-nates	SiC	Al oxide	Saffil	Atta short	Atta long	Wollast-onite	Aramid	Carbon / graphite	Cellu-lose
Non-inhalation animal studies:																			
intraperi-toneal or intrapleural cancer	yes	yes	yes	--	no	yes	--	yes	no	yes	yes	±	no	no	yes	no	±	±	±
intratrache al cancer	yes	no	no	no	--	yes	--	--	--	--	--	--	--	--	--	no	--	--	--
Animal inhalation studies:																			
relative solubility	very low	high	mod - erat e	hig h	very high	low	very high	low	low	low	low	low	low	low	low	high	low	low	low
fibrosis	yes	no	no	no	--	yes	no	yes	--	±	yes	--	no	no	yes	no	yes	--	yes
cancer	yes	no	no	no	--	yes	no	no	--	±	yes	--	no	no	yes	no	no	--	--
meso-thelioma	yes	no	no	no	--	yes	no	yes	--	--	yes	--	no	no	yes	no	no	--	--
Human studies:																			
skin itch, and/or eye, respiratory discomfort	yes	yes	yes	yes	yes	yes	--	--	yes	--	--	--	--	--	--	--	--	--	yes
asthma	no	no	no	no	--	--	--	no	yes	--	--	--	--	--	--	--	--	--	--
abnormal lung function	yes	no	no	no	--	±	--	no	--	--	--	--	--	--	--	--	±	--	--
cancer	yes	no	no	no	--	--	--	no	no	--	±	--	--	--	--	--	--	--	--
meso-thelioma	yes	no	no	no	--	--	--	no	no	--	--	--	--	--	--	--	--	--	--

1. Background and scope

1.1 This document is a report on the assessment of the health effects of alternative materials, in the event of a phase-out of the uses of chrysotile asbestos in Australia. In particular this document reviews the alternative materials identified in the NICNAS Full Public Report on *Priority Existing Chemical No. 9* Chrysotile Asbestos, February 1999 (PEC 9).

1.2 In this review, the alternate materials identified in PEC9 have been rearranged as follows into structural groupings similar to that used by the International Labour Organisation in its booklet on *Safety in the use of mineral and synthetic fibres*[1], rather than the alphabetical format:

A. Synthetic vitreous (mineral) fibres:

(i) insulation wools - glass wool, rock (stone) wool, slag wool, and new bio-soluble insulation wools

(ii) special purpose glass fibres

(iii) refractory ceramic fibres (RCF)

(iv) refractory fibres other than RCF

(v) calcium magnesium silicate (CMS) high temperature wools

(vi) continuous filament glass fibres

B. Natural mineral fibres (other than asbestos):

(i) attapulgite

(ii) wollastonite

C. Synthetic organic fibres:

(i) aramid fibres

(ii) carbon and graphite fibres

D. Natural organic fibres:

(i) cellulose fibres

1.2 The use of this grouping of the alternate materials also reflects the way the world usage has evolved and the generation of scientific data concerning the health aspects of the substitutes. It will be readily obvious that there are far more available data on the synthetic vitreous fibres than the other categories combined; but in practice, there are far more people exposed to these materials than others so the disproportionate amounts of data are to be expected.

1.3 As far as practicable, original scientific papers have been used in this review since some of the major reviews, whilst they may still be relevant in a regulatory sense,

are now many years old and the scientific data base has developed greatly since they were written.

1.4 References

1. International Labour Organisation (1990) *Safety in the use of mineral and synthetic fibres. Occupational Safety and Health Series No. 64*. ILO, Geneva, Switzerland.

2. Synthetic vitreous fibres – General

2.1 Synthetic vitreous fibres (SVF), otherwise known as synthetic mineral fibres (SMF) (in some reports as man-made mineral fibres) is the generic term applied to a range of fibrous materials manufactured mostly from glass, natural rocks, slag, and kaolin clay. The most common types of SVF are insulation wools (glass, rock and slag wool), continuous filament glass fibres, special purpose glass fibres, and refractory (including ceramic) fibres. The health effects of SVF have been the subject of detailed reviews in official publications: the International Agency for Research on Cancer (IARC)[1] in 1988; the International Programme on Chemical Safety (IPCS)[2] in 1988; and the International Labour Organisation (ILO)[3] in 1990. Since the publication of these reviews there have been numerous international meetings specifically on the subject of fibre toxicology including the NATO Advanced Research Workshop on Mechanisms in Fibre Carcinogenesis[4] in 1990, a Workshop on Approaches to Evaluating the Toxicity and Carcinogenicity of Man-Made Fibres (MMF)[5] in 1991, an IARC Workshop on Biopersistence of Respirable Synthetic Fibres and Minerals in 1992[6], and an International Symposium on the Health Effects of Fibrous Materials (excluding asbestos) used in Industry, organised by the Australian Insulation Wools Research Advisory Board, in 1995[7]. In 2000, the ILO held a meeting of experts and published a Code of Practice on safety in the use of synthetic vitreous fibre insulation wools (glass wool, rock wool and slag wool)[8].

2.2 Whilst the various types of SVF are all amorphous silicates, there are great differences in physical form (particularly in mean and range of length and diameter) and chemical properties (particularly solubility at physiologically important pHs), which affect biopersistence. These differences have resulted in the variability of health effects associated with SVF, ranging from clear evidence of carcinogenicity in animal inhalation studies for refractory ceramic fibres, but absence of a cancer risk in comparable studies for the insulation wools. None of the fibrous materials considered in this review has been shown to cause cancer or other serious health effects in humans, but they all remain occupational and environmental health issues because of their widespread use, and the inevitable comparisons with asbestos.

2.3 References

1. International Agency for Research on Cancer. (1988) *IARC monographs on the evaluation of the carcinogenic risks of humans. Vol. 43. Man-made mineral fibres and radon*. IARC Press, Lyon, France.

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

3. International Labour Organisation (1990) *Safety in the use of mineral and synthetic fibres. Occupational Safety and Health Series No. 64*. ILO, Geneva, Switzerland.

4. NATO Advanced Science Institute Series. (1991) *Mechanisms in fibre carcinogenesis*. Plenum Press, New York, USA.

5. McClellan R , Miller F, Hesterberg T, Warheit D, Bunn W, Kane A, Lippman M, Mast R, McConnell E, Reinhardt C. (1992) Approaches to evaluating the toxicity and carcinogenicity of man-made fibres. Summary of a workshop held November 11-

13, 1991, Durham, North Carolina. *Regulatory Toxicology and Pharmacology*, **16**: 321 - 364.

6. Bignon J, Saracci R, Touray J-C. (1994) Introduction: INSERM-IARC-CNRS Workshop on Biopersistence of Respirable Synthetic Fibers and Minerals. *Environmental Health Perspectives*, **102**(Suppl 5): 3 - 5.

7. Insulation Wools Research Advisory Board. (1996) Symposium on the health effects of fibrous materials (excluding asbestos) used in industry: 30-31 October 1995, Sydney, Australia. *The Journal of Occupational Health and Safety, Australia and New Zealand*, **12**(3): 243 - 385.

8. International Labour Organisation. (2000) *Code of Practice on safety in the use of synthetic vitreous fibre insulation wools (glass wool, rock wool, slag wool).* ILO, Geneva, Switzerland.

3. Synthetic vitreous fibre insulation wools – glass wool, rock (stone) wool, slag wool

3.1 Introduction

3.1.1 Glass wools have been produced for more than fifty years from mixtures of minerals and industrial chemicals in order to provide a composition consisting mostly of oxides in the following approximate concentrations: silicon (54 - 65%), aluminium (4%), magnesium (5%), calcium (20%), barium (3%), sodium (14%), potassium (2%), and boron (6%). Rock wool and slag wool have generally been prepared from single minerals such as basalt or diabase, with limestone added to improve melting qualities. The chemical composition of rock wools and slag wools are similar to glass wool, but generally less SiO_2 and more Al_2O_3 and CaO.

3.1.2 The raw materials are melted in either a glass melting tank furnace or a cupola furnace. The melts are fiberised usually by one of three processes: the Owens blowing process; the centrifugal cascading process; and the rotary process. The fibres produced are mostly in the range of 4 - 8 microns diameter and 3 - 10 centimetres long. The fibres are treated with resin binders and dust suppressing oils, formed into the desired shapes and thickness, and cured in an oven. Depending on the use and purpose of the products, insulation wools are sometimes covered on one or more sides with coatings including aluminium foil, paint, plastic, or glass tissue.

3.1.3 The binders used are phenol-formaldehyde resins, often modified with urea or melamine. The final products typically consist of 90 - 99% fibrous material, up to 10% resin binder, and up to 1% solvent refined mineral oil. Some insulation wools, used for blowing into cavities, contain no resin binders.

3.1.4 During the 1990s, manufacturing processes worldwide have aimed at producing insulation wools with chemical compositions that result in fibres that are even more soluble in body fluids than those produced in previous decades. Typically, the composition of these “bio-soluble” glass wools is: SiO_2 62%, Al_2O_3 1%, FeO 0.1%, MgO 3%, CaO 7%, Na_2O 16%, K_2O 1%, B_2O_3 9% and TiO_2 0%; and that of the ”bio-soluble” rock and slag wools (known as stone wool in Europe) is typically: SiO_2 40%, Al_2O_3 33%, FeO 7%, MgO 2%, CaO 15%, Na_2O 0.2%, K_2O 1%, B_2O_3 0% and TiO_2 2%;

3.1.5 Insulation wools are used extensively in domestic, commercial and industrial buildings for thermal and acoustic insulation, low to medium (800^{o}C) temperature pipe insulation, ventilation and air-conditioning ducting, and acoustic ceiling tiles or panels. During handling and installation, some coarse dust may be generated, but the levels of airborne respirable fibres have generally been found to be very low; with the airborne levels found in monitoring over the past 20 years found to be less than 0.1 f/mL[1, 2]. These low levels are due to the low percentage of respirable fibres in the bulk products, and the use of resins which bind the fibrous materials together. Higher exposures may occur during the installation of blowing wools containing no resin binders, when average exposures greater than 1.0 f/mL may be expected with peak concentrations as high as 20 f/mL[3].

3.2 Health effects – general considerations

3.2.1 There are a variety of parameters and mechanisms that influence fibre toxicity, and the potential for insulation wool fibres and dust to have an impact on health. These are all important in the explanation of the differences in observed effects between the different types of insulation materials[4].

(i) **fibre inhalation and deposition** - in order to cause health effects, fibres and/or particles must be inhaled, deposited and retained in the body, particularly the respiratory tract[5, 6].

(ii) **biopersistence (durability in biological tissues)** - experimental data clearly indicate that fibres that are not readily eliminated by respiratory clearance mechanisms or subject to breakdown and dissolution, are potentially more fibrogenic and carcinogenic[7, 8, 9] ie they have the potential to cause scarring and cancer.

(iii) **physicochemical** parameters - the penetration and deposition of fibres depends on their physical dimensions, ie length, diameter and aspect ratio. Whilst respirable fibres have been defined as having diameter less than 3 microns, lengths greater than 5 microns, and aspect ratios greater than 3:1[10], experimental studies have demonstrated that the most carcinogenic fibres, particularly for the mesothelium (layer of cells on the lung lining), have lengths greater than 15-20 microns and diameters less than 0.25 microns[11, 12]. Apart from durability, the chemical properties of the surface of the fibres may play a part in potential biological reactivity[13, 14].

(iv) **dose** - although complex, the concept of dose is important in any consideration of fibre toxicology and potential for human disease. The concentration of respirable fibres (f/mL or f/m^3), as measured by the WHO[10] or similar method, provides a crude estimate of potential dose; estimation of airborne concentrations of fibres less than 0.25 microns diameter and greater than 15-20 microns long (f/mL or f/m^3) would provide an estimate of the potential dose of biologically active (at least for the deep lung and lining of the lung ie pleura) fibres; estimation of the mass amount (mg/m^3) of inspirable fibrous dusts may also be important for considering the potential dose which is relevant for the upper airways and bronchi (air passages in the lung). However, all of these estimates of airborne concentrations may also require consideration of factors related to knowledge on biopersistence and chemical leaching[15].

3.2.2 Based on experimental comparative studies, insulation wools (glass, rock and slag wool) have been shown to be more soluble *in vitro* and less biopersistent *in vivo* than refractory ceramic fibres and special purpose glass fibres[16, 17, 18]; and developments in the manufacturing processes in the 1990s have resulted in insulation wools even more soluble than those which have been manufactured in previous decades[9, 19].

3.3 Health effects – animal studies

Introduction

3.3.1 The earliest recorded animal experiments studying the potential health effects of insulation wools occurred in the 1930s when cats were exposed by inhalation to slag[20] and, guinea pigs and rabbits were exposed by intratracheal instillation (ie instilled into the main windpipe) to glass wool[21]. The slag wool study found "no significant pathological change". The glass wool study, included in a major investigation into the toxicity of asbestos fibres, not only found an absence of fibrosis (lung scarring) and lung tumours following intratracheal instillation, but also led the researchers to conclude that "the fibrous filamented structure of asbestos appears to play an essential part in the irritating action, since the solid fibers of glass wool do not produce fibrosis (or cancer)". They also noted that long asbestos fibres were far more toxic than short fibres.

3.3.2 Animal experiments involving insulation wools were not pursued following these negative studies, until a variety of glass fibres were included in research involving the direct implantation of fibrous and particulate (fine solid particles) materials into the chest cavities of rats in the 1970s[22]. These materials, mostly special purpose fine fibres provided by the production industry as a courtesy to researchers, were used for comparison with asbestos. These experiments not only aroused worldwide interest in the potential health effects of glass fibres and other insulation wools, but also set the initial parameters for the mechanisms involved in fibre toxicology, and indicated directions for future research. Stanton et al (1972 and 1977) stated:

- *in all experiments yielding few or no mesotheliomas* [tumours arising from the cells of the lining of the lung]*, irrespective of the material used, fibrosis* [scarring] *was negligible;*
- *the extent of the fibrosis roughly correlated with the incidence of pleural neoplasms* [tumours]*;*
- *the simplest incriminating features for both fibrogenesis and carcinogenesis seems to be a durable fibrous shape, perhaps in a narrow range of size;*
- *neoplastic* [new tumour growth] *response correlated well with the dimensional distribution of the fibres - < 1.5 microns diameter and > 8 microns length yielded the highest probability of pleural tumours;*
- *clearly, fibres must have the opportunity to reach the target tissue to cause cancer. Our experiments are inappropriate for evaluating many aspects of the environmental hazard, since they circumvent those factors that might inhibit or enhance exposure through natural routes;*
- *inhalation experiments with glass fibres in narrowly limited dimensional ranges, particularly those ranges found to be the most carcinogenic in this*

study, should offer a broad base from which guidelines of safety might be determined.

3.3.3 The Stanton hypotheses have now been well tested in numerous animal inhalation studies, and the risks of fibrogenesis and carcinogenesis found to be related to fibre diameter (less than 1.0 micron), fibre length (more than 20 microns) and durability. But not all researchers and commentators have adhered to the Stanton advice concerning the relevance of the intracavity tests (intrapleural and intraperitoneal) for use in human risk assessment[23].

3.3.4 In this review, the collective views of scientists on the validity of the different research methods currently available for the assessment of fibres[24, 25] has been followed:

- *A tiered approach to toxicity evaluation is recommended that includes:*

  (a) in vitro [test-tube] *screening for durability, surface properties, cytotoxicity* [cell toxicity]*;*

  (b) short-term inhalation or other in vivo [in living organisms eg animals] *studies;*

  (c) chronic inhalation studies are the "gold-standard" and provide most appropriate data for risk characterisation.

- *the rat is the most appropriate species for inhalation studies;*

- *serial lung-burden analyses are an essential component of inhalation studies and are essential for understanding exposure - dose-response relationships;*

- *studies oriented to understanding mechanisms of toxicity and carcinogenicity are important adjuncts to fundamental toxicity studies; and*

- *intracavity studies are inappropriate for risk characterisation but can play a useful screening role in initial toxicity assessment.*

Intracavity studies

3.3.5 **Intrapleural** studies (inside the space between the lining of the lung and the chest wall) using commercial glass wool, as distinct from special purpose glass fibres, have all been negative in a variety of test animals: Osborne-Mendel rats[22], Sprague-Dawley rats[26], Wistar rats[27], and BALBc mice[28]. Similarly, intrapleural studies using rock wool[26, 29], and slag wool [22, 26] were all negative.

3.3.6 **Intraperitoneal** studies (inside the space between the lining of the abdomen and pelvis and the intestine and organs) using commercial glass wool except for three types of Bayer fibre[14], were not reported prior to 1996. In the study of Bayer fibre, the importance of durability and fibre diameter was nicely shown: the moderately soluble coarse fibre (B1, diameter more than 2.0 microns) and the

very soluble fine fibre (B2, diameter less than 1.0 micron) were both negative, but the durable fine fibre (B3, diameter less than 1.0 micron) was positive in intraperitoneal tests using Wistar rats. A positive intraperitoneal study of glasswool (MMVF 11) was reported in 1996 [30]. The new 'bio-soluble' glass wool formulations have also been tested by this most sensitive intraperitoneal route of administration and found to produce negative results[31].

3.3.7 **Intraperitoneal** studies of commercial rock wool[29] and slag wool[32-34] were all negative except a 1996 rockwool study using MMVF 21 [30]. Positive results were obtained using experimental rock wools[32]. The new 'bio-soluble' stone wool formulations have also been tested by this most sensitive intraperitoneal route of administration and found to produce negative results[31].

Intratracheal instillation studies

3.3.8 **Intratracheal** (inside the windpipe) instillation studies using glass wools, not special purpose glass fibres, were negative in Fischer-344 rats[35] and Syrian hamsters[36]. Negative results were also obtained with rock wool instillation in Wistar rats[37] and Syrian hamsters[36]. Studies on slag wool have not been reported.

Inhalation studies

3.3.9 All the chronic inhalation studies ever done in experimental animals using commercial glass wool have been negative. The studies published during the 1980s26, 38-40 have been summarised in Table 1.

3.3.10 Rock wool and slag wool were also tested during the 1980s by chronic inhalation studies in Wistar rats[39], Fischer 344 rats[38], Osborne-Mendel rats[26], and Syrian Golden hamsters[26]. Wagner grade 4 fibrosis scores were found in 9/55 (16%) rats and 1/69 (1.4%) hamsters exposed to slag wool, but no mesothelioma or lung tumour risks were found in any of the studies (Table 2).

3.3.11 All the above chronic inhalation studies had been subject to criticism, mostly because the samples of insulation wools contained significant percentages of fibres with diameters greater than 1.0 micron, and therefore not respirable by rats and hamsters. Because of this, additional inhalation studies of glass wool[41], and rock wool and slag wool[42] have been done at the Research Consulting Company (RCC) in Geneva in accordance with the currently accepted "gold standard" test protocols[43, 44, 45]. In these, and all the recent studies done at the RCC in Geneva, "state-of-the-art" techniques were used in fiber preparation, aerosolization, exposure measurement, and determination of the actual target organ dose. It was important to use fibres with dimensions that permitted deposition into the deep lung regions. In addition, nose-only rather than whole-body exposure was used in these studies to allow greater control of the exposure levels and to provide more uniform dosing of animals. To permit comparison of biological effects between the different fiber types, the fibrous glasses used in this study were prepared to have dimensions as close as possible to the refractory ceramic fibre studies at the RCC" [41].

3.3.12 The glass wool study exposed Fischer 344 rats to MMVF 10 (Manville 901 glass wool) and MMVF 11 (CertainTeed B glass wool). These two materials represent "over 90% of the commercial glass wools in widespread use". The study found that the glass wools tested did not cause lung fibrosis (scarring) and there was no statistically significant increase in lung tumour incidence when compared with an air-only control group. The authors concluded that (i) the inhalation model provided a sound basis to identify the potential hazards of airborne fibrous materials in humans, (ii) the results suggested that glass wool represents no significant hazard for fibrotic or neoplastic disease in humans, and (iii) the chemical composition of synthetic mineral fibres is a critical determinant of their potential for inducing adverse biological results.

3.3.13 The rock wool and slag wool studies exposed Fischer 344 rats to MMVF 21 (Rockwool International basalt-based rock wool) and to MMVF 22 (USG Interiors blast-furnace slag wool) which are also commonly used insulation materials. Crocidolite asbestos was used as a positive control, and unexposed chamber controls were also observed. The fibres used in the study were size-selected to be respirable in rats. Exposure to crocidolite asbestos was terminated after 10 months because of increased morbidity and mortality. Exposure to rock and slag wool, while producing a dose-related non-specific inflammatory response (rock and slag) and minimal focal pulmonary fibrosis (rock only), showed no evidence of carcinogenic activity in either the lung or pleura, in contrast to crocidolite asbestos, which induced neoplasms (tumours) in both tissues. Since workplace airborne levels are several orders of magnitude lower than even the lowest exposure level to which the animals were exposed, the authors concluded that these results suggest that rock wool and slag wool do not pose a significant health risk to humans[42].

3.3.14 The combined results from the insulation wool chronic inhalation studies done at the RCC in Geneva have been summarised in Table 3[46]. No test group had a tumour rate significantly higher than its air control, and there were no significant trends in tumour rate with increasing dose.

3.3.15 Commercial glass wool insulation (MMVF10a) similar to that tested in rats, has also been studied in chronic inhalation studies on hamsters[47]. The results in this species were the same as in the rat inhalation studies in that the glass wool insulation did not cause lung fibrosis or lung cancers in the hamsters, even at doses as high as 300 f/mL.

Table 1. Animal inhalation studies done in the 1980s - glass wool

Researcher	Species	Exposure Level	Type of Glass	Fiber Dimension D-diameter/L-length	No. of Animals	Percentage of Tumors	Wagner Lung Grade
Le Bouffant et al (1984)[39]	Wistar rats	Air controls	Not applicable	Not applicable	47	0	No fibrosis
		48 f/mL	St. Gobain insulation wool	D 69% <1 micron; L 42% <10 microns	45	2.2 NS	No fibrosis
Wagner et al (1984)[26]	Fischer 344 rats	Air controls	Not applicable	Not applicable	48	0	No fibrosis
		1436 f/mL	Pilkington insulation wool	D 52% 1 micron; L 72% 5-20 microns	48	2.1 NS	No fibrosis
		323 f/mL	Pilkington insulation wool	D 47% 1 micron; L 58% 5-20 microns	47	2.1 NS	No fibrosis
Mitchell (1986)[40]	Fischer 344 rats	Air controls	Not applicable	Not applicable	100	0	No fibrosis
		15 mg/m^3	OCF insulation wool	D 4-6 microns; L > 20 microns	100	0	No fibrosis
		15 mg/m^3	OCF air filter media	D 0.5 - 3.5 microns; L > 10 microns	100	0	No fibrosis
		5 mg/m^3	OCF air filter	D <3.5 microns; L > 10 microns	100	0	No fibrosis
Smith et al (1987)[38]	Osborne-Mendel rats	Air controls	Not applicable	Not applicable	60	0	No fibrosis
		100 f/mL	InsulSafe II blowing wool	D 1.2 microns mean; L 24 microns mean	52	0	No fibrosis
Smith et al (1987) *cont.*		100 f/mL	JM insulation wool	D 1.1 microns mean; L 20 microns mean	57	0	No fibrosis
		10 f/mL	JM insulation wool	D 1.1 microns mean L 20 microns mean	61	0	No fibrosis

Table 1. Animal inhalation studies done in the 1980s - glass wool

Researcher	Species	Exposure Level	Type of Glass	Fiber Dimension D-diameter/L-length	No. of Animals	Percentage of Tumors	Wagner Lung Grade
		25 f/mL	OCF insulation wool	D 3.0 microns mean; L 80 microns mean	58	0	No fibrosis
Smith et al (1987)[38]	Syrian golden hamsters	Air controls	Not applicable	Not applicable	58	1.7	No fibrosis
		100 f/mL	InsulSafe II blowing wool	D 1.2 microns mean; L 24 microns mean	60	0	No fibrosis
		100 f/mL	JM insulation wool	D 1.1 microns mean; L 20 microns mean	66	0	No fibrosis
		10 f/mL	JM insulation wool	D 1.1 microns mean; L 20 microns mean	65	0	No fibrosis
		25 f/ML	OCF insulation wool	D 3.0 microns mean; L 83 microns mean	61	0	No fibrosis

Table 2. Animal inhalation studies done in the 1980s - rock wool and slag wool

Researcher	Species	Exposure level	Type of glass	Fiber dimension D-diameter/L-length	No. of animals	Percentage of tumours (adenomas)	Wagner lung grade
Le Bouffant et al (1984)[39]	Wistar rats	5.4 mg/m^3 41 f/mL	Saint Gobain rock wool	D: 23% < 1 micron L: 60% > 10 microns	47	0	No fibrosis
Wagner et al (1984)[26]	Fischer 344 rats	9.61 mg/m^3 214 f/mL	Swedish experimental rock wool	D: 58% < 1 micron L: 71% 5-20 microns	48	4.2% NS	No fibrosis
Smith et al (1987)[38]	Osborne-Mendel rats	7.8 mg/m^3 200 f/mL 90 f/mL rat respirable	USG slag	D: mean 0.9 microns L: mean 22 micron	55	0	No fibrosis
Smith et al (1987)[38]	Syrian Golden hamsters	7.8 mg/m^3 200 f/mL 90 f/mL respirable	USG slag	D: mean 0.9 microns L: mean 22 microns	69	0	No fibrosis

3.3.16 Developments in the manufacture of insulation wools in the past decade have resulted in modifications to the chemical formulation of some insulation wools leading to even more soluble fibres9, 19. Results of chronic inhalation studies in these fibrous materials have not yet been reported; but a study at the RCC in Geneva in which Fischer 344 rats were exposed to 200 f/mL of “X607" fibres (high temperature, highly soluble insulation glass fibres) has been completed. Unlike high temperature RCF fibres, the X607 did not result in lung fibrosis, pleural mesothelioma or an increased risk of lung tumours in the experimental animals48.

Biopersistence studies

3.3.17 The ground-breaking studies at the Saranac Laboratories in the 1930s not only started an ongoing investigation into the potential health effects of insulation wools, but raised questions about the mechanisms by which fibres might exert their toxicity. Since then, most of the studies referenced above have included observations on mechanisms of action, particularly in relation to factors responsible for fibre deposition, dissolution, translocation, and clearance - that is, factors responsible for the biopersistence of fibres. In 1992, a Workshop on the Biopersistence of Respirable Synthetic Fibers and Minerals was held at the International Agency for Research on Cancer to consider in detail the current state of knowledge on biopersistence[49]. Since then, a range of sophisticated studies, designed specifically to study biopersistence, have been published in which a variety of insulation wools have been examined by intratracheal and inhalation

methods[9, 18, 19, 50-53]. The most recent review[54] stated: available experimental data from long-term experiments are consistent with the hypothesis that the oncogenic (cancer) potential of synthetic vitreous fibres is determined completely by their biopersistence.

Table 3. Multi-dose chronic inhalation studies on Fischer 344 rats done by the RCC, Geneva - combined glass wool, rock wool and slag wool results

Exposure group	No. of animals*	Lung tumours (adenoma & carcinoma) (%)	Mesothelioma (%)
Glass MMVF 10			
0 mg/m^3 (air controls)	131	4 (3.1%)	0
3 mg/m^3 (~30 f/mL)	119	0	0
16 mg/m^3 (~145 f/mL)	121	1 (0.8%)	0
30 mg/m^3 (~230 f/mL)	121	7 (5.8%)	0
Glass MMVF 11			
0 mg/m^3 (air controls)	131	4 (3.1%)	0
3 mg/m^3 (~40 f/mL)	122	4 (3.3%)	0
16 mg/m^3 (~155 f/mL)	122	9 (7.4%)	0
30 mg/m^3 (~250 f/mL)	117	3 (2.6%)	0
Rock MMVF 21			
0 mg/m^3 (air controls)	126	2 (1.6%)	0
3 mg/m^3 (~34 f/mL)	114	5 (4.4%)	0
16 mg/m^3 (~145 f/mL)	115	5 (4.3%)	0
30 mg/m^3 (~247 f/mL)	114	5 (4.4%)	0
Slag MMVF 22			
0 mg/m^3 (air controls)	126	2 (1.6%)	0
3 mg/m^3 (~27 f/mL)	116	2 (1.7%)	0
16 mg/m^3 (~123 f/mL)	115	0	0
30 mg/m^3 (~230 f/mL)	115	3 (2.6%)	0

* Number includes all rats exposed for 12 months, or controls surviving for 12 months.

3.4 Health effects – human studies

Introduction

3.4.1 Since insulation wools have been manufactured and used in increasing amounts for more than sixty years, hundreds of thousands of people worldwide have been exposed to glass wool, rock wool and/or slag wool during manufacture, use and removal. Accordingly, the extent of epidemiological and other data on the human health effects of insulation wools is comprehensive, with research into potential

human health effects concentrated on non-malignant and malignant respiratory disease outcomes through morbidity (illness) and mortality studies. However, acute reversible skin, eye and respiratory irritation have been recognised as potential health effects, and research papers have also been published on these.

Skin and eye irritation

3.4.2 Ever since insulation wools were first manufactured, cases of skin, eye and respiratory irritation have been reported. One US manufacturer commissioned a study in 1942 which investigated glass wool dermatitis by experiments on rabbits and humans[55]. This study demonstrated that the skin reactions associated with glass wool were transitory, of a superficial nature, and easily relieved by "ordinary washing with water". No evidence of skin sensitisation was found. A 1973 British study found 40% of 70 workers experienced "glass fibre rash" when first exposed to glass wool[56]. Rock wool irritation was investigated in 1977 by patch testing 315 human volunteers, of whom 79 (25%) reacted positively to the fibres[57]. This result was similar to 1975 experiments involving glass wool[58]. These and other studies[59, 60] all indicated that the skin irritation and dermatitis associated with insulation wools was an irritant reaction due to the mechanical (microtrauma) effect of relatively large, non-respirable, fibres with diameters > 4 microns.

3.4.3 Eye irritation has also been investigated in a cross-sectional study of 15 workers exposed to rock wool and compared with 15 non-exposed controls61. Significantly higher frequencies of eye symptoms, and cellular changes in the eye, both related to working conditions, were found among exposed workers. It was found that the rock wool fibres exerted the same mechanical and reversible effects on the eyes as on the skin.

Respiratory irritation and disease

3.4.4 Since 1945, numerous epidemiological studies have investigated the respiratory health of people exposed in the manufacture and use of insulation wools. The studies have concentrated on non-malignant respiratory diseases including asthma, bronchitis and lung fibrosis, and on malignant conditions such as lung cancer and mesothelioma. None of the studies has demonstrated a causal association between exposure to glass wool, rock wool and/or slag wool fibres and the development of these or other health effects. The principal investigations have been summarised in the following paragraphs.

3.4.5 No evidence of pneumoconiosis (lung disease due to inhaling dust) or fibrosis (scarring of the lung) was found in people producing rock and slag wool in a 1945 study62. No relationships between exposure to glass wool and lung abnormalities were found in three studies conducted in the years 1968 - 1971 63-65. No respiratory conditions, including asthma, associated with exposure to glass wool were found in a 1982 study of Australian workers employed in the manufacture of insulation wools66.

3.4.6 No lung abnormalities associated with exposure to glass wool or slag wool fibres, were found in a 1983 study with a follow-up in 1990 67, 68. The authors reviewed their studies again in 1995 69 and provided the following summary.

Investigations of employed insulating wool manufacturing workers began in 1979 with two studies of workers in five fibrous glass and two mineral wool plants in the US, with reports published in 1983 (1,000 workers) and 1993 (1,400 workers). Average exposures ranged from below the limit of detection to 1.4 fibres/mL. In both studies, mean lung function levels were normal and related to smoking; levels of function were not associated with indices of fibre exposure; and respiratory symptoms were related to smoking and not to exposure.

3.4.7 A survey of former workers in a factory using glass wool in a manufacturing process suggested lung changes associated with glass wool exposures. However, the design of the study did not permit such a conclusion70. As a result of telephone interviews, the authors of a US study (1993) concluded that members of the Sheet Metal Workers International Association (SMWIA) who had had high insulation wool exposure whilst removing insulation, had an increased risk of bronchitis symptoms, but were not at risk from obstructive airways disease based on lung function testing71. Although the report lacked essential information, it was likely that the symptoms of irritation were related to general dustiness, rather than to fibre exposure. A similar conclusion was reached in a 1998 study of Swedish construction workers that found no effect on lung function from exposure to insulation wools, but symptoms of persistent cough with exposure to mixed dusts72.

3.4.8 A detailed lung function and chest X-ray study (1996) of 670 people employed in the Australian glass wool and rock wool manufacturing industry found no evidence of occupational asthma, pulmonary fibrosis, lung cancer, or occupational pleural disease73. The population consisted of glass wool and rock wool production and clerical workers, as well as 1,840 community referents. Factory exposures were generally well below the Australian Standard of 0.5 f/mL.

Mortality studies

3.4.9 Studies of the causes of mortality, particularly from respiratory system cancers and non-malignant respiratory disease, began in the US in the 1970s and covered workers employed in the manufacture of glass wools (including special purpose glass fibres and continuous filament (textile) glass fibres), rock wool and slag wool. None of these studies found any causal links between exposure to the various fibres and the development of respiratory system cancers, mesothelioma, or chronic respiratory disease74-77. These and other populations of manufacturing plant workers became the cohort (group of workers) for what is now generally referred to as the ongoing US mortality study. It was first reported by Enterline and Marsh in 1987 78.

3.4.10 The US mortality study in 1987 included over 17,000 men employed between 1945 and 1963 in the production of all types of glass fibres, rock wool and slag wool in 17 manufacturing plants78. Analysis of deaths occurring between 1946 and 1982 resulted in statistically significant raised standardised mortality ratios (SMR – see glossary for explanation) for all cancers (SMR = 108) and lung cancer (SMR = 113). The lung cancer SMRs, when analysed by fibre type, were not statistically significant but were elevated being 111 for glass wool, and 131 for

rock wool and slag wool. There were several features which were not consistent with a causal relationship between fibre exposure and raised lung cancer SMRs: (a) lack of relationship with duration of exposure; (b) lack of relationship with cumulative dose of fibres; (c) inconsistencies in the relationship between time since first exposure and death from lung cancer; and (d) in rock/slag workers, those most recently employed experienced the greatest lung cancer excess; and smoking was found to be a confounding factor ie smoking was a likely alternative cause of the lung cancer excess.

3.4.11 Analysis of deaths was extended to cover the period 1946 to 1985 and reported in 1990 79. There were statistically significant raised SMRs for all causes of death (SMR = 103), all cancers (SMR = 110), lung cancer (SMR = 120), non-malignant respiratory disease (SMR = 112), and nephritis and nephrosis (SMR = 146). The data on lung cancer and non-malignant respiratory diseases were then studied in more detail to see whether the raised SMRs could have been caused by specific occupational factors: production process; year of hire; time since first employment; duration of employment; type of plant; age and year of death; intensity of fibre exposure; and cumulative fibre exposure. There were no data on smoking. The authors of the study drew the following conclusions: (a) the raised SMRs for lung cancer and non-malignant respiratory diseases were less than in previous analyses; (b) if there ever had been an occupational cause for the raised SMRs, that cause was present in the distant past and was no longer affecting current workers; (c) detailed analyses demonstrated that raised SMRs were not related to exposure data, so fibres had not been demonstrated to be the cause of disease; (d) the raised SMRs arose mostly from the 1940-50s operations of slag wool plants, and could have been influenced by arsenic from the slag or other confounding (ie alternative) exposures; and (e) there were no raised SMRs from mesothelioma.

3.4.12 In 1991, the principal researcher of the US mortality study commented on the statistically significant lung cancer SMR of 112 for glass wool workers80, based on using the local populations as standard for calculation of the SMRs. The statistical significance was not weighted heavily in the overall assessment of lung cancer risks for the following reasons: (a) the SMR of 112 was only marginally statistically significant because the lower bound of its associated 95% confidence interval of 100.3 - 124.4 barely exceeded the baseline SMR value of 100; (b) an SMR of 112 is of little practical significance because it could be due simply to the inability to control for confounding factors such as cigarette smoking, lifestyle characteristics, racial composition, and occupational and environmental exposures to agents other than fibres; and (c) most occupational epidemiologists regard SMRs below 150 as being difficult to interpret because they were more likely than larger SMRs to be influenced by simple random variability as well as by bias due to confounding. Some epidemiologists believe that true associations between exposure and disease that amount to less than an SMR of 120 are too weak to be detected by epidemiological methods. The author reiterated that detailed analyses revealed no statistically significant patterns of increased lung cancer SMRs associated with any of the indicators of fibre exposure. Compared with the previous 1982 follow-up, the 1985 update revealed somewhat weaker cumulative

evidence overall of a relationship between lung cancer and factors related to work in the glass wool industry.

3.4.13 An explanation for the raised lung cancer SMR in one plant was provided in 199081: In the plant from the US study with the highest lung cancer rate, amosite asbestos fibres at concentrations greater than 1,000,000 per gram of lung tissue were found in four out of six cases of lung cancer, but in none of their matched referents (unexposed workers in the comparison group).

3.4.14 A further update of the US mortality study was published in 1996 82. The 1946 to 1989 mortality experience of an updated rock wool and slag wool subcohort was analysed, and reported that SMRs for all causes combined and for respiratory system cancers were “unremarkable”. They showed no consistent evidence of a causal association with any of the measurements of respirable fibre exposures, with or without adjustment for potential confounding factors that included: year of hire, plant, and co-exposures such as arsenic, asbestos, formaldehyde, phenolics, polycyclic aromatic hydrocarbons, radiation, silica dust, and urea. These findings were corroborated in a nested case-control study that adjusted for tobacco smoking. There were no deaths from malignant mesothelioma in the extended follow-up period.

3.4.15 A mortality study of 2500 people employed between 1955 and 1977 in glass wool and continuous glass filament manufacture in Canada was reported in 1987 83. Analysis of deaths to the end of 1984 has resulted in a statistically significant SMR of 176 for lung cancer. But the interpretation of this raised SMR was difficult because length of exposure and time since first exposed were not consistent with a causal relationship. Follow-up analyses have not been done.

3.4.16 An ongoing large-scale mortality study has also been conducted in Europe, covering more than 20,000 people employed in 13 plants in 7 countries manufacturing glass wool, rock wool, slag wool and continuous filament glass fibres between 1933 and 1961 84. Analysis of deaths to the end of 1982, using local rates as standard for calculation of SMRs, and reported in 1987, resulted in statistically significant raised SMRs for all causes of death (SMR = 111), all cancers (SMR = 111), lung cancer (SMR = 125), accidents, poisoning and violence (SMR = 153), and suicide (SMR = 130). SMRs for mesothelioma, non-malignant respiratory diseases and pneumoconiosis were not significantly raised. For glass wool workers, the SMR for lung cancer was 103 for all workers, but 138 for those first employed thirty or more years before death. The corresponding SMRs for rock/slag wool workers were 124 and 185. None of these raised SMRs was statistically significant. In neither glass wool nor rock/slag wool workers was there any relationship between duration of exposure, nor any evidence of a dose-response relationship.

3.4.17 The European cohort mortality study was extended to include all deaths up to 1990 and reported in 1995 85. The person-years at risk had increased to 409,000 with 4,521 deaths from all causes. Statistically significant results included raised SMRs for: all causes (114); all malignant tumours (113); trachea, bronchus and lung (132) based on 344 deaths; cirrhosis of the liver

(158); accidents, poisonings and violence (148) based on 546 deaths; and suicide (150) based on 187 deaths. SMRs for respiratory system cancer were 148 for those employed less than one year, and 129 for those employed longer than one year. There were no findings suggesting a causal relationship between duration of employment or type of employment and increased SMRs for respiratory system cancer. In contrast to the original 1987 report, there was no clear relationship between lung cancer mortality and first employment in the early, intermediate or late technological phases in either glass wool or rock/slag wool production workers. In both the glass wool and rock/slag wool sectors of the cohort, lung cancer SMRs between 1983 and 1990 were lower than SMRs up to 1982. The authors suggested that any "excess risk may be concentrated among workers starting their employment in the industry more than 40 years ago". Their overall conclusion was that "the issue of confounding by tobacco smoking and other occupational exposures should now be addressed, combined with as accurate as possible assessment of past individual exposure to respirable fibres, in a case-control analysis nested in the cohort".

3.4.18 A further follow-up of the European mortality study was reported in 1997 86. Twenty-two thousand production workers were followed over time with 4,521 deaths. Workers with less than one year of employment had an increased mortality rate with an SMR of 145 and the SMRs for cancer of trachea, bronchus and lung in workers employed > 1 year were as follows: rock or slag wool: 134, glasswool: 127, and glass wool adjusted for local mortality rates: 112. The excess of lung cancer in the glass wool workers did not persist when local (not national) mortality rates were applied. In the rock/slag wool group, the lung cancer was concentrated among workers in maintenance and in secondary production. The trend from previous studies that showed that lung cancer risk was mainly in those working in the early technological phase of rock and slag wool production was less marked in this follow-up. The authors postulate that tobacco smoking, social class, and carcinogenic exposures outside the insulation wool industry are other possible explanations of the association between lung cancer, but it appeared unlikely that the potential confounders explained the whole increase in lung cancer risk associated in employment with rock and slag wool.

3.4.19 The European study team have also reported the latest update of cancer incidence among workers employed in the manufacture of glass wool, rock wool, and slag wool during the years from 1933 to 1995 87. The factories were in Denmark, Finland, Norway and Sweden and the report was part of the continuing analyses being done by the International Agency for Research on Cancer (IARC). Small, non-significant, increased rates of lung cancer were found, as previously, in both the glass wool and rock or slag wool workers, but exposures to fibres did not show any causal association: "As in the mortality analysis, the increased risk of lung cancer among insulation wool workers cannot be attributed to fibre exposure. We have so far been unable to disentangle the contributions to the increase in lung cancer of extra-occupational factors, such as tobacco smoking".

3.4.20 Another publication from the IARC on-going research reported on non-cancer causes of death of workers exposed to glass wool, rock wool and slag wool during

production in factories in Denmark, Finland, Norway, Sweden, United Kingdom, Germany and Italy88. The study population comprised 11,373 workers employed for at least one year between the years 1933 to 1992 – in total they contributed 256,352 person-years of observation. Overall, no increased risks were found for any of the diseases of concern, particularly bronchitis, emphysema, asthma and all non-malignant respiratory diseases.

Case-control studies

3.4.21 In a case-control study published in 1991, a cohort of 4,841 men were identified who had worked more than one year at one of the nine slag wool plants89. Of 504 deaths that occurred between 1970 and 1989, 61 were attributed to lung cancer. Fifty-five of these were traced and matched with 98 controls. The controls were individually matched controls randomly selected from the 443 deaths other than lung cancer. The authors found no increased lung cancer risk associated with exposure to slag wool, and analysis by cumulative fibre exposure did not indicate any trend. As expected, cigarette smoking was found to be responsible for the observed increased lung cancer mortality in this group of workers, and the risk increased with increasing pack-years of cigarette smoking.

3.4.22 The largest of the 17 plants in the US mortality study (Newark, Ohio which produces glass wool fibres) has been investigated thoroughly since 1990 to identify possible risk factors within and external to the plant90-92. In relation to the external non-occupational risk factors, the authors concluded that smoking was the most important non-workplace factor for risk of lung cancer in this group of workers. Smoking did not appear to play such an important part in the mortality from non-malignant respiratory disease. Another important finding was that the prevalence of smoking for Newark in 1955 appeared to be sufficiently greater than the corresponding United States data in 1955 to suggest that some of the previously reported excess of lung cancer for Newark based on US mortality may be accounted for by differences in the prevalence of cigarette smoking90.

3.4.23 In a 1993 report on occupational risk factors at the Newark plant, results of the investigation clearly indicated that neither respirable fibres nor any of the substances investigated as part of the plant environment were statistically significant factors for lung cancer risk91. Smoking was the most important factor in risk for lung cancer in the population.

3.4.24 A third report (1995) based on the Newark plant described the results of a case-control study conducted at the glass fibre plant which comprised 38% of the workers in the US cohort92. The authors concluded that adjustment of the national-based SMR for the confounding effect of smoking reduced the lung cancer SMR to a non-statistically significant level. When the information from the case-control study was considered, plant exposures, including respirable glass fibres, did not appear to be responsible for the non-statistically significant raised SMR for lung cancer. It was concluded that the raised SMR was likely to be due to some unknown set of social, demographic or chance factors.

3.4.25 In a 1987 study of 135,000 Swedish construction workers, a case-control study was carried out on 518 cases of lung cancer93. The overall lung cancer incidence was below that expected, but there was a risk associated with high asbestos exposure. There was no lung cancer excess associated with insulation wool exposures.

3.4.26 A smaller, single user industry mortality study (1992) has been done in the Swedish prefabricated house industry94. The aim of the study was to investigate the lung cancer risk after exposure to insulation wool in an occupational environment where confounding exposures were less pertinent. The conclusion of the study was that lung cancer mortality was somewhat lower than expected, and there was no correlation with exposure levels or duration of employment. Analysis of cancer incidence gave similar results.

Comments on US and European mortality studies

3.4.27 Even after the latest completed follow-up studies, the authors of the European cohort mortality studies remain equivocal in their interpretations of the patterns of lung cancer observed. Particularly for the rock and slag wool production workers in Europe, the excess of lung cancer has been considered as a possible result of exposure to airborne fibres. “Despite the difficulty to rule out the possibility of a confounding effect by tobacco smoking or occupational exposures outside the [rock/slag wool] industry, a carcinogenic effect of exposures occurring in the [rock/slag wool] working environment is a credible explanation of the findings. ..... The ensemble of these results is not sufficient to conclude that the increased lung cancer risk is related specifically to exposure to MMVF: however, insofar as respirable fibres were a significant component of the ambient pollution of the working environment, they may have contributed to the increased risk.”85, 86

3.4.28 However, as described above in paragraph 4.13, there was clear evidence of asbestos exposure at one of the US plants. The latest update of the US study considered that plant separately, and there was then no evidence of an excess of lung cancer in the remaining rock/slag wool plants, except among the short-term workers95.

3.4.29 There is now similar evidence in Europe that there was asbestos-exposure and asbestos-related lung cancers and mesotheliomas at one of the rock wool plants. Additional epidemiological analyses have been carried out excluding that plant. As in the American study, there was an excess of lung cancer among the short-term workers. For the longer-term workers, excluding the plant with asbestos exposure, the overall lung cancer rate was not significantly raised, nor was there any significant association with time since first employment or duration of employment95.

3.4.30 A lung cancer case-control study in the European stone wool production sector commenced in late 1996. The study includes enquiries from next-of-kin concerning smoking habits, and estimates of exposure to a range of possible environmental contaminants. This study should help resolve the interpretation of

the European mortality study, which has not yet included adjustment of estimated lung cancer risk for smoking habits in any of its analyses.

3.5 Summary and conclusions

3.5.1 The International Agency for Research on Cancer (IARC), in its Monograph No. 43 published in 1988 96, evaluated glass wool (including special purpose glass fibres), rock wool, and slag wool as Group 2B, possibly carcinogenic to humans. Since the IARC evaluations, there has been extensive research into the multiple factors which determine whether varieties of insulation wool could be potentially toxic and/or carcinogenic to humans. In particular, data have been gathered on mechanisms of action and biopersistence from inhalation experiments; state-of-the-art animal inhalation models have been developed for chronic toxicity and carcinogenicity studies; and human epidemiology studies on morbidity and mortality, updated by additional analyses, case-control studies, and detailed characterisation of exposures and smoking histories, have provided enhanced information on tens of thousands of exposed workers.

3.5.2 The available studies published on possible health effects of insulation wools were reviewed in this report. It should be noted that all types of insulation wools, particularly the coarse fibres and dusts, may cause acute, reversible symptoms including itching of the skin, and discomfort of the eyes, nose and respiratory system. An evaluation of each type of insulation wool in terms of toxicity (respiratory disease), and carcinogenicity (lung cancer and/or mesothelioma) is as follows:.

Insulation wools - glass wool, rock wool, and slag wool

- sufficient evidence for the non-toxicity of glass wool and slag wool, and the non-carcinogenicity of glass wool, slag wool and rock wool in experimental animals;
- sufficient evidence for the toxicity of rock wool in experimental animals;
- sufficient evidence for the non-toxicity and non-carcinogenicity of glass wool, rock wool and slag wool in human morbidity studies; and
- sufficient evidence for the non-toxicity and non-carcinogenicity of glass wool, rock wool and slag wool in human mortality studies.

New ‘bio-soluble’ insulation wools

- sufficient evidence for the non-toxicity and non-carcinogenicity of the even more soluble ‘bio-soluble’ insulation wools in experimental animals; and
- no data on toxicity and/or carcinogenicity in humans.

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4. Synthetic vitreous fibres – special purpose glass fibres

4.1 Introduction

4.1.1 Special purpose glass fibres are made from molten glass and fiberised by the flame attenuation process. Whilst similar to glass wools, they contain more aluminium oxide and are made to much finer diameters (0.1 micron - 3.0 microns). These differences have been shown to result in the potential for high concentrations of respirable fibres during use such as in aircraft insulation - range 0.4 - 24.4 f/mL; mean 4.6 f/mL[1]. However, the total production of special purpose glass fibres is less than 1% of all SVF, and they are used in limited applications such as in aeronautical insulation and special air filters.

4.2 Health effects – animal studies

Intracavity studies

4.2.1 Numerous intraperitoneal and intrapleural studies (see glossary) have been conducted, mostly using JM100 and JM104 (formulation 475) special purpose glass fibres with diameters generally in the range 0.1 – 0.5 microns. Intrapleural tests were positive in Osborne-Mendel rats2, Wistar rats3, and Sprague-Dawley rats4, 5, with malignant tumour incidences ranging from 8% to 62%.

4.2.2 Intraperitoneal tests have also been positive in Wistar rats6, 7, Sprague-Dawley rats6, and Osborne-Mendel rats8. The tumour incidence rates for these positive tests ranged from 25% to 80%. Several negative studies were also reported in both intrapleural2 and intraperitoneal9 studies.

Intratracheal instillation studies

4.2.3 Numerous intratracheal instillation studies in rats and hamsters using coated and uncoated special purpose glass fibres (JM100) of 1.0 micron or less median diameter were negative10, 11. Negative results were also obtained with fine diameter (0.45 m) JM100 special purpose glass fibres in Osborne-Mendel rats, though in this study 7/22 (32%) developed pulmonary fibrosis.

4.2.4 Positive results were found in intratracheal instillation studies using finer diameter (< 0.2 micron) special purpose glass fibres (JM 104/475) in Wistar rats - 5/34 (15%) tumours in one group of rats6, 10/55 (18%) in a second group12, and 17/38 (45%) in a third group of rats12. Positive results were also obtained with similar fibres in Syrian hamsters13.

Inhalation studies

4.2.5 Animal inhalation studies prior to using special purpose glass fibres (mostly JM100 and JM104/475) have all been negative in rats4, 8, 10, 14, 15-17, hamsters8, 10, 11, and monkeys16. However, a chronic inhalation study in Syrian Golden hamsters was completed by the Research Consulting Company (RCC) in Geneva in accordance with the “gold-standard” protocols18. In this chronic toxicity and carcinogenicity inhalation study19 of a typical building insulation glass wool (MMVF 10a), hamsters were shown to be highly sensitive to

the induction of mesotheliomas with RCF. A special purpose glass fibre (MMVF 33) and amosite asbestos were used for comparative purposes. Groups of 140 weanling male Syrian golden hamsters were exposed via nose-only inhalation for 6 hours/day, 5 days/week for 78 weeks to either filtered air (chamber controls) or MMVF 10a, MMVF 33, or amosite asbestos at 300 WHO fibres/mL, (see glossary for definition of WHO fibres) with two additional amosite asbestos groups at 25 and 125 WHO fibres/mL. After 13, 26, 52, and 78 weeks, various pulmonary parameters and lung fibre burdens were evaluated. Groups of hamsters were removed from exposure at 13 and 52 weeks and were held until 78 weeks (recovery groups). Initial lung deposition of long fibres more than 20 microns after a single 6-hour exposure was similar for all three fibres exposed to 300 fibres/mL. Glass wool showed inflammation (which regressed in recovery hamsters) but no pulmonary or pleural fibrosis (lung scarring) or neoplasms (tumours). Special purpose glass fibres induced more severe inflammation and mild interstitial and pleural fibrosis by 26 weeks that progressed in severity until 52 weeks, after which it plateaued. While the inflammatory lesions regressed in the recovery animals, pulmonary or pleural fibrosis did not. A single multicentric mesothelioma (cancer arising out of the lining of the lung) was observed at 32 weeks. No neoplasms were found in the remainder of the study. Amosite asbestos produced dose-related inflammation and pulmonary and pleural fibrosis as early as 13 weeks in all three exposure levels. The lesions progressed during the course of the study, and at 78 weeks severe pulmonary fibrosis with large areas of consolidation was observed in the highest two exposure groups. Progressive pleural fibrosis with mesothelial hypertrophy and hyperplasia was present in the thoracic wall and diaphragm in most animals and increased with time in the recovery hamsters. While no pulmonary neoplasms were observed in the amosite exposed hamsters, a large number of mesotheliomas were found; 25 f/mL, 3.6%; 125 f/mL, 25.9%; and 250 f/mL, 19.5%. For the three fibre types, the severity of the lung and pleural lesions generally paralleled the cumulative fibre burden, especially those over 20 microns in length, in the lung, thoracic wall, and diaphragm. They also inversely paralleled the in vitro dissolution rates; that is, the faster the dissolution, the lower were the cumulative lung burdens and the less severe the effects.

4.3 Health effects – human studies

4.3.1 Exposure to special purpose glass fibres has been limited since these materials have been manufactured in small amounts for limited speciality uses. Refractory ceramic fibres (RCF) were first produced commercially forty years ago, and although production and use has grown in the past 20 years, relatively few people have been exposed when compared with insulation wools. Accordingly, the extent of epidemiological and other data on the human health effects of SVF is variable with comprehensive data on insulation wools, but sparse data on other fibres.

4.3.2 Human health effects associated with special purpose glass fibres have been investigated as part of the study populations in the major US morbidity and mortality studies set up to study insulation wools. As appropriate, reference has been made to special purpose glass fibres in the following sections.

Skin, eye, and respiratory irritation

4.3.3 No studies have reported skin, eye or respiratory irritation associated with the manufacture and use of special purpose glass fibres.

Respiratory disease morbidity studies

4.3.4 No lung abnormalities associated with exposure to glass wool or slag wool fibres, including special purpose glass fibres, were found in a 1983 study with a follow-up in 1990. There was a suggestion of an association between slight X-ray abnormalities and exposure to special purpose fine glass fibres in 1983, but the 1990 follow-up showed no abnormalities20, 21. The authors reviewed their studies again in 199522 and provided the following summary. Investigations of employed insulating wool manufacturing workers began in 1979 with two studies of workers in five fibrous glass and two mineral wool plants in the US, with reports published in 1983 (1,000 workers) and 1993 (1,400 workers). Average exposures ranged from 0.0032 to 1.4 fibres/mL. In both studies, mean lung function levels were normal and related to smoking; levels of function were not associated with indices of fibre exposure; and respiratory symptoms were related to smoking and not to exposure.

4.3.5 In the earlier (1983) study, minimum duration of employment was five to ten years, depending on the size of the plant. Small opacities (shadows) on chest X-ray were of low prevalence (3.3%) and low profusion - 1/0 or 1/1 by median of readings, indicating the lowest density of small shadows that can be detected on chest X-ray, using the International Labour Office Classification of the Pneumoconioses. Opacities were related significantly to age, smoking and lung function and there were significant differences in prevalences (more than or equal to 1/0) across the plants: 7.5% for workers in two plants producing both ordinary (nominal diameter = 1 – 3 microns) and fine (nominal diameter = 1 micron) glass fibres, 1.7% for workers in the other five plants combined22.

4.3.6 For current smokers, there were relationships between small opacities (more than or equal to 0/1) and several indices, beyond age and amount smoked, within the two ordinary/ fine fibre plants. However, there were no significant relationships between small opacities (more than or equal to 1/0) and any exposure indices. Because of the confounding between plants and geographic region and X-ray facility, the second study (1990) was undertaken using a modified study design. No minimum employment time was required, resulting in a younger cohort with shorter exposure duration for each location; comparison blue-collar workers were included (using the same X-ray facility); and five readers were used22. A lower prevalence of small opacities was found than earlier. There were no significant differences in prevalences among the MMVF and comparison workers and no clear evidence of exposure relationships with small opacities on X-ray.

Cohort mortality studies

4.3.7 Studies of the causes of mortality, particularly from respiratory system cancers and non-malignant respiratory disease, began in the US in the 1970s and covered workers employed in the manufacture of glass wools (including special purpose

glass fibres and continuous filament (textile) glass fibres), rock wool and slag wool. None of these studies found any causal links between exposure to the various fibres and the development of respiratory system cancers, mesothelioma, or chronic respiratory disease23-26. These and other populations of manufacturing plant workers became the cohort for what is now generally referred to as the ongoing US mortality study, first reported by Enterline and Marsh in 198727.

4.3.8 The US mortality study in 1987 included over 17,000 men employed between 1945 and 1963 in the production of all types of glass fibres, rock wool and slag wool in 17 manufacturing plants27. Analysis of deaths occurring between 1946 and 1982 resulted in statistically significant raised standardised mortality ratios (SMR) for all cancers (SMR = 108) and lung cancer (SMR = 113). The lung cancer SMRs, when analysed by fibre type, were not statistically significant but were elevated being 111 for glass wool, and 131 for rock wool and slag wool. There were several features which were not consistent with a causal relationship between fibre exposure and raised lung cancer SMRs: lack of relationship with duration of exposure; lack of relationship with cumulative dose of fibres; inconsistencies in the relationship between time since first exposure and death from lung cancer.

4.3.9 Analysis of deaths was extended to cover the period 1946 to 1985 and reported in 199028. There were statistically significant raised SMRs for all causes of death (SMR = 103), all cancers (SMR = 110), lung cancer (SMR = 120), non-malignant respiratory disease (SMR = 112), and nephritis and nephrosis (SMR = 146). The data on lung cancer and non-malignant respiratory diseases were then studied in more detail to see whether the raised SMRs could have been caused by specific occupational factors: production process; year of hire; time since first employment; duration of employment; type of plant; age and year of death; intensity of fibre exposure; and cumulative fibre exposure. There were no data on smoking. The authors of the study drew the following conclusions: the raised SMRs for lung cancer and non-malignant respiratory diseases were less than in previous analyses; if there ever had been an occupational cause for the raised SMRs, that cause was present in the distant past and was no longer affecting current workers; detailed analyses demonstrated that raised SMRs were not related to exposure data, so fibres had not been demonstrated to be the cause of disease; the raised SMRs arose mostly from the 1940-50s operations of slag wool plants, and could have been influenced by arsenic from the slag or other confounding exposures; and there were no raised SMRs from mesothelioma.

4.4 Summary and conclusions

4.4.1 The International Agency for Research on Cancer (IARC), in its review in monograph No. 43 published in 1988 29, evaluated special purpose glass fibres as Group 2B, possibly carcinogenic (cancer causing) to humans. Since the IARC evaluations, there has been extensive research into the multiple factors that determine whether varieties of SVF could be potentially toxic and/or carcinogenic to humans. In particular, data have been gathered on mechanisms of action and biopersistence from inhalation experiments; and state-of-the-art animal

inhalation models have been developed for chronic toxicity and carcinogenicity studies.

4.4.2 The available studies published on possible health effects of special purpose glass fibres were reviewed in this chapter, and evaluated in terms of toxicity (respiratory disease) and carcinogenicity (lung cancer and/or mesothelioma) as follows.

- sufficient evidence for the toxicity and carcinogenicity of special purpose glass fibres in experimental animals;
- sufficient evidence for the non-toxicity of special purpose glass fibres in human morbidity studies;
- sufficient evidence for the non-toxicity and non-carcinogenicity of special purpose glass fibres in human mortality studies.

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5. Synthetic vitreous fibres – refractory ceramic fibres

5.1 Introduction

5.1.1 The term refractory ceramic fibres (RCF) refers to high-purity aluminosilicate wool fibres which are made by spinning a melt of calcined kaolin or pure alumina and silica[1]. Five compositions are in common use: 50/50 wt% alumina/silica (maximum use temperature of 1250°C), 60/40 wt% (1400°C), and chromia-, boria-, or zirconia-modified 50/50 wt% alumina/silica (also for use at 1400°C). Most RCF products have mean diameters in the range of 2-3 microns.

5.1.2 The principal use for RCF is for hot-face insulation of pottery kilns and metal working furnaces. Most commonly, they are manufactured as low density flexible blanket, but alternatively, rigid boards and shapes can be created by vacuum-forming wet slurries of raw fibres with a refractory binder such as silica sol. Resin binders are unable to be used in RCF products because of the high in-use temperatures, with the result that it is relatively easy to generate airborne fibres during installation and removal.

5.2 Health effects – animal studies

Intracavity studies

5.2.1 Intraperitoneal studies (space between the lining of the abdomen and pelvis and the intestine and internal organs) have found that two types of refractory ceramic fibres, when injected into the peritoneum of female Wistar rats at doses of 45mg and 75mg, have resulted in tumour (mesothelioma or sarcoma) incidences of 33/47 (70%) and 12/54 (22%)2. In another study, RCF fibres were injected into the peritoneum of two groups of Syrian hamsters and one group of Osborne-Mendel rats. All animals each received 25mg of fibres; 100% of the animals developed abdominal fibrosis/reactive tissue; and 2/15 (13%) and 5/21 (24%) of hamsters, and 19/23 (83%) of rats developed abdominal malignant tumours3. One intrapleural study (in the cavity between the lining of the lung and chest wall) of RCF was negative4.

Intratracheal instillation studies

5.2.2 Intratracheal instillation (in the windpipe) studies, using refractory ceramic fibres of 1.8 microns diameter, were done on Syrian hamsters and Osborne-Mendel rats3. None of the animals (0/25 hamsters and 0/22 rats) developed lung tumours. However, 6/22 rats had “bronchiolar epithelial polypoid lesions“ (ie polyps in the air passages of the lung) which were considered to be a chronic inflammatory response and not tumour formation, and 16% of hamsters and 9% of rats developed pulmonary fibrosis (lung scarring).

Inhalation studies

5.2.3 Early long-term inhalation studies of RCF fibres in experimental animals found a lung tumour incidence rate of 8/48 (17%) in Wistar rats5, 0/55 in Osborne-Mendel rats3, and 1/70 in Syrian hamsters3. In the Osborne-Mendel rats, 12/55

(22%) were reported as having reversible fibrosis (Wagner Grade6 less than 4 – see glossary for explanation), and the one tumour in the hamsters was a "mesothelioma of the lung".

5.2.4 Because of limitations in these studies (presence of non-rat-respirable fibres and non-fibrous particulates), inhalation experiments developed by the Research and Consulting Company (RCC) in Geneva used size selected RCF fibres with diameters 1.0 microns and approximately 25 microns length. Three types of RCF have been tested at the RCC - Kaolin based aluminium silicate (RCF1), aluminium zirconia silica (RCF2), high purity aluminium silicate (RCF3), and an "after-service" Kaolin fibre, obtained by heating RCF1 in a furnace at 2400oC for 24 hours (RCF4). RCF4 contained approximately 27% free crystalline silica, cristobalite. Maximum tolerated dose chronic inhalation studies (30 mg/m3 equivalent to 200-260 f/mL), using all four fibre types, were conducted in Fischer 344 rats5; a single dose chronic inhalation study (30mg/m3 or approximately 220 f/mL) using RCF1 was conducted on Syrian Golden hamsters7, and multiple-dose chronic inhalation studies (3 mg/m 3, 9 mg/m 3, 16 mg/m 3 or approximately 36, 91 and 162 f/mL) using RCF1 was conducted on Fischer 344 rats8.

5.2.5 In the rats: all types of RCF, when tested at the high exposure of 260 f/mL, resulted in irreversible grades of fibrosis (Wagner scale averaging 4.2 to 4.6), lung tumour incidences of 3.4% to 15.7% (RCF1 16/123; RCF2 9/121; RCF3 19/121; RCF4 4/118), and mesothelioma incidences of 0.8% to 2.4% (RCF1 2/123; RCF2 3/121; RCF3 2/121; RCF4 1/118). The multidose study of RCF1 (kaolin based aluminium silicate fibres) demonstrated dose-dependent lung fibrosis and lung tumours, and found a random incidence of mesothelioma and mesothelial proliferation with 8.9% mesotheliomal abnormalities at the highest exposure.

Table 1 Multidose study of Kaolin RCF in F344 rats

group (mg/m^3)	number at risk	fibrosis (Wagner Grade)	lung tumours (%) (adenoma + carcinoma)	mesothelial proliferation (%)	mesothelioma (%)
0	129	1.0	1 (0.8)	1 (0.8)	0
3	123	2.9	2 (1.6)	0	0
9	127	3.8	5 (3.9)	1 (0.8)	1 (0.8)
16	124	4.0	2 (1.6)	1 (0.8)	0
30	123	4.3	16 (13.0)	9 (7.3)	2 (1.6)

NB: Number at risk is the number of animals surviving 12 months of exposure.

5.2.6 In the hamsters, lung fibrosis was also demonstrated at the Wagner Grade 4.0 level, but lung tumours were not found. However, the outstanding finding of this study was mesothelioma in 42/102 (41%) of the animals.

5.3 Health effects – human studies

Introduction

5.3.1 The extent of epidemiological and other data on the human health effects of SVF is variable with comprehensive data on insulation wools, but sparse data on RCF and other fibres. Overall, research into potential human health effects has concentrated on non-malignant and malignant respiratory disease outcomes through morbidity and mortality studies. Whilst acute reversible skin, eye and respiratory irritation have been well recognised symptoms, few research papers have been published on local irritant effects.

Skin, eye, and respiratory irritation

5.3.2 Because RCF consists mostly of fine fibres in the 2 - 3 microns diameter range, and resin binders are not used, local irritation would not be expected as a significant health concern. However, a European respiratory health study found frequent skin and eye symptoms in workers manufacturing RCF9. In a study population of 628, 36% reported skin irritation, 41% eye irritation, and 55% nasal stuffiness.

Respiratory disease morbidity studies

5.3.3 Pleural changes were found on the standard chest radiographs of some workers manufacturing RCF in the United States during an industry-wide respiratory health study10. Data were collected from 652 current workers at three facilities and from current and former workers at two. This case-control study used a comprehensive characterization of possible asbestos exposure to investigate asbestos as the potential causative agent of chest-radiographic changes. Chest radiographs of 20 workers (3.1%) demonstrated 19 pleural plaques and one diffuse pleural thickening. Nine of 72 workers (12.5%) with more than 20 years since their first fibre-production job had plaques (odds ratio [OR] = 9.5; 95% confidence interval [CI] = 1.9 to 48.2). Five of 19 workers with more than 20 years in fibre-production work (26.3%) had plaques (OR = 22.3; 95% CI = 3.6 to 137.0). Similarly, adjusted ORs demonstrated a progressive relationship between cumulative fibre-months per millimeter (fibre-mo/mL) exposure and plaques. The case-control study confirmed that asbestos exposure did not account for the observed association between fibre exposure and plaques. A validity review of historical films demonstrated biologic plausibility for the association, since sufficient latency (lag time) existed from the time of first RCF exposure to the development of plaques. There was no significant increase in parenchymal (lung tissue) changes consistent with interstitial fibrosis (scarring). There have been no reports that the radiographic changes have been further investigated by the use of high-resolution CT scans.

5.3.4 In the European study9, the respiratory health of 628 current employees in the manufacture of refractory ceramic fibres in seven plants in three countries was studied by means of a respiratory questionnaire, lung function tests, and chest radiography. Exposure estimates were obtained by combining occupational histories with occupational hygiene data obtained from personal fibre and dust

monitoring done at the time of the respiratory health study. The authors concluded that exposure to ceramic fibres was associated with frequent symptoms of local skin, nose and eye irritation, and that cumulative exposure could, by promoting the effects of cigarette smoke, cause obstructive airways disease. After adjustment for smoking, age, sex and plant, shortness of breath more than or equal to grade 2 and wheeze increased significantly with exposure, particularly in the highest exposure group. No radiographic changes attributable to exposure were reported. A significant correlation was found between cumulative exposure to respirable fibres and decrements (loss) in FEV1 and FEF25 - 75 in current smokers, and FEV1 in ex-smokers, after adjusting for potential confounding by past dust exposures. Lung function in never-smokers was not found to be modified by fibre exposure.

5.3.5 The European study also investigated the role of dust exposure, rather than fibre exposure, as the cause of the respiratory health effects11. Odds ratios (see glossary for explanation of ORs) were calculated for symptoms and current exposure by multiple logistic regression, and multiple linear regression coefficients for lung function related to cumulative exposures controlled for the effects of respirable fibre and inspirable mass separately and together. The authors concluded that: (i) acute symptoms (skin, nose, eye, and/or respiratory irritation) were related to both inspirable dust and respirable fibre exposure; and (ii) decrements (loss) of lung function were related to the fibre constituent of the exposure.

5.3.6 An industry-wide respiratory health study has been undertaken in the United States12 of employees manufacturing refractory ceramic fibres at five US sites between 1987 and 1989. Of the 753 eligible current employees, 742 provided occupational histories and also completed the American Thoracic Society respiratory symptom questionnaire; 736 also performed pulmonary function tests. Exposure to refractory ceramic fibres was characterised by classifying workers as production or non-production employees and calculating the duration of time spent in production employment. The risk of working in the production of refractory ceramic fibres and having one or more respiratory symptoms was estimated by adjusted odds ratios (see glossary for explanations of ORs, confidence intervals, p values) and found to be 2.9 (95% confidence interval 1.4 – 6.2) for men and 2.4 (95% confidence interval 1.1 – 5.3) for women. The effect of exposure to refractory ceramic fibres on tests of lung function (see glossary for explanation of FEV1, FVC and FEF) including forced vital capacity (FVC), forced expiratory volume in 1 second (FEV1), the ratio of the two (FEV1/FVC), and forced expiratory flow (litres/second) between 25% and 75% of the FVC curve (FEF25-75) was evaluated by multiple regression analysis using transformed values adjusted for height, by dividing by the square of each individual's height. For men, there was a significant decline in FVC for current and past smokers of 165.4 mL (p less than 0.01) and 155.5 mL (p = 0.04), respectively, per 10 years of work in the production of refractory ceramic fibres. For FEV1, the decline was significant (p less than 0.01) only for current smokers at 134.9 mL. For women, the decline was greater and significant for FVC among nonsmokers, who showed a decrease of 350.3 mL (p = 0.05) per 10 years of employment in the production of refractory ceramic fibres. That is, both men and

women exposed to RCF in manufacturing were found to have declining lung function, but the decline was greater in women, even in the absence of smoking. These findings indicate that there may be important sex differences in response to occupational and/or environmental exposure.

5.3.7 In addition to the study of respiratory health, a study was done of airborne fibre dimensions found on 118 personal samples collected over a 20-year period in the US RCF manufacturing industry13. All samples were analysed by transmission electron microscopy (TEM). The fibre characteristics were diameters ranging from less than 0.19 to 1.0 micron, of which 75% were less than 0.6 microns; and lengths ranging from less than 0.6 to more than 20 microns, with 68% of fibres between 2.4 and 20 microns. The authors concluded that exposures in RCF manufacturing included airborne fibres with dimensions historically associated with biological effects in the lung lining. This study gave no quantitative data on RCF fibres/mL.

5.3.8 Whilst health effects have not been reported from exposure to dusts and fibres during the removal of RCF products, there may be an added risk from this type of work because of the partial conversion, during use at high temperatures, of RCF to cristobalite, a form of crystalline silica14.

Mortality studies

5.3.9 No mortality studies of RCF exposed workers have been reported. However, as part of the US morbidity study10, a concurrent study was established to analyse the mineralogical content of lung tissue obtained from participants in the main study. 426 participants provided informed consents for the donation of lung tissue at the time of elective surgery or death15. Mineralogical analysis has been performed on tissue collected from three male workers who spent a total of 13, 16 and 17 years working in RCF production. All three demonstrated increased lung fibre burdens when compared with controls, and 20% to 80% of the fibres counted were RCF. Some RCF had a “moth eaten” appearance suggesting disintegration. Diffuse interstitial fibrosis was not found, but the lung tissue in all three cases had “patchy fibrosis of respiratory bronchioles and the adjacent interstitium” ie patchy scarring of the small air passages and lung tissue.

5.4 Summary and conclusions

5.4.1 The International Agency for Research on Cancer (IARC) in its review in Monograph No 43 published in 198816, evaluated refractory ceramic fibres (RCF) as Group 2B, possibly carcinogenic (causing cancer) to humans. Since the IARC evaluation, there has been extensive research into the multiple factors that determine whether varieties of SVF, including RCF, could be potentially toxic and/or carcinogenic to humans. In particular, data have been gathered on mechanisms of action and biopersistence from inhalation experiments, and state-of-the-art animal inhalation models have been developed for chronic toxicity and carcinogenicity studies.

5.4.2 The available studies published on the possible health effects of RCF were reviewed for this chapter, and evaluated in terms of toxicity (respiratory disease) and carcinogenicity (lung cancer and/or mesothelioma) as follows:

- sufficient evidence for the toxicity and carcinogenicity of RCF in experimental animals;
- limited evidence for the toxicity of RCF in humans;
- no data on the carcinogenicity of RCF in humans.

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6. Synthetic vitreous fibres – refractory fibres other than RCF

6.1 Introduction

6.1.1 Refractory fibres, which are also used at temperatures above 1000°C, are distinguishable from RCF by their greater durability at high temperatures and by the fact that they have polycrystalline microstructures rather than being amorphous[1]. A wide variety of fine diameter refractory fibres have been developed during the past twenty-five years and include: titanates (potassium octatitanate and hexatitanate); silicon carbide whiskers (diameter 0.1-0.5 micron); silicon nitride whiskers (0.5-2.0 microns); and high-alumina fibres (1.0-5.0 microns). Additionally, continuous filament yarns with diameters up to 150 microns are made using similar chemical formulations. All refractory fibres other than RCF have complex compositions and microstructures so that each should only be referred to by its unique trade name, such as “Tokomax”, “Fibermax”, “Silar SCS9", “Saffil RF”, etc.

6.1.2 Although manufactured and used in relatively small quantities compared with RCF and other SVF, these fibres, particularly the whiskers, pose the greatest potential health risks because of their similarities to amphibole asbestos: fine diameters; crystalline structure; and resistance to dissolution.

6.2 Health effects – animal studies

Intracavity studies

6.2.1 Intrapleural studies have been done on a variety of refractory fibres other than RCF using female Osborne-Mendel rats2, resulting in malignant tumour (sarcoma) incidences: two samples of potassium titanate fibres yielded incidences of 21/29 (72%) and 20/29 (69%); silicon carbide fibre 17/26 (65%); and five samples of aluminium oxide fibres ranged from 4/22 (18%) to 15/24 (63%). Four other aluminium oxide fibres and one zirconium oxide fibre all resulted in one or two sarcomas (tumours) each. The incidences of malignant tumours (sarcomas) were found to correlate well with the number of fibres with diameters less than or equal to 0.25 micron; and lengths more than 8 microns in the test materials. Another intrapleural injection study using Fischer 344/N rats found that silicon carbide whiskers (fibre diameter less than 1 micron) were of similar potency to crocidolite asbestos in the induction of mesothelioma3. In the same study, injection of coarse (10-30 micron diameter) continuous ceramic filaments did not result in mesothelioma. Negative results, ie no malignant tumours in treated animals or controls, were obtained when Saffil® fibres (more than 95% alumina with 3-4% silica, median diameter 3.3 microns) were implanted into the pleural cavities of female rats - 24 rats treated with new fibres, 24 treated with fibres following treatment at more than 1000oC, and 48 controls4. Intraperitoneal studies with refractory fibres other than RCF have not been reported.

Intratracheal instillation studies

6.2.2 No data on intratracheal instillation studies have been reported.

Inhalation studies

6.2.3 Three-month inhalation studies in Sprague-Dawley rats, using high concentrations (approximately 3000 f/mL) of potassium octatitanate (19% fibres less than 3.0 microns diameter), and potassium titanate (46% less than 3.0 microns diameter), were considered negative. No lung tumours were found in the potassium titanate group (0/45), 1/45 in the potassium octatitanate group, and 3/45 in an amosite exposed control group5. In a study in which AF/HAN rats inhaled fibres in concentrations of 1000 f/mL seven hours a day, five days a week, for approximately one year, silicon carbide whiskers of 0.45 micron mean diameter and more than 5.0 microns length were found to have similar fibrogenic and carcinogenic potency to amosite fibres6. The silicon carbide whiskers also produced mesothelioma in 24% (10/42) of the rats compared with 5% (2/42) exposed to amosite. In the only other reported study of refractory fibres, rats were exposed for 18-months by inhalation to alumina (Saffil®) fibres with median diameters of 3.3 microns. No lung tumours were found in the 40 test animals or in 34 air controls, but 9/39 exposed to chrysotile developed lung tumours4.

6.3 Health effects – human studies

6.3.1 Studies of human health effects associated with refractory fibres other than RCF have not been reported, though the findings from one study of post-mortem lung tissue from former silicon carbide workers suggested an increased number of silicon carbide fibres in those with lung fibrosis (scarring) and lung cancer7.

6.4 Summary and conclusions

6.4.1 There are limited available data on the toxicity and carcinogenicity of refractory fibres other than RCF, but the references cited above, together with an assessment by Vu et al8, provide the basis for the following evaluation:

- sufficient evidence for the toxicity and carcinogenicity of silicon carbide whiskers and titanate fibres in experimental animals;
- limited evidence for the toxicity and carcinogenicity of aluminium oxide fibres in experimental animals;
- sufficient evidence for the non-carcinogenicity of Saffil® fibres in experimental animals;
- limited evidence for the toxicity and carcinogenicity of silicon carbide whiskers in humans; and
- no data on the toxicity or carcinogenicity of titanates, aluminium oxide or Saffil® in humans.

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7. Synthetic vitreous fibres – calcium magnesium silicate (CMS) high temperature wools

7.1 Introduction

7.1.1 The refractory ceramic fibre (RCF) manufacturing industry has also developed fibrous materials for high temperature applications which are designed to be more soluble and less biopersistent in the lung than "traditional" RCF products. Whereas the composition of RCF consists predominantly of silicon dioxide and aluminium oxide, the composition of the new high temperature wools consists of silicon dioxide and oxides of magnesium and calcium. Two examples of these materials have been described by Maxim et al[1] as Isofrax and Insulfrax.

7.1.2 Isofrax is described as being composed of 72 to 77% silicon dioxide (SiO2) and 19 to 26% magnesium oxide (MgO) with trace amounts of other oxides. Insulfrax is a fibre composed of 65% SiO2, 32% calcium oxide (CaO), and 3% MgO with trace amounts of other oxides. Both materials were designed to have high rates of dissolution, since studies on fibre toxicology have demonstrated that the presence of oxides of sodium, magnesium and calcium (ie alkali and alkaline earths) enhance fibre solubility and reduce biodurability, whilst aluminium oxide, a major constituent of RCF, appears to contribute to enhanced durability and lower solubility.

7.1.3 The role of fibre durability was well recognised by the International Agency for Research on Cancer (IARC) when it stated in the introductory general remarks to its evaluation of synthetic vitreous fibres in 19872: Present scientific knowledge indicates that the major determinants of the carcinogenic potential of fibres are biological durability, dimensions/length and diameter) and as for any other agent, dose to the target organ. This view has scientific support from research spanning the past two decades3-12, and influenced the development of these new SVF materials.

7.2 Health effects – animal studies

Intracavity studies

7.2.1 No data are available on intracavity studies using SVF calcium magnesium silicate (CMS) wools.

Intratracheal instillation studies

7.2.2 No data are available on intratracheal studies using SVF calcium magnesium silicate wools.

Inhalation studies

7.2.3 Sub-chronic inhalation studies on rats with calcium magnesium silicate wools at high concentrations (150 f/mL of fibres more than 20 microns in length) for 90 days with follow-up for one year are reported to have shown neither lung fibrosis

(scarring) or cancer, and early signs of inflammation in the rats' lungs returned to normal after cessation of exposure13.

7.2.4 In a lifetime carcinogenicity (cancer) study, rats were exposed by inhalation for two years for 5 days a week and 6 hours per day to CMS wool at 200 respirable f/mL. It was reported that there was neither fibrosis nor carcinogenic response14.

Biopersistence studies

7.2.5 In-vitro dissolution tests, which measure the dissolution rate constant, have been reported on these materials1. According to Zoitos et al11 the dissolution rate constant (KDIS) is a relevant parameter for measuring the potential bio-persistence of new fibres, and KDIS is measured in in-vitro flow experiments using simulated lung fluid. The KDIS results are described in units of mass/surface area/time, and expressed in units such as nanograms of silicon dioxide dissolved from a square centimeter of fibre per hour (ng/cm2/hr).

7.2.6 The authors1 predicted that, based on comparisons with KDIS values for other SVF and for amosite and crocidolite asbestos, and based on the extensive scientific data base for the health effects of SVF and asbestos, CMS wools such as Isofrax and Insulfrax would, if tested fully, produce the following results:

(i) they would dissolve rapidly in the lungs because of their chemical composition and K_{DIS};

(ii) because the dissolution rate constants (KDIS) were relatively high compared with other SVFs, and well above the threshold values at which fibrosis or lung cancer has been observed in well designed chronic inhalation animal studies, they would not be expected to cause fibrosis or cancer if tested in a chronic inhalation animal study.

7.3 Health effects – human studies

7.3.1 No studies of CMS wools in humans have been reported.

7.4 Summary and conclusions

7.4.1 The limited data on the new high temperature SVF known as calcium magnesium silicate (CMS) wools forms the basis for the following evaluation:

- sufficient evidence for the non-toxicity and non-carcinogenicity of SVF calcium magnesium silicate (CMS) wools in experimental animals
- no data on the toxicity and carcinogenicity of CMS wools in humans

7.5 References

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13. European Cermic Fibre Industry Association. (1999) Report on sub-chronic inhalation study of CMS fibres in rats. ECFIA, London.

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8. Synthetic vitreous fibres – continuous filament glass fibres

8.1 Introduction

8.1.1 Continuous filament, or textile, glass fibres, is a collective term for fibres possessing an approximately uniform circular cross section, made from molten glass[1]. The chemical composition of the textile glass fibres varies: eg multi-purpose E-glass - 55% SiO_2, 15% Al_2O_3 and 20 - 25% CaO and MgO; and quartz glass, 100% SiO_2. The most widely used are E-glass fibres especially in glass reinforced plastic (GRP) products, and acid resistant E-CR-glass fibres used in pipe and cement reinforcement. Most commonly, glass filaments are made by a direct melt process which draws single filaments of 10 – 20 microns diameter from a "bushing" consisting of 400 - 1600 holes. The filaments are wound into strands, and each strand consists of 50, 100, 200 or more filaments.

8.1.2 The strands are then formed into continuous strand mats, chopped strands, glass rovings or other forms depending on their ultimate, wide-ranging uses. Because the glass filaments can be made to consistent diameters of 10 microns and greater, the use of these materials rarely results in measurable concentrations of airborne respirable fibres. However, coarse abrasive dusts may be generated, and inspirable dust levels as high as 60 mg/m3 have been found during GRP manufacture2.

8.2 Health effects – animal studies

Intracavity studies

8.2.1 Intrapleural and intraperitoneal studies of continuous filament glass fibres have been negative3, 4.

Intratracheal instillation studies

8.2.2 No data on intratracheal instillation studies have been reported.

Inhalation studies

8.2.3 No data on inhalation studies have been reported.

8.3 Health effects – human studies

Skin, eye and respiratory irritation

8.3.1 For more than thirty years there have been publications demonstrating that the acute irritant effects (skin, eye and respiratory irritation) associated with synthetic vitreous fibres are related to fibre diameters5. Materials of diameter greater than 4.3 microns are more likely to cause irritation than fibres of finer diameter. Accordingly, the continuous filament glass fibres, which consist of coarse fibres greater than 10 microns diameter would be expected to act as severe mechanical irritants if in contact with the skin, eye and respiratory tract.

8.3.2 One study has found respiratory symptoms and asthma associated with the manufacture of continuous filament glass fibres6. Seven cases of work-related asthma occurring in a continuous filament glass fibre plant were described, and all but one had no past history of asthma. Additionally, work-related rhinitis (itchy, runny nose) was complained of by 20% of the workforce, and appeared to be related to airborne continuous filament glass fibre dusts. There were no available previous or subsequent reports of asthma associated with these materials.

Morbidity studies

8.3.3 There are no available data on studies specifically looking at the health of workers manufacturing or using continuous filament glass fibres.

Mortality studies

8.3.4 Some populations of workers exposed to continuous filament glass fibres have been included in the major US and European mortality studies reported in Section 3.4 of this report7, 8, 9. None of the studies have demonstrated an increased risk of lung cancer or mesothelioma in these workers.

8.3.5 Additional detailed mortality studies specific to the continuous filament glass fibre industry have been done in the United States10, 11 and results reported as negative. The results of a case-control investigation within the cohort mortality study confirmed that respirable glass fibres were not associated with an increased lung cancer risk in the population studied.

8.4 Summary and conclusions

8.4.1 The available data cited above on the health effects of SVF continuous filament glass fibres provides the basis for the following evaluation:

- limited evidence for the non-toxicity and non-carcinogenicity of continuous filament glass fibres in experimental animals;
- sufficient evidence for the toxicity of continuous filament glass fibres in human morbidity studies;
- sufficient evidence for the non-toxicity and non-carcinogenicity of continuous filament glass fibres in human mortality studies.

8.5 References

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9. Natural mineral fibres

9.1 General

9.1.1 A wide range of naturally occurring minerals exist in fibrous form, that is, they contain particles which conform to the occupational hygiene definition of a fibre as any particle with a length to breadth aspect ratio equal to or greater than 3:1. Included in this definition are single crystals and crystal aggregate patterns or arrangements. Fibrous particles may also result from avulsion or cleavage of discrete particulate material.

9.1.2 The list of minerals containing fibrous particles is extensive and includes attapulgite (correct mineralogical name: polygorskite) and wollastonite. These are the subject of this document because of their potential for significant occupational exposure, and because they have been extensively reviewed by the International Programme on Chemical Safety (IPCS)2 and the International Agency for Research on Cancer (IARC)3, 4. But there are many others, including epsomite, pectolite, pyrophyllite, anhydrite, fibrolite, zoisite, epidote, pistacite, sepiolite, halloysite, nemalite, magnesite, apjohnite, gypsum, gedrite, celestite, halotrichite and many more1.

9.1.3 Very few of the fibrous minerals have been tested in experimental systems, and there have been few studies of people exposed to them. However, the limited evidence suggests that the potential health effects differ widely. This section highlights the fact that many naturally occurring minerals contain fibrous particles.

9.2 References

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10. Natural mineral fibres – Attapulgite

10.1 Introduction

10.1.1 Attapulgite (correct mineralogical name: palygorskite) is a magnesium aluminium silicate similar in structure to the minerals of the amphibole group and is very similar to sepiolite. The structural arrangement of attapulgite results in long, thin or lath-like crystals occurring in bundles that comprise thin sheets composed of minute interlaced fibres[1]. Attapulgite is found in association with sepiolite, phosphates, carbonates, opal, quartz, cristobalite, and other clay minerals and the purity of marketed products is dependent on the mined ore. It is mined in many countries with the largest producer being the USA, where attapulgite is known as "fullers' earth". Attapulgite deposits are mined by open-pit techniques. It is then refined by conventional milling and screening techniques to produce various grades of clay products.

10.1.2 Attapulgite, as a component of various naturally occurring clays, was probably used in ancient times, and currently the main uses for attapulgite are in pet waste absorbents, oil and grease absorbents, drilling muds, pesticides and related products, fertilizers and cosmetics and pharmaceutical products1.

10.1.3 In 1976, about 200 dust samples were collected at various milling operations in a USA attapulgite production plant. During crushing, milling, drying and screening, the average concentrations in the workers' breathing zone ranged from 0.05 to 2.1 mg/m3 for total dust and from 0.02 to 0.32 mg/m3 for respirable dust. Except for some individual samples, respirable free silica exposures calculated for each job category were below 0.05 mg/m3. As determined by transmission electron microscopy, airborne attapulgite fibres had a count median diameter of 0.07 micron and a median length of 0.4 micron, with ranges of 0.02 to 0.1 micron in diameter and 0.1 to 2.5 microns in length2, 3.

10.1.4 Dust concentrations were measured in several hundred air samples in two USA companies mining and milling attapulgite clay. The mean concentration of total dust ranged from 0.6 to 3.1 mg/m3 in mining and from 0.1 to 23 mg/m3 in milling and shipping operations. On average, the concentration of respirable dust was reported to be below 5 mg/m3 in all job categories4.

10.2 Health effects – animal studies

Intracavity studies

10.2.1 Intrapleural studies in which male and female Fischer 344 rats were injected with "long" attapulgite fibres (greater than 6.0 microns long and less than 0.5 microns diameter) found high incidences of mesotheliomas in the treated animals (61%) compared with the controls (3%); whereas similar studies using "short" fibre attapulgite (less than 2.0 microns long) found a mesothelioma incidence of 5%5.

10.2.2 Intraperitoneal studies by Pott et al reported similar findings. Attapulgite from three sources with short fibre length (less than 5.0 microns) were shown to be carcinogenic, but an attapulgite with longer fibres (more than 5.0 microns)

increased the incidence of mesothelioma6. The authors commented that the carcinogenic potency of inorganic fibres depends on their biopersistence, dimensions, and possibly also on surface properties.

Intratracheal instillation studies

10.2.3 The authors of one study, in which attapulgite fibres were instilled into the tracheal lobe of sheep, noted that the attapulgite was a fibrous mineral used in industry at the rate of over a million tons per year, but the biological activity of the material was not fully known7. In their intratracheal study, the authors stated that the attapulgite (fibre length less than 1.0 micron) produced a severe inflammatory response and led them to conclude that the material was not inert and required longer follow-up studies.

10.2.4 In contrast, Wagner et al found a more severe response in intratracheal studies in Fischer rats when longer fibre attapulgite (20% of sample greater than 6 microns long) produced fibrosis similar to, or more severe than that from UICC crocidolite5.

Inhalation studies

10.2.5 In an inhalation study limited by a relatively small number of Fischer rats per exposure group (28), Wagner et al demonstrated a greater incidence of lung fibrosis, lung cancer and mesothelioma following inhalation of long fibre attapulgite (length more than 6.0 microns) compared with short fibre (less than 2.0 microns) material5.

10.3 Health effects – human studies

10.3.1 The only available human epidemiological study is that by Waxweiler et al3 who conducted a cohort study on over two thousand men employed for at least one month between 1940 and 1975 at an attapulgite mining and milling facility in the Unites States. The attapulgite fibres were short, with 99% less than 5.0 microns long. Although non-statistically significant increased death rates for lung cancer (SMR 119) and stomach cancer (SMR 120) were found, the authors were unable to attribute causation by attapulgite and stated that the observed increases were not related to duration of employment, or intensity of exposure. Follow-up studies have not been reported.

10.4 Summary and conclusions

10.4.1 In its Monograph Volume 68 in 1997, the International Agency for Research on Cancer re-evaluated palygorskite (attapulgite)1. That evaluation, together with evidence from the references cited above, forms the basis for the following evaluation:

- sufficient evidence for the toxicity and carcinogenicity of long attapulgite fibres (more than 5.0 microns) in experimental animals;

- limited evidence for the toxicity of short attapulgite fibres (less than 5.0 microns) in experimental animals;
- sufficient evidence for the non-carcinogenicity of short attapulgite fibres in experimental animals; and
- inadequate evidence for the toxicity and carcinogenicity of short fibre attapulgite in humans; and no data on the toxicity and carcinogenicity of long fibre attapulgite in humans.

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11. Natural mineral fibres - Wollastonite

11.1 Introduction

11.1.1 A description of the mineralogical aspects of the natural mineral material known as wollastonite (named after W H Wollaston, an English chemist and mineralogist) has been provided in the 1997 IARC Monograph Volume 68 [1]. Wollastonite is composed of calcium dioxide and silicon dioxide, although iron, magnesium or manganese may partially substitute for calcium. It occurs as coarse-bladed masses, rarely showing good crystal form. Fragments of crushed wollastonite tend to be acicular, lath-shaped or fibrous. Wollastonite rarely occurs in pure form, but in association with other minerals such as calcite, quartz, garnet, and diopside.

11.1.2 In general, wollastonite is chemically inert, but in a water slurry has a naturally high pH of 9.9. The acicularity of particles is defined by their aspect ratio (length: diameter), and in wollastonite deposits, even the smallest individual particles have an aspect ratio of about 8:1 and average diameter of 3.5 microns. Low-aspect ratio wollastonite products, known as powder or milled grades, with aspect ratios of 3:1 to 5:1 are used as general fillers, in ceramics and in metallurgical fluxing. High-aspect ratio products, with ratios of 15:1 to 20:1 are used as functional fillers in the reinforcement of polymer compounds, and as a replacement for asbestos1.

11.1.3 Wollastonite was probably first mined in the 1930s for mineral wool production, but significant commercial production did not commence until about 1950. Since then wollastonite has become widely used, especially in the ceramics industry. The other main areas of use are in paints, plastics and rubber, abrasives and in metallurgy. Synthetic wollastonite in powder grade only has been produced for specialist uses requiring high levels of purity and performance.

11.1.4 In a Finnish quarry producing wollastonite as a side-product of limestone mining, mixed exposures to wollastonite fibres and granular calcite dust were measured. On average, the quarried stone contained about 15 per cent wollastonite and 2 – 3 per cent quartz. A similar mean composition was also found for the respirable fraction of dust samples from mining and milling operations. In drilling, crushing and sorting, the concentration of total dust ranged from 2 to 99 mg/m3 and the levels of airborne fibres from 1 to 45 f/mL, as measured by phase-contrast optical microscopy. In the flotation and bagging plant, dust was mainly composed of wollastonite, and workplace concentrations ranged from 15 to 30 mg/m3 for total dust and from 8 to 37 f/mL for fibres, as counted by phase-contrast optical microscopy. In all operations, the mean level of respirable quartz was below 0.1 mg/m3. The counting criteria were the same as those most commonly used for asbestos: all fibres over 5 microns in length, less then 3 microns in diameter and with an aspect ratio over 3:1 were counted. When studied by scanning electron microscopy, the thinnest wollastonite fibres were characteristically 0.2 – 0.3 micron in diameter. The median fibre lengths and median diameter were 4 microns and 0.8 micron in crushing operations and 2 microns and 0.4 micron in bagging work.

11.1.5 Similar results have been reported from the United States wollastonite production plant. In open-cast and underground mining, crushing, packing and maintenance, the mean concentration of total dust ranged from 0.9 to 10 mg/m3. Bulk samples contained less than 2 per cent free silica, and respirable silica concentrations ranged from less than 0.01 to 0.13 mg/m3. In the same operations, airborne fibre counts by phase-contrast optical microscopy showed a mean of 0.3 f/mL in the mine, and a range of 0.8 – 8.5 f/mL in the mill. Fibrous particles had a median diameter of 0.2 micron and a median length of 2.5 microns.2

11.1.6 The only available data on occupational exposures during the use of wollastonite refer to its use in the production of fibre-reinforced cement sheets. Airborne fibre levels ranging from 0.02 to 0.2 f/mL have been measured during stacking and mixing.2

11.2 Health effects – animal studies

Intracavity studies

11.2.1 Intrapleural administration of wollastonite to Osborne-Mendel rats resulted in rates of pleural cancers above controls (10% versus 3%), but well below crocidolite asbestos 48% 3.

11.2.2 Intraperitoneal injection studies in Wistar rats using wollastonite fibres with median length 8.1 microns and median diameter 1.1 microns found no abdominal cancers (mesothelioma or sarcoma), whereas actinolite asbestos resulted in 42% of the rats with abdominal cancers 4. Further intraperitoneal injection studies with Wistar rats and wollastonite from another source (median length 5.6 microns and diameter 0.7 microns) provided similar negative results for wollastonite, but 64% with cancer when injected with crocidolite asbestos5. The authors stated that all wollastonite fibre types were fairly soluble probably because of the very high content of calcium6.

Intratracheal instillation studies

11.2.3 Intratracheal instillation studies in Wistar rats found that wollastonite fibres were rapidly cleared from the lungs (half time about 10 days) compared with crocidolite asbestos (more than 300 days)7. The authors of another study in Wistar rats reported that the instillation of a 25 mg bolus of wollastonite (as a mixture of particles and fibres) resulted in lung changes consistent with fibrosis (scarring), but less marked than that following crocidolite or quartz instillation8. A further review by another pathologist stated that the fibrotic changes found were due to the relatively large (25 mg) mass of dust given in one dose, and fibrosis would not have occurred if the fibres had been given by inhalation9.

Inhalation studies

11.2.4 In one short-term inhalation study in Crl:CD-BR rats, wollastonite fibres (length greater than 4.0 microns and diameter from 0.2 to 3.0 microns; airborne concentration 835 f/mL) caused reversible inflammatory responses in the lungs

which returned to control levels within one month of ceasing exposure. It was also reported that the wollastonite fibres were cleared rapidly from the lungs, with a clearance half-time of one to two weeks10.

11.2.5 One long-term inhalation study has been reported. "Groups of Fischer rats were exposed to wollastonite fibres (length greater than 5 microns, diameter less than 3 microns, aspect ratio greater than 3:1) by inhalation at a concentration of about 54 f/mL for 12 or 24 months. Overall, the incidence of lung fibrosis was 0% in the group exposed for 12 months, 2% in those exposed for 24 months, and 96% in a chrysotile asbestos control group. The incidence of bronchial adenoma [cancer of the airway] or carcinoma (combined) was 0% in those exposed for 12 months, 2% in those exposed for 24 months, 2% in controls exposed to air only, and 38% in the chrysotile asbestos control group."

11.3 Health effects – human studies

Skin, eye and respiratory irritation

11.3.1 No data are available on the short-term health effects of wollastonite.

Respiratory morbidity studies

11.3.2 The respiratory health (lung function and chest X-rays) of workers exposed to wollastonite dust in a mine and mill was tested in 1976 and again in 1982, and compared with unexposed workers in a neighbouring industrial group ie a control group. Three percent of the wollastonite exposed group showed evidence of pneumoconiosis (lung scarring) on chest X-rays; and dust-related lung function changes were found when compared with the controls. The authors concluded that long-term cumulative exposure to wollastonite may impair ventilatory function as reflected by changes in FEV1/FVC ratio and peak flow rate (lung function tests – see glossary). The contribution of mixed mine and mill dusts, compared with wollastonite fibres, was not calculated. Similar studies have not been done in workers using wollastonite.

11.3.3 A study of 46 men who had been exposed to wollastonite a limestone-wollastonite quarry for more than ten years in 1981 concluded that fourteen (30%) had X-ray evidence of lung fibrosis (scarring), and 28% had X-ray evidence of pleural thickening ie thickening of the lining of the lung (both conditions are also found in asbestos exposure)13. However, a follow-up study published in 1997 concluded that no evidence was found that long-term exposure to wollastonite causes parenchymal (lung tissue) fibrosis. Furthermore, the findings indicate that wollastonite fibres are poorly retained in the lungs14. The conclusions were based on more detailed study techniques, including high-resolution computerised tomography (HRCT – a type of X-ray) of the lungs, and bronchoalveolar lavage (BAL – collecting fluid from the lungs and examining it under microscope) to assess fibrosis of the lung and pleura and to determine exposure to wollastonite. In addition, lung tissue specimens obtained at autopsy were available from two wollastonite workers14.

Mortality studies

11.3.4 One mortality study of all 238 people employed in a Finnish limestone-wollastonite quarry for at least one year has been reported15, and the low statistical power of the study noted by the IARC1. Nevertheless, the study showed an overall mortality deficit with 79 deaths observed compared with 96 expected, and no excess cancer deaths. There was one rare abdominal tumour suggestive of peritoneal mesothelioma.

11.4 Summary and conclusions

11.4.1 In its Monograph Volume 68 in 1997, the International Agency for Research on Cancer re-evaluated wollastonite1. That evaluation, together with evidence from the references cited above, forms the basis for the following evaluation:

- sufficient evidence for the non-toxicity and non-carcinogenicity of wollastonite fibres in experimental animals;
- inadequate evidence for the toxicity and carcinogenicity of wollastonite fibres in humans.

11.5 References

1. International Agency for Research on Cancer. (1997) *IARC Monographs on the evaluation of carcinogenic risks to humans. Vol. 68. Silica, some silicates, coal dust and para-aramid fibres.* IARC Press, Lyon, France.

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12. Synthetic organic fibres

12.1 General

12.1.1 Most synthetic organic fibres (SOF) such as polyamides, polyesters, polyolefins, and polytetrafluoroethylenes are used in the textile industry with well recognised trade names including nylon, dacron, orlon, lycra, and teflon. During the past twenty years, some SOF have been developed with improved properties such as durability, strength and resistance to chemicals, making them useful as asbestos substitutes in some applications. The principal examples of these are aramid fibres (a polyamide) and carbon and graphite fibres consisting predominantly of carbon.

12.2 References

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13. Synthetic organic fibres – aramid

13.1 Introduction

13.1.1 Aramid fibres are products formed from a long chain polyamide[1]. There are currently two types of aramid fibre in world production. The first, para-aramid, is composed of a polymer of p-phenylenediamine and terephthaloyl chloride. It is manufactured under the trademarks Kevlar®, and Twaron®. The second type, meta-aramid, is composed of a polymer of m-phenylenediamine and isophthaloyl chloride. It is manufactured under trademarks Nomex® and Teijinconex®. The two aramid types are both manufactured to diameters of approximately 12 microns. The polymer is prepared in solution, spun, and then extruded through spinnerets. Both types are stated to have high tensile strength, resistance to heat, flame and most chemicals, and are stated to be very good electrical insulators; but the first type, Kevlar®/Twaron®, is very much stronger. The other very important difference is that the first type can generate fine fibres (fibrils) of less than 1.0 micron diameter.

13.1.2 Kevlar®/Twaron® is manufactured as continuous multi-filament yarn, cut fibre (staple), staple yarn, fabrics, and pulp. Pulp is made of strands chopped to lengths of 2 – 8 mm. The chopping process generates fine fibres known by the manufacturers as “fibrils”, and the pulp manufacturing process strives to produce a fibrillated surface as this enhances the usefulness of the product. The fine fibres are of a diameter of more than 0.1 micron and 3 – 1000 microns long. Both the mixing and reinforcing properties of the product are improved by the fine fibres because of their great length to breadth ratio 2,3.

13.1.3. In its 1997 evaluation of para-aramid fibrils, the International Agency for Research on Cancer (IARC) stated that exposure levels during US manufacturing processes resulted in mean para-aramid fibre exposures ranging from less than 0.05 f/mL; and maximum exposures of 2.9 f/mL when water-jet cutting3. A UK occupational hygiene study of a wide range of para-aramid users (processors of continuous filament yarn, users of pulp, users of staple and processors of resin impregnated cloth composites) counted fibre samples with both phase contrast optical microscopy (PCOM) and scanning electron microscopy (SEM)4. The fibre lengths ranged from 2.3 to 13.8 microns, and diameters from 0.3 to 1.3 microns, and the geometric mean airborne fibre concentrations ranged from 0.005 f/mL to 0.4 f/mL. It was stated that the processes were carried out in well-ventilated work places.

13.2 Health effects – animal studies

Intracavity studies

13.2.1 **Intraperitoneal** injection studies in Wistar rats by Pott et al were regarded as negative with mesothelioma found in 3 of 53 test animals (6%) compared with 2 of 102 controls (2%). The para-aramid fibres were of mixed dimensions, with 50% greater than 4.9 microns long and less than 0.5 microns diameter[5]. No

mesotheliomas were found following intraperitoneal injection of aramid fibres of unstated dimensions into Sprague-Dawley rats[6].

13.2.2 An unpublished intraperitoneal injection study commissioned by the asbestos industry, in which much finer aramid (Kevlar) pulp fibrils (96% less than 1.0 micron diameter; 56% less than 0.25 microns diameter) were injected into laboratory rats concluded: "Histological examination of peritoneal tissues taken at varying dates after Kevlar injection demonstrated that the cellular reaction to Kevlar fibrils is very vigorous. Large cellular granulomas [mass of inflammatory tissue] develop in which the injected Kevlar is embedded. Fibrosis [scarring] eventually occurs in these granulomas. Two peritoneal mesotheliomas developed in animals injected with Kevlar. Both of these tumours occurred in the group of animals receiving the highest dose. It is concluded that the Kevlar preparation used in these studies possessed a definite carcinogenic (cancer) potential.7 These conclusions were supported in a subsequent report of in-vitro (test-tube) toxicity studies on hamster tracheal epithelial cells (cells lining the windpipe) and rat lung fibroblasts (scar tissue cells)8. The authors concluded that "when tested over a respirable size range, aramid exhibited many of the same effects on epithelial cells in vitro as did asbestos.

Intratracheal instillation studies

13.2.3 No data are available on the intratracheal instillation of aramid fibres.

Inhalation studies

13.2.4 One whole-of-life (two year) inhalation study in Sprague-Dawley rats has been reported as showing a mild, but dose-related lung fibrosis (scarring) at doses of 25 f/mL and 100 f/mL, and a 4% incidence of a rare tumour in female rats at the highest dose9. The rare tumour type was subject to detailed review subsequent to the inhalation study, and the IARC included in its 1997 evaluation that they were not cancers, but a rare type of lung cyst3.

13.2.5 Short term inhalation studies in both rats and hamsters, in which the animals were exposed to aramid fibres (diameter less than 1.0 micron and length greater than 11 microns) for five days at high airborne concentrations (approximately 1000 f/mL), have found that aramid fibrils have low durability in the lungs when compared with chrysotile asbestos. These studies also found that the fibres caused an initial inflammatory response in both species, but the inflammation subsided after cessation of exposure10,11.

13.3 Health effects – human studies

13.3.1 There are no available data on the health effects of aramid fibres in human populations.

13.4 Summary and conclusions

13.4.1 In its Monograph Volume 68 in 1997, the International Agency for Research on Cancer evaluated para-aramid fibrils3. That evaluation, together with evidence from the references cited above, forms the basis for the following evaluation:

- limited evidence for the toxicity and carcinogenicity of aramid fibres in experimental animals;
- no data for the toxicity or carcinogenicity of aramid fibres in humans.

13.5 References

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14. Synthetic organic fibres – Carbon and graphite

14.1 Introduction

14.1.1 Although carbon is an element, carbon and graphite fibres are dealt with in this chapter because of the production of carbon and graphite fibres predominantly from organic compounds. They are made by high temperature processing (carbonization) of one of three precursor materials: rayon (regenerated cellulose), pitch (coal tar or petroleum residue), or polyacrylonitrile (PAN). PAN-based carbon fibres are the most common[1]. The terms carbon and graphite are often used interchangeably, but there are differences. Graphite fibres require higher temperatures for their production, usually 2000 – 3000^{0}C, compared with carbon fibres which are manufactured at about 1300^{0}C. Graphite fibres are stronger and stiffer than carbon fibres.

14.1.2 Carbon and graphite fibres have a wide range of uses because of their properties of high mechanical strength and elasticity, low density and high heat and chemical resistance. They are mainly used as reinforcing materials in structural composites and in high temperature applications. The original impetus for the development of advanced composites was the performance improvement and weight savings in materials designed for aerospace systems and military aircraft; but other applications now include their use in sporting goods, motor vehicle parts and medical prosthetic devices2.

14.1.3 These fibres are made to nominal diameters of 5 to 8 microns, but have up to 25% of the product less than 3 microns in diameter. Additionally, they may break up during processing to generate respirable dust particles. Results of airborne respirable fibre monitoring are not available, but dust concentrations have been reported in manufacturing plants in the United Kingdom and in the USA. In the former, the mean levels for the dustiest group (laboratory workers) were 0.39 mg/m3 total dust and 0.16mg/m3 respirable dust3. In the USA studies done in aircraft manufacturing plants, airborne exposures to composite fibres were measured4. It was found that the dust consisted mostly of particulates with few fibres, and the authors concluded that occupational hygiene measurements should concentrate on geometric measurements rather than fibre counts. The concentrations of respirable composite dust ranged from 1.0 mg/m3 in sanding operations to 6.5 mg/m3 when routing or milling.

14.2 Health effects – animal studies

Intracavity studies

14.2.1 Intraperitoneal injection studies have been reported to have been done at the US Air Force Aerospace Medical Laboratory when Fischer rats were injected with fibre samples of 1, 1 to 2, and 2 to 5 microns diameter. No mesotheliomas (cancer of the lining of the abdominal and pelvic cavity) were found after two years of observation after the initial single injection, but the significance of the study was stated to be limited by the small number of rats in each group5.

Intratracheal instillation studies

14.2.2 Intratracheal instillation studies were also done on Fischer rats using the same fibre preparations as those used for the intraperitoneal studies5, and reported to give negative results.

14.2.3 Intratracheal studies have also been used to evaluate the toxicity of composite dusts as opposed to the toxicity of dusts from raw carbon fibre6. The composite dusts were administered to "specific pathogen-free" rats by intratracheal instillation; and crystalline silica (quartz) used as a positive control, and aluminium oxide and saline used as negative controls. Examinations of the lungs one month after the instillation was reported to show that composite dusts did not cause lung inflammatory responses as severe as quartz, but the responses were more severe than those caused by aluminium oxide dust. Composite dusts consisting of graphite-PAN and graphite-pitch fibres in resin were more reactive than continuous filament glass fibre resin composites.

Inhalation studies

14.2.4 Two short-term inhalation studies have been reported to be negative, though both used relatively coarse fibrous material. In one study, Sprague-Dawley rats were exposed to 20 mg/m3 of carbon fibres of 7 microns diameter and 20 to 60 microns in length. No signs of inflammation or fibrosis (scarring) were found7. Similar negative findings were reported when rats were exposed to carbon-PAN fibres of 3.5 microns in diameter and 10 to 60 microns in length for six hours a day, five days a week, for 16 weeks8.

14.3 Health effects – human studies

14.3.1 The only available data on human health effects are from a study of process workers in a UK factory producing continuous filament carbon fibre, when it was reported that no evidence of dust or fibre related respiratory disease was found3. Problems with health based research have been described by Luchtel2 as due both to the proprietary nature of many of the composites, and to the fact that "while the reinforcing fibre in present day composites is usually a PAN-based carbon fibre, resins count for more than 50% of binders used, composites are complex mixtures toxicologically. Even within a specific class of resin, there are many different formulations with varying amounts of monomer, solvent curing agents and additives".

14.4 Summary and conclusions

14.4.1 An evaluation of the health effects of carbon/graphite fibres, and the composites in which they are used, on the evidence cited above, is as follows:

- limited evidence for the toxicity of carbon/graphite fibres in experimental animals;
- inadequate evidence for the carcinogenicity of carbon/graphite fibres in experimental animals; and

- inadequate evidence for the toxicity and carcinogenicity of carbon/graphite fibres in humans.

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15. Natural organic fibres – Cellulose fibres

15.1 Introduction

15.1.1 Cellulose fibres are derived from wood and plants, and wood-based products such as paper and cardboard. They are used to impart structural strength to cement products (as substitutes for asbestos in fibre-cement boards), and shredded paper cellulose fibres are used as a thermal insulating material. Whilst the health effects of wood and wood dust have been the subject of major research in the past forty years, with wood dust evaluated by the International Agency for Research on Cancer (IARC) as Group 1, carcinogenic (cancer causing) to humans[1], little research has been done on cellulose fibres even though the range of products and uses has increased with the decline of asbestos use[2].

15.1.2 Potential occupational exposures to cellulose fibre have been tested in simulated conditions in a laboratory and found to vary with the type of product. Airborne respirable fibre concentrations for most products ranged from 1 to 4 f/mL with one product generating 18 f/mL (compared with chrysotile asbestos in the same laboratory generating 20 f/mL)3. Actual exposures have been measured during installation of blown shredded paper cellulose insulation into houses, when very high dust and fibre levels were reported4. Mean airborne respirable fibres (length equal to or greater than 5 microns, diameter equal to or less than 3 microns, and aspect ratio equal to or greater than 3:1) were reported to be 10.9 f/mL and 22.6 f/mL when measured by optical microscopy in two blowing applications.

15.2 Health effects – animal studies

Intracavity studies

15.2.1 One intraperitoneal injection study has been reported in which a cellulose derived from European conifers for use in the fibre-cement industry was injected into Wistar rats. Although cancers occurred in the abdominal cavities of the rats, the incidence was reported as not statistically significantly different from controls. Precise fibre dimensions were not provided, though it was stated that at least some of the cellulose fibres were of respirable (less than 3 microns) diameter5.

Intratracheal instillation studies

15.2.2 One intratracheal instillation study, in which 15 mg of European cellulose fibre was instilled into Sprague-Dawley rats, reported the results after examining the rats one day, one week and one month after the instillation. A rapidly progressive inflammatory response was observed (no pathological changes in control animals), with a “tendency to fibrosis[scarring]” after one month6. In quartz exposed positive controls the fibrotic reaction was more vigorous and advanced after one month. The researchers concluded that the results of their “experiments have proved that cellulose in the lungs cannot be regarded as an inert harmless powder.” In another intratracheal study in hamsters, in which respirable cellulose was used as an expected inert control in a study of cotton dust, hamsters received six weekly instillations of 0.75 mg cellulose dust per 100g of body weight. Eight weeks after the exposure the hamsters were killed

and the lungs examined. Those dosed with cellulose showed an advanced inflammatory response with early fibrotic changes7.

Inhalation studies

15.2.3 No long-term whole-of-life inhalation studies have been reported. One 28 day inhalation exposure study found that cellulose building insulation (35 to 40% rat respirable dimensions) caused an acute inflammatory response in SPF rats. At the highest dose level (2.0 mg/mL) early changes of fibrosis were noted8.

Biopersistence

15.2.4 Because of the findings of inflammatory changes in both intratracheal and inhalation studies, the durability of both wood and cellulose fibres and shredded newspaper cellulose fibres has been investigated in Wistar rats in an intratracheal instillation study9. The size distributions were determined by electron microscope to be median length 4.2 microns and median diameter 0.9 microns for wood cellulose fibres, and 7.6 microns and 0.5 microns for cellulose insulation. The test materials were suspended in saline and 2 mg per animal was instilled into 30 animals per group. After one year there had been little clearance of the wood cellulose fibres from the lungs, while the cellulose insulation fibres had split into finer fibres, with no evidence of dissolution of either fibre. The authors concluded that: “cellulose fibres show a higher bio-durability in lungs than ceramic fibres tested by the same protocol, and therefore have the potential to accumulate in the lungs. Pathology results and published data show inflammatory reactions and fibrotic lesions in the lungs, and it is recommended that a long-term inhalation study be performed to study chronic effects.”

15.3 Health effects – human studies

15.3.1 There are no available data on studies of the health effects of either wood-based cellulose fibres or shredded paper cellulose insulation fibres in those manufacturing or using these fibres. However, a prevalence study of respiratory symptoms and asthma in workers at a soft paper mill in Sweden reported an increased risk of respiratory symptoms but drew no conclusions about asthma prevalence10.

15.4 Summary and conclusions

15.4.1 Based on the evidence from the references cited above, the evaluation of the health effects of cellulose fibres is as follows:

- sufficient evidence for the toxicity of cellulose fibres in experimental animals;
- inadequate data on the carcinogenicity of cellulose fibres in experimental animals; and
- limited data on the toxicity, and no data on the carcinogenicity of cellulose fibres in humans.

15.5 References

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Glossary

Adenocarcinoma - malignant cancer arising out of the glands of the skin and internal organs eg bowel, lung, lining of the nasal passages.

Alveolus (plural = alveoli) - air sacs in the lung where oxygen is absorbed.

Alveolitis - inflammation of the air sacs in the lung leading to cough and wheeze.

BAL - see bronchoalveolar lavage.

Breathing zone - the worker's breathing zone is described by a hemisphere of 300mm radius extending in front of his/her face and measured from the midpoint of an imaginary line joining the ears.

Bronchi - the branching airways (or windpipes, breathing tubes) into which the trachea (main windpipe) divides and which terminate in the lungs.

Bronchial - of the bronchus/breathing tubes and airways in the lung.

Bronchial hyperresponsiveness - irritation which cause the wind pipes and air passages of the lungs to be "twitchy" and narrow, causing breathing problems such as wheeze and tightness in the chest.

Bronchiole – small airway in the lung that connects to air sacs.

Bronchoalveolar lavage - a procedure in which a tube (bronchoscope) is passed down the windpipe (trachea) and into the lung under anaesthesia; fluid is passed into the lung and recollected for examination under microscope. It usually contains some white blood cells, lung macrophages (scavenger cells) plus any mineral fibres and particles.

Carcinogen - anything which causes cancer.

Carcinogenic – cancerous/cancer causing.

Carcinogenesis - the process of inducing cancer.

Carcinogenicity – the property of being able to cause cancer

CAT scan (or CT scan) (Computerised Axial Tomography) - is a series of pictures (X-rays) of the internal structures of the body taken at various depths in order to build-up a more detailed picture of a particular area of the body.

Cohort – see Epidemiology - cohort.

Confounding bias - Distortion in the size of relative risk seen due to the presence of other agents which may affect disease status in addition to the one of interest. eg Smoking is a **confounder** for lung cancer.

Control group - Also known as the "**referent group**" this group is used as a comparison to the group of workers for whom disease rates are being investigated.

Cytotoxicity – the property of being toxic to cells

Dermatitis - inflammation of the skin resulting in redness, peeling or blistering.

DNA - deoxyribonucleic acid, the basic building blocks of genes which make up chromosomes.

Dysplasia - abnormal development of cells (or a part of the body).

Emphysema - is lung disease in which the air spaces in the lungs enlarge because of destruction of the walls of connecting air sacs, resulting in shortness of breath as there is less surface area of lung tissue for oxygen to be absorbed.

Epidemiology - is the study of the factors which cause disease, and their distribution in the human population.

Common terms used in epidemiology:

1. ***Cohort*** - is a group of people (eg a group of workers) who, because of their pre-determined characteristics, make up a study base which can be followed over a period of time.

2. ***Standardised Mortality Ratio (SMR)*** - is the ratio of the number of deaths observed in a study population when compared with a non-exposed reference population (National or regional populations are frequently chosen as reference populations), after standardising for age, sex and other factors.

3. ***Relative risk*** - is the ratio of the number of people exposed to a particular hazard who develop disease compared with the number of people who develop the disease but are not exposed.

4. ***Confounder*** - is a factor which, if it is not controlled, distorts the estimated effect of an exposure on a study group.

5. ***Confidence interval*** - a calculated range of values for an outcome of interest eg percent with silicosis, constructed so that this range has a specified probability of including the true value of the variable. The specified probability is called the confidence level, and the end points of the confidence interval are called the confidence limits.

6. ***Odds ratio*** - is the ratio of people who experience an event compared to those who do not.

Erythrocytes - red blood cells.

Exposure standard - represents an airborne concentration of a particular substance in the worker's breathing zone, exposure to which, according to current knowledge, should not cause adverse health effects nor cause undue discomfort to nearly all workers. The exposure standard can be of three forms: time-weighted average (TWA), peak, or short term exposure limit (STEL).

f/mL - fibres per millilitre of air

FEF_{25-75} – the airflow rate as measured during the middle part of a forced exhalation

FEV_1 - forced expiratory volume in one second, the volume of air that can be expelled in one second of a forced expiration starting from full inspiration. The FEV_1 should be greater than 75% of the forced vital capacity (FVC) for normal healthy adults.

FVC - forced vital capacity, the maximum volume of air a person can expel from the lungs after first filling their lungs to the maximum extent and then expiring to the maximum extent (about 4.6 litres in a 40 year old male, non-smoker, 173cm in height).

Fibre - is defined as a particle with length to width ratio of at least 3 : 1 ie the object is at least three times or more as long as it is wide.

Fibrogenic – able to cause scarring

Fibrogenicity –the property of being able to cause scarring

Fibrosis - scarring of tissue as a result of injury (physical or chemical).

Fibrotic – adjective describing scarred tissue.

Granuloma – a mass of inflammatory tissue.

Hyperplasia - increase in the volume of a tissue or organ caused by the formation and growth of new cells.

IARC - International Agency for Research on Cancer. A group funded by the World Health Organisation, which commissions independent reviews of hazardous substances, pharmaceutical drugs and infectious agents for their potential to cause cancer.

The IARC classifies substances/agents into:

Group 1 -the agent (mixture) is carcinogenic to humans. The exposure circumstance entails exposures that are carcinogenic to humans.

Group 2A - The agent (mixture) is probably carcinogenic to humans. The exposure circumstance entails exposures that are probably carcinogenic to humans.

Group 2B - The agent (mixture) is possibly carcinogenic to humans. The exposure circumstances entails exposures that are possibly carcinogenic to humans.

Group 3 - The agent (mixture or exposure circumstance) is not classifiable as to its carcinogenicity to humans.

Group 4 - The agent (mixture) is probably not carcinogenic to humans.

Intrapleural – describing the space between the lining of the lung and the lining of the chest wall.

Interstitial – describing the space between cells in living tissue.

Interstitium – the space between cells in living tissue.

Intraperitoneal – describing the space between the lining of the abdominal and pelvic cavity and the lining of the intestine and organs.

Lung function tests - measure the function of the lung. The most commonly used instrument is a spirometer. The results are compared with a set of normal values. Common tests are:

1. *FEV_1 (forced expiratory volume in one second)* - measures the volume of air a person is able to force out of his/her lungs in one second after taking a full breath.

2. *FVC (forced vital capacity)* - measures the total volume of air a person can force out of his/her lungs after taking a full breath.

Lymphocyte - white blood cells arising out of lymph nodes which can fight infection, especially viral infection.

Macrophages - cells which form the first line of defence for fighting foreign substances which enter the body eg alveolar macrophages (AM) help remove particles such as dust from the air sacs (alveoli) in the lung. They can also engulf bacteria.

Measurement bias - Distortion in the size of relative risk seen due to systematic errors made in classifying persons in relation to their disease or exposure status.

Mesothelioma – cancer arising out of the cells of the lining of the lung or abdominal cavity.

Mesothelium – the cells which make up the lining of the lung and abdominal cavity

Micrometre (☞m) - one thousandth of a millimetre.

Micron - see micrometre.

Mucosa - the cells lining the nose and throat (and other internal structures such as the intestine).

Mutagenesis - the process of causing inheritable change in genetic material

which can be transmitted to daughter cells and to succeeding generations, provided such changes are not a dominant lethal factor.

Nasopharyngeal cancer - cancer of the nasal cavities behind the passages of the nose and back of the throat.

Necropsy - a post-mortem examination of the body.

Neoplasm – a mass of newly formed tissue, a new growth or tumour.

Neoplastic – pertaining to new tumour growth.

nm - nanometre = one billionth of a metre.

Odds ratio - ratio of people who experience an event (eg lung cancer) with those who do not.

Oncogenic – causing tumour formation.

Parenchyma – the essential or functional elements of an organ

Particulate – fine solid particles.

Peritoneal – of the lining of the abdominal and pelvic cavity.

Peritoneum - the membrane which lines the abdominal and pelvic cavity containing the stomach, intestines etc.

Personal samples - atmospheric samples collected within the breathing zone of the worker are called personal samples.

Pharyngeal - of the pharynx (throat).

Pleura - the membrane covering the lungs and lining the walls of the chest cavity.

Pneumoconiosis - scarring of the lung due to breathing in dusts or fibres such as coal, silica, asbestos.

Pneumonitis - inflammation of the lung tissue.

Polypoid – shaped like a polyp.

Pulmonary - of the lung.

RCC – Research Consulting Company, an independent non-government research facility based in Geneva – it specialises in animal inhalation studies.

Referent group – see Control group.

Respirable fibre - defined as a particle with a diameter equal to or less then 3 microns, length equal to or greater than 5 microns, and with a length to width ratio equal to or greater than 3 : 1. These fibres can reach the deepest part of the lung.

Respirable particle - a particle with a diameter less than 7 microns that can reach the deep lung.

Respirator - dust mask.

Sarcoma – a tumour arising out of the mesenchymal cells, often highly malignant

Selection bias - Distortion in the size of relative risk seen in a working population when compared with its control population. This occurs because, the working population was initially at greater or lesser risk of the investigated disease, irrespective of the amount of exposure to the causative agent received. eg The general population usually has a greater rate of disease than the working population because the former contains the old, young and unhealthy.

Sister chromatid exchange (see also Chromatid) - the two strands of chromosomes (ie each chromatid) are joined at a point called the centromere; during cell replication, these strands can break and reform so that genetic material from one strand can be

translocated to the other strand and vice versa.

Standardised mortality ratio – see SMR and Epidemiology – standardised mortality ratio

SMR - Standardised mortality ratio - the ratio of the death rate due to a particular disease in the exposed population as compared with that in an unexposed population (often the general population). eg SMR of 200 for lung cancer means that this group is twice as likely to die of lung cancer than the general population. SMRs for the general population are all equal to 100.

Threshold limit value (TLV) - is a proprietary name registered by the American Conference of Governmental Industrial Hygienists (ACGIH) and refers to airborne concentrations of substances or levels of physical agents to which it is believed that nearly all workers may be repeatedly exposed day after day without adverse effect.

Time-weighted average (TWA) - the average airborne concentration of a particular substance when calculated over a normal eight-hour working day, for a five-day working week.

Trachea - the main airway (windpipe) leading from below the nose and mouth to the region of the lungs where it divides into the bronchi.

☞**m** - micron = one millionth of a metre.

Wagner scale – is a scale used to describe the appearance of lung tissue under the microscope, and is used to classify and grade changes in the lung tissue related to the inhalation of fibres: eg normal tissue is grade 1, grades 2 and 3 are reversible inflammatory changes, grade 4 shows some deposition of collagen in the small airways and airsacs whilst grade 7 is marked fibrosis (scarring) and grade 8 is complete destruction of most airways

WHO fibre – see respirable fibre.

X-ray (radiograph) - is a single picture of the internal structures of the body produced by exposing specially sensitised film to X-rays.