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The Nordic Expert Group for Criteria Documentation of Health Risks from Chemicals

121. Refractory Ceramic Fibres

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Nordic Council of Ministers

ARBETE OCH HÄLSA VETENSKAPLIG SKRIFTSERIE

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Preface

The Nordic Council is an intergovernmental collaborative body for the five countries, Denmark, Finland, Iceland, Norway and Sweden. One of the committees, the Nordic Senior Executive Committee for Occupational Environmental Matters, initiated a project in order to produce criteria documents to be used by the regulatory authorities in the Nordic countries as a scientific basis for the setting of national occupational exposure limits.

The management of the project is given to an expert group. At present the Nordic Expert Group consists of the following member:

Vidir Kristjansson	National Board of Occupational Health, Iceland
Petter Kristensen	National Institute of Occupational Health, Norway
Per Lundberg (chairman)	National Institute for Working Life, Sweden
Vesa Riihimäki	Institute of Occupational Health, Finland
Adolf Schaich Fries	National Institute of Occupational Health, Denmark

For each document an author is appointed by the Expert Group and the national member acts as a referent. The author searches for literature in different data bases such as Toxline, Medline, Cancerlit and Nioshtic. Information from other sources such as WHO, NIOSH and the Dutch Expert Committee is also used as are handbooks such as Patty's Industrial Hygiene and Toxicology. Evaluation is made of all relevant scientific original literature found. In exceptional cases information from documents difficult to access are used. The draft document is discussed within the Expert Group and is finally accepted as the Group's document.

Editorial work is performed by the Group's Scientific Secretary, Gregory Moore, and technical editing by Ms Karin Sundström both at the National Institute for Working Life in Sweden.

Only literature judged as reliable and relevant for the discussion is referred to in this document. Concentrations in air are given in mg/m^3 and in biological media in mol/l. In case they are otherwise given in the original papers they are if possible recalculated and the original values are given within brackets.

The documents aim at establishing a dose-response/dose-effect relationship and defining a critical effect based only on the scientific literature. The task is not to give a proposal for a numerical occupational exposure limit value.

The evaluation of the literature and the drafting of this document on Refractory Ceramic Fibres was made by Dr Vidar Skaug at the Norwegian National Institute of Occupational Health. The final version was accepted by the Nordic Expert Group 22nd May,1995, as its document.

Gregory Moore
Scientific Secretary

Per Lundberg
Chairman

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1. Introduction

Mineral fibres, such as various types of asbestos, and synthetic mineral fibres differ in toxicity, mainly related to their size, morphology and durability (45). Since these fibres pose different levels of human risk, it is generally accepted that durable fibrous minerals presenting airborne particles in the respirable size range, should be examined for possible adverse health effects in workers exposed to these fibres. Thus, during the latest 20 years, man-made mineral fibres (MMMF) have been extensively examined for any effects similar to those caused by some naturally occurring mineral fibres, notably asbestos. Among MMMFs, the vast majority are mineral wools produced from glass, rock or slag. They have been extensively studied in man and animals.

During the latest years there has also been concern about toxicological data on another group of these synthetic mineral fibres, the refractory ceramic fibres (RCFs). This group comprises of fibres with various chemical compositions and dimensions. Although ceramic fibres are much less extensively in use compared with mineral wools, concern as to their hazard has been raised from a limited number of toxicological studies in the eighties. Available information on RCFs has been included in reports on MMMFs from two World Health Organisation meetings (113, 114, 115) and by several scientific workshops and meetings (7, 10, 68, 78, 79). Animal studies published recently contributes to further clarification of the health risk issue.

2. Substance identification

2.1. Definitions

RCFs are classified among the man-made inorganic fibres which are commonly referred to as MMMF (36, 46). Other fibres in this group are the continuos filaments, the insulation wools (glass wool, stonewool, slagwool) and special purpose fibres (glass micro fibres and aerospace insulation fibres). The term MMMF is, however, not precise for this group of products since mineral denotes a crystalline inorganic compound with a specific chemical composition (50). The Nomenclature Committee of the Thermal Insulation Manufacturers Association (TIMA) (100) has recommended the term man-made vitreous fibres (MMVFs) for the group of man-made glass fibres. This group contains the largest number of products among the man-made inorganic fibres. They are manufactured from oxide melts, as glassy or non-crystalline compounds with different physical properties and fibre dimensions. They may be classified according to chemical composition, fibre morphology and their usage. The classification of fibres as proposed by TIMA is shown in Figure 1.

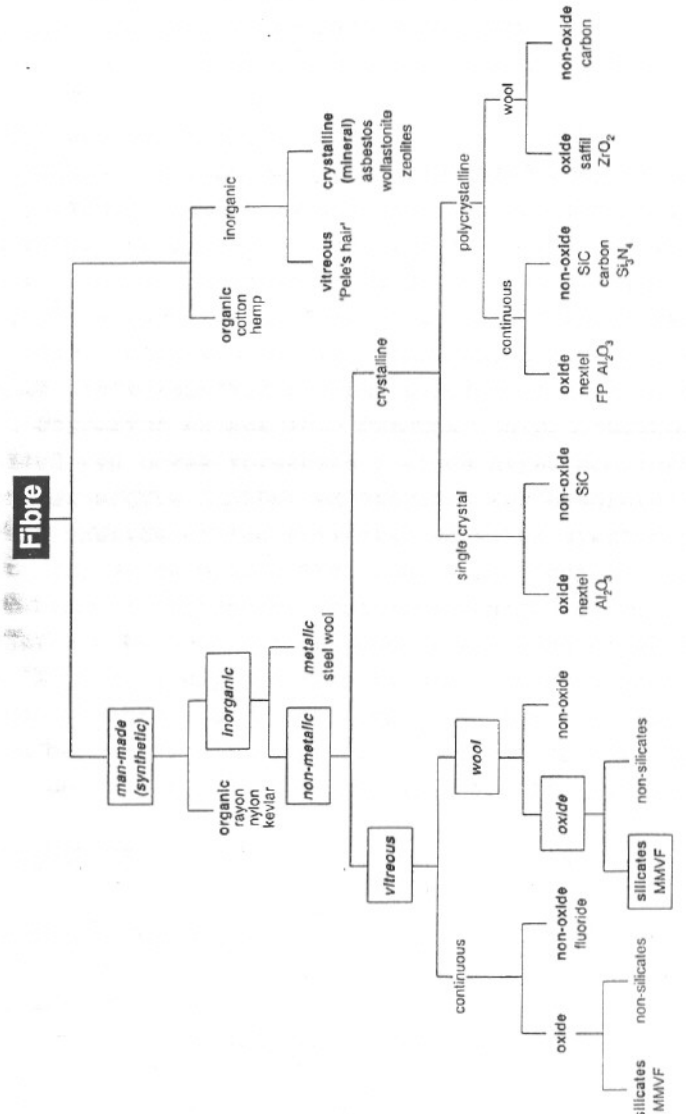

Figure 1. Classification tree based on state matter, composition and fibre morphology (TIMA, 1991) (60).

One subgroup of MMVFs is highly resistant to heat. These products are therefore often referred to as refractory fibres (RFs). Two further subgroups have been proposed: ceramic fibres (CFs) and other fibres (36). The term "refractory" is derived from the heat resistant nature of these fibres, and "ceramic" from the fired pottery clay origin of the materials (25).

The terms refractory fibre and ceramic fibre are sometimes used interchangeably (25). This seems justified for the majority of RCFs which are mainly non-crystalline fibres derived mainly from kaolin clay, oxides of aluminium or silicon. However, other types of refractory fibres also exists; i.e. the less common fibres or acicular particles with predominant crystalline structures. Crystalline aluminium oxide fibres, such as produced under the trade name SAFFIL, has different properties to RCFs (2). It is included only to a minor extent in this document, for comparison with the RCFs. Refractory fibres may also be manufactured from non-oxide materials, such as silicon carbide (SiC) and silicon nitride (Si_3N_4) (45). Such fibres are less commercially important and are not considered further in this document.

The quantitatively most important RCFs, vitreous alumino-silicate fibres, are mainly produced from kaolin clay or from the oxides of aluminium or silicon. Oxides such as zirconium oxide, ferric oxide, titanium oxide, magnesium oxide, calcium oxide and others may be added. By definition, monoxide ceramics such as aluminium ceramics are composed of at least 80% oxides. More often they contain 90% or more of base-oxides. The ratios of mixtures of two or more oxides can vary over large ranges. To separate ceramic fibres from glass, the amount of sodium, lithium, or potassium (with the exception of potassium titanate) in the final product is limited to less than two per cent (4).

2.2. Synonyms and Trade names:

Other terms for RCFs are high-temperature resistant synthetic fibres. The term ceramic fibre has also been used. The fibres included in this document have also been denoted vitreous siliceous fibres. Some trade names are listed in Table 1.

3. Physical and chemical properties

3.1. General

RCFs are synthetic vitreous fibrous structures. RCF-products and some of their properties are described in the literature (4, 41, 42, 45, 50).

RCFs show the following properties (4): i) high temperature resistance and resistance to thermal shock; ii) resistance to most chemicals including strong acids; iii) efficient electrical insulation properties at high temperatures; iv)

Table 1. Commercial ceramic fibres

Trade-names	Bulk sample: fibre diameter	Compositon
Cartolane	2.0 µm [b]	Alumino-silicate
Cera blanket	1 -20 µm [a]	Alumino-silicate
Cera chrom felt	0.75 - 12 µm [a]	Alumino-silicate
Cera chrom form	0.5 - 15 µm [a]	Alumino-silicate
Cera felt	0.75 - 10 µm [a]	Alumino-silicate
Cera fibre bulk	0.75 -20 µm [a]	Alumino-silicate
Cera form	2 - 10 µm [a]	Alumino-silicate
Cera paper	1 - 6 µm [a]	Alumino-silicate
Fiberfrax® bulk	2 - 3 µm [c]	Alumino-silicate
Fiberfrax® HSA	1.2 µm [c]	Titanium-iron-alumino-silicate
Fiberfrax® long staple	5.0 µm and 13 µm [c]	Zirconium-alumino-silicate
Fibremax® bulk	2 - 3.5 µm [c]	Alumino-silicate
Fiberfrax®	0.5 - 15 µm [a]	Boron-sodium- aluminium silicate
Keranap	1.4 µm [b]	Alumino-silicate
Kerlan 45 and 50	0.2 - 25 µm [a]	Alumino-silicate
Nextel® 312 fibre	8 -12 µm [c]	Boron-alumino-silicate
Pyroblock	2.0 µm [b]	Alumino-silicate
Pyronap	2.4 µm [b]	Zirconium-alumino-silicate
Saffil® Alumina bulk	3.0 µm [c]	Alumino-silicate
Triton kaowool	0.3 - 20 µm [a]	Alumino-silicate
Zirconia bulk	3 - 6 µm [c]	Zirconium-ytrium-(alumino-silicate)
Zirlane	0.3 - 18 µm [a]	Zirconium-Alumino-silicate

[a] fibre diameter interval as analysed by Jørgensen 1994 (50)
[b] mean fibre diameter as analysed by Krantz et al., 1994 (51)
[c] mean fibre diameter; from IARC 1988 (45)

Table 2. Compositions and thermal limitations of some RCFs [1)]

Name	Composition	Melting point °C	Service Temp °C
Alumino-silicate-zirconia	Al_2O_3-SiO_2-ZrO_2	1,790	1,260
Alumino-silicate	Al_2O_3-SiO_2	1,760	1,300
Alumino-silicate-chromia	Al_2O_3-SiO_2-Cr_2O_3	1,760	1,427
Alumino-silicate-boria	Al_2O_3-SiO_2-B_2O_3	1,740	1,427

1) modified from Hodgson (42)

excellent acoustical characteristics at temperatures up to 1,300°C or higher; and, v) heat insulation by diffusion, reflection and blocking of infrared radiation. Different fibre qualities results from the various manufacturing processes and raw materials used. The biological relevant physical and chemical properties of the fibres are related to chemical composition, aspect ratio (which is length/width), solubility and surface chemistry.

3.2. Chemical composition

The chemical composition of RCFs, depends to a great extent on the intended use of the various fibre types. They are typically produced from kaolin clay or from

oxides of aluminium, silicon or other metal oxides (4). Most RCFs are composed of a 50/50 mixture of oxides of aluminium and silicon. Monoxide RCFs, such as oxides of aluminium and zirconium, are composed of at least 80% of one oxide. Other RCFs prepared for special applications may incorporate oxides of thorium, zirconium, magnesium, beryllium, titanium, hafnium, yttrium, but also potassium titanate or fused silica (4). Table 2 shows the chemical compositions and thermal limitations of some RCFs.

3.3. Fibre dimensions

The distribution of lengths and widths of fibres in the bulk sample is a major determinant for size distributions in the airborne dust cloud, and hence for lung, deposition, elimination and biological effects (57). In general, the term width will be used throughout this document instead of diameter.

According to the US Environmental Protection Agency (103) the alumino-silicate ceramic fibres may be produced in two types which differ by size: The refractory ceramic fibres (mainly manufactured as wools) and ceramic textile fibres. The latter are longer, ranging from about 155 to 250 mm in length. Their widths are in the range from 11 to 20 µm. Only 10% of the US production is textile fibres. These broad fibres are potential irritants to the skin and mucous membranes. They do not readily penetrate into the lung, and do therefore not pose inhalation risks as the first group of RCFs might do. They are not commented further in this document.

The non-textile RCFs present a wide range of widths in bulk materials, such as melt spun alumino-silicate fibres (2.5-5.5 µm), continuous filament alumino-silicate fibre (7-12 µm), and oxides of aluminium and zirconium fibres (3 µm) (42). Widths in the submicron have also been detected, see Table 1. It has also been stated that the approximate range of mean widths for RCFs is 2-3 µm, and the approximate overall range of widths is 1-10 µm (36). There is a wide variation in fibre widths in each sample (15). RCFs also vary in widths along the length of the fibre from less than 1 to over 6 µm. Most have a length weighted geometric mean diameter (LWGD) in the range from 1-3 µm (the value of the LWGD is largely independent on the sample preparation method for microscopic examination). Lengths may vary from several microns to several centimetres (2).

One ceramic fibre insulation blanket, when ripped apart, showed no difference in nominal width between bulk samples and airborne samples (11). A part from this observation, the relationship between RCF fibre dimensions in the original products and in the air samples, has not received much attention in the literature. Widths of RCFs in air-samples are discussed in Section 6.

3.4. Specific surface area

The specific surface area (i.e. the total surface area of the fibres divided by the mass of the sample) for two types of carborundum fibres and cerachem fibres ranged from 0.187 to 0.256 m^2/g. The values do not differ from typical glass wool

or rock and slag wool insulation materials (15, 110). The values for Fiberfrax® HSA are 0.5, 7.5 and 2.5 m^2/g, respectively. Data are not obtainable for many RCFs.

3.5. Non fibrous particulate

In RCF products the fraction of non fibrous material or shot, ranges from 31-43 weight percent for three different RCFs, compared to 0-5 for typical glass wool insulation and 16-55 weight percent for rock and slag wool insulation materials (15). The percentage of shot in RCF is in general 40-60 according to TIMA 1991 (100). This must be taken into consideration when assessing RCF-toxicity. See also Section 11.4.1.1.

3.6. Durability

3.6.1. Thermal properties

Typically service temperatures for RF-containing products vary from 1,060°C for pure silica fibre, to 1,650°C for oxides of aluminium and zirconium. Heat resistance is additionally determined by fibre width; finer fibres giving lower thermal conductivity (45). Compositions and thermal limitations of some RCFs are shown in Table 2.

The vitreous alumino-silicate RCFs may partially devitrify when exposed to temperatures exceeding approximately 1,000°C. During this process there may be formation of mullite, a crystalline aluminium silicate formed at temperatures in excess of 980°C and silica in the form of β-cristobalite (a highly fibrogenic crystalline silica) notably above about 1,080°C (11, 26, 106). A summary of the phases and phase changes in alumino-silicate fibres with increasing temperature is seen in Table 3. Maximum possible cristobalite in devitrified fibres are calculated to be between 23 and 37% for some of the RCFs (11).

The crystallisation process is reported to have weakened the fibres (27) and to have resulted in fibre structure collapse (21). Levels of cristobalite measured during removal of RCFs are reported in Section 6.2.

3.6.2. Chemical (solubility)

The chemical composition of the various RCFs also determines their chemical resistance and solubility (45). Clearance and consequently biopersistence, which depends mainly on fibre solubility and fibre dimensions, differs among fibres. Few studies with RCFs are reported in Gambles artificial extra-cellular fluid ceramic fibres (not further specified) released a small amount of silicon; less than other MMVFs (52). They are more durable than most other MMVFs (1, 64, 68). Compared to asbestos they are less durable in vitro and in vivo (33, 94).

Sebastien (95, 96) examined transformed fibres in bronchoalveolar cell lavage recovered from seven voluntary workers in a ceramic fibre plant. Some of the fibres retained typical ceramic chemistry and other had hollow tube morphology

Table 3. Changes in alumino-silicate fibres with increasing temperatures [1)]

Temp. (°C)	Phases and phase changes
<840	Glassy alumino-silicate fibre
840	Glass transition temperature
840-980	Supercooled alumino-silicate liquid
980	Devitrification. Formation of mullite crystals, shrinkage of fibres and reduction in proportion of supercooled liquid component
≈1,080	Onset of formation of cristobalite
980-1,200	Increasing proportions of cristobalite and mullite
1,200-1,370	Decreasing proportion of cristobalite which transforms to silica rich supercooled liquid
1,370	Disappearance of cristobalite resulting in mullite and silica-rich supercooled liquid
1,790	Melting point

[1)] From (11)without any of the normal major ceramic elements. Beds of silicious leachate were observed. It has been proposed that the RCFs in the human lung first is coated with iron-containing granules, followed by dissolution of the structural elements.

3.6.3. Mechanical properties

MMVF in general do not split longitudinally into fibrils of smaller width, but may break transversally into shorter segments (115). Specific reference to RCFs is not available.

3.7. Refractive Index

Optical polarising microscopy may be used to determine the refractive index (RI) which may help to differentiate fibre samples on filters. For RCFs of pure alumino-silicate the RI range from 1.5347 to 1.5378 (50).

4. Occurrence, Production and Use

4.1. Occurrence

Ceramic fibres do not occur naturally.

4.2. Production

Ceramic fibre production constitutes a small, but increasing portion (less than 1-2%) of the man-made mineral fibre industry output (23, 28). RCF-production is the most recent addition to this industry. Although RCFs were known in the 1940s, commercial production commenced first in the 1950s. The fibres at that time were mainly made from clay or slag (by-products of the steel industry) and then made into low-cost fibrous wools or bats for insulating purposes. Historically

such battings contained a significant amount of particles, or shot, from the manufacturing process, which is an undesirable feature for insulating applications. Consumption of RCFs has increased in metallurgic industry since the ban on asbestos in the Nordic and other countries. The European production of RCFs has doubled from 1986 (16,000 tons) to 1991 (40,000 tons) (3). In the European Union Member States, RCFs are produced in UK, Germany, France and Italy. The production volume is growing by around 5% per year (2).

4.2.1. Main methods

RCFs are made from either a molten stream or by attenuation of a chemical solution. In the melting operation one may use either calcinated kaolin or a combination of the oxides of aluminium and silicon (Al_2O_3 and SiO_2, respectively) in approximately equal proportions. Oxides of zirconium, barium or titanium may also be added to improve properties such as temperature resistance. Fibres are produced by processes of blowing or spinning. In the steam-blowing process, the raw materials are fused in an electric arc furnace to produce a molten mixture which is drawn off and blown by pressurised steam or gas. The fibres are collected on a screen and may be processed to remove palletised material or shot (4, 73). In the spinning process the melt is forced onto rapidly rotating discs, which throw off the molten material tangentially, transforming it into a fibrous form (4, 73).

4.2.2. Other methods

Ceramic fibres have been produced by other methodologies, which are not relevant for most fibres included in this document.

RCFs of oxides of aluminium, zirconium, silicon, mixtures of zirconium and silicon, and thorium have been prepared through evaporation of a colloidal suspension (70).

Also RCFs of aluminium, zirconium, aluminium-silicon mixed oxide, zirconia and titania have been produced by a wet spinning process (this rayon spinneret method involves dissolution of the raw materials in a liquid bath, where a filament is formed by a combination of precipitation, coagulation and regeneration). Subsequent firing at 1,150°C, yields polycrystalline fibres (70).

4.3. Use

After manufacture, the fibres can be used in many product forms such as bulk fibre, mat or blanket, rope, paper, continuos fibre and in woven materials. Added to other materials they may be a constituents of fibreboards, castables and molables. Major product groups with RCFs are insulation materials, heat resistant and high performance textiles, friction materials, reinforced plastics, packings and jointings (45).

RCFs are used in industries where high temperature resistance is required. They are heat resistant materials at high temperatures in the range of 700-1,800°C, where asbestos fibres are no longer useful. They are used for insulation of furnaces, heaters, crucibles and other high temperature equipment. In industry they

may replace the "hard" refractories for the insulation of high temperature kilns and furnaces. Cast-shaped ceramic end-products are widely used in smelting, casting and foundry operations as riser sleeves, feeder tubes and reusable surface insulation tiles (73). They are also used in the papermaking industry (4). Thus, for high temperature resistance purposes most of the RCFs do not compete for a place as alternatives to asbestos (42).

Light weight and low heat storage are other qualities for industrial applications of RCFs. Other applications are fire protection and heat shields on aircraft's, military equipment such as tanks and cruise missiles. They are also used in the automobile industry (42, 73, 103, 108).

In Europe the major user countries are Germany, UK, France and Italy, and it has been estimated that in 1994 less than 5% of the annual sales in Europe was to the Nordic Countries (2).

Other MMVFs, such as mineral wools, are much more widely used at lower temperatures for thermal and acoustic insulation.

5. Measurement and Analysis of Workplace Exposure

5.1. General on measurement and analysis.

The levels of RCFs in the working atmosphere have been determined by collecting personal samples from workers or stationary samples. Air is drawn through a membrane filter in the same way as for asbestos sampling detailed in the HSE Guidance note EH10 (37). RCF levels in the working atmosphere have also been determined by the NIOSH method 7400 (81); Fibres are collected on membrane filters and analysed by optical microscopy methods. Care should be taken during sampling to prevent deposition of fibres to the conductive sampling cowl (16).

Reference methods for measuring airborne MMMF has been published by WHO (111). A new WHO recommended method for the determination of airborne fibre number/concentration by phase contrast microscopy (the membrane filter method) in workplace atmospheres has been devised, but not yet published.

Data on the relationship between total suspended particulate matter expressed in mg/m^3, and total fibre exposures, expressed in fibres/ml has been published. Esmen (23) found an excellent correlation between average exposure to total suspended particulate matter and fibre concentrations in three US ceramic fibre production plants. This could not be confirmed by Friar (25) who in a survey of occupational exposure to ceramic MMMFs identified exposure ranges from 1 mg/m^3 for light tasks to over 10 mg/m^3 for some insulation workers. Exposures above 10 mg/m^3 were not necessarily associated with high fibre counts. Head & Wagg (36) have shown for fibres whose bulk mean widths are at or just below 3 µm that both gravimetric and fibre count measurement appear to give a good indication of exposure levels. The relative importance of the two methods of monito-

ring will depend on the significance to be placed on fibre size and the numerical value of fibre concentration.

6. Occupational Exposure

Occupational exposure to RCFs may take place in industry during manufacturing, processing and during end use of RCF containing material. The European RCF industry directly employs approximately 1,050 workers and additionally some 25,000 workers are estimated to be exposed as workforce in the user industries (2). In the United States no more than 33,000 persons are exposed (28). Exposure to RCFs may also occur from brazing mats during welding operations (109).

6.1. RCF exposures in the production Industry

RCF-concentrations in three production plants in the USA showed average exposure of employees in the range 0.05 to 2 fibres/ml (24). In this study 95% of the fibres in air samples presented widths <4 µm, and lengths <50 µm, with a geometric mean width of 0.7 µm and geometric mean length of 13 µm. In another study, alumino-silicate fibres from two different plants showed count median width of 1.16 and 0.86 µm, and count median length of 14.7 and 12.5 (43). Both aluminium and alumino-silicate ceramic fibres monitored in fibre production processes, gave total dust concentrations ranging from 4.9 to 8.3 mg/m^3 with mean respirable fibre counts of 1.09 to 1.27 fibres/ml. The individual range was 0.09-5.64 fibres/ml (36).

Exposures to RCFs have been reported by Friar (25) in some manufacturing processes such as fibre chopping (>10 mg/m^3 or 0.8 fibres/ml), bagging/chopping of raw fibres (>10 mg/m^3 or 1.2 fibres/ml), packing of products (0.7 mg/m^3 or 0.002 fibres/ml) and in baling raw fibre (1.5 mg/m^3 or 0.4 fibres/ml).

6.2. Exposures in the user industry

Exposure to RCFs have been determined during installation and removal of RCF blankets, modules and bulk fibres in 13 RCF insulated furnaces (14). Typically, for tasks at the furnaces, outside of an enclosed space, workers were exposed to less than 0.2 fibres/ml of RCF. There was an increased risk of higher exposure when working within an RCF insulated furnace. Tasks creating an access of 0.2 fibres/ml includes both removal and installation of RCF-blankets, modules and bulk fibres. Tasks that only indirectly cause RCF release, such as erecting scaffolding, repairing refractory material and welding within a furnace , can create exposures above 0.2 fibres/ml.

In applications involving single fibre types overall mean gravimetric concentrations of total airborne dust were in the range 1.0-12.6 mg/m^3 (individual range 0.7- 22.9 mg/m^3), with mean respirable fibre concentrations of 0.44-2.39 fibres/ml (individual range 0.09-5.64 fibres/ml). The size distribution of diameters for airborne ceramic fibres up to 10 µm were as follows: <1 µm: 18%, 1-2 µm: 52%, 2-3 µm: 14% and 3-10 µm: 16%.

In another study by Hori et al (43) of exposures in two alumino-silicate ceramic processing workplaces, the geometric mean of fibre concentrations were 0.27 (GSD 1.93) and 0.66 (GSD 1.21) fibres/ml, respectively, as determined from stationary samples by phase contrast optical microscopy. The personal exposure levels from these factories were twice or more the average fibre concentrations by the stationary sampling. Widths and lengths of these fibres determined by scanning electron microscopy; count medium diameter was 0.85-1.2 µm and count median length was 11-18.8 µm. Similar values has been reported (median width 0.5-1 µm, median lengths 8-23 µm) when air samples were analysed by transmission electron microscopy (90). About 15% of the fibres would fall into the high carcinogenicity category (l >8 µm, d <0.25 µm) (86, 98).

Ceramic fibre brazing mats damaged during welding operations released levels of airborne fibres less than 0.05 fibres/cm^3 (109). High exposures to RCFs have been reported by Friar (25) in some user operations such as insulation work using blanket (10 mg/m^3 or 1 fibres/ml) or when stripping and relining furnace panel (10.5 mg/m^3 or 1.2 fibres/ml). Lower exposures are described in machining and ventilation control of ceramic fibreboard (0.4 mg/m^3 or 0.6 fibres/ml).

During removal of refractory ceramic lining inside a large furnace of an oil refinery, air concentrations up to 50 fibres/ml (mean 18 fibres/ml) were measured as a part of a monitoring program on many dust hazards (104).

In a Swedish study (51) the highest concentrations are encountered during RCF-insulation or during dismantling of insulation walls (0.26-1.2 fibres/ml, with extreme values up to 210 fibres/ml). Levels of 0.003-0.24 fibres/ml are observed among workers not directly handling RCFs. The German studies also demonstrates that the highest exposures are among dismantling workers (63, 99).

6.3. Cristobalite exposures

Bulk samples of alumino-silicate RCFs may contain up to 37% cristobalite (11), whereas 4-15% has been detected in air samples after removing insulation material exposed to temperatures from 500-2,550°C, for 130-471 hours (26, 63).

7. Toxicokinetics (humans, animals)

There are few observations on toxicokinetics of RCFs. Other MMVFs and asbestos have, however, been extensively studied. It is reasonable to assume that fibre dimensions and durability, much in the same way, also determines RCF deposition and persistence. The effects of fibre characteristics on lung deposition, retention and disease has been reviewed by Lippmann (57).

7.1. Uptake and distribution

In general respirable mineral fibres are deposited in the conducting airways and non-ciliary airspaces according to aerodynamic behaviour which depends mainly on fibre width and density. There are no reports on deposition pattern of RCFs, nor on the role of surface chemistry or charge for deposition in the airways. However, after inhalation of MMVFs and RCFs in rats it has been shown that the apical region of the right lung has a higher relative concentration; for RCFs the disproportion of fibres between lobes increased with aerodynamic diameter (92). Retention of RCFs is treated further in Section 7.3.

The topographic distribution of alumino-silicate ceramic fibres in human tissue is largely unknown. Alumino-silicate RCF have been identified in broncho-alveolar fluids of workers (95).

Migration of mineral fibres, other than RCFs, to other sites are described after injection into the pleural cavity of rats (74). There are no observations on translocation of RCFs to extra-pulmonary sites subsequent to animal inhalation exposures.

7.2. Biotransformation

Non native iron coatings have been identified on the surface of alumino-silicate RCFs recovered from bronchoalveolar fluids in a few exposed workers, indicative of interaction between fibres and macrophages. The biological significance of this is, however, not clear, see Section 10.1.2.

The disintegration of man-made mineral fibres in general, depends on the degree of subdivision into smaller segments, partial dissolution of the matrix creating a more porous fibre of relatively unchanged external width, or surface etching creating a change in the external dimensions of the fibres. The breakdown of man-made fibres in the lungs, is virtually all by length (115). The breakdown into smaller width fibrils which is characteristic of asbestos fibres, is seldom seen. Few data are available specifically for RCFs, see Section 7.3.

7.3. Elimination

In general the fate of fibres deposited on the airway linings depends on the sites of deposition, the characteristics of the fibres and the rate of disintegration. Most mineral fibres deposited on the linings of the tracheo-bronchial airways are carried proximal on the muco-ciliary escalator to the larynx within the first day, and subsequently eliminated through the gastro-intestinal tract (57).

Fibres deposited in the non-ciliated airways beyond the terminal bronchioles are in general slowly cleared from their deposition sites to other sites by movements along the epithelial surface either as intact fibres or within macrophages, depending on size. The clearance rates depends not only on the fibres lengths and widths at the time of deposition in the lungs, but also on the rate of disintegration of the fibres as described above.

The clearance of ceramic alumino-silicate fibres from lungs of inhalation-exposed animals has been analysed by scanning electron microscopy of the ashed lung residues. Nine week old animals were exposed to an average fibre concentration of 20.7 mg/m^3 (standard deviation 4.5 mg/m^3): mass median aerodynamic diameter 4.2 µm with geometric standard deviation 2.0, 6 hours/day, 5 days/week for two weeks, and then killed at one day, three months and six months after end of exposure. There was no difference in geometric mean length at these time points. The geometric mean width decreased, however, with increased duration of clearance time, indicating that solubility of fibre contributes most in the clearance of inhaled ceramic fibres from the lungs (117). This view is not supported by studies demonstrating that RCFs are resistant to biodegradation (33).

Rats were studied over two years after intratracheal instillation of various glasswool, rockwool and RCF. In all cases fibres <5 µm were removed more rapidly than longer fibres. RCF had the longest residence time: half-life was 780 days for fibres >5 µm in length, compared to 280 days for rockwool fibres >5µm in length and for thicker glasswool (5).

The rat inhalation study (30 mg/m^3) conducted at the Research and Consulting Company Ltd, Geneva, (38, 65, 67) showed that the glass fibres which produced no tumours nor fibrosis, were not more efficiently cleared than the pathogenic kaolin-based ceramic fibres (RCF1). Recovery of these fibres from the rat lungs showed that both lengths and widths were approximately halved compared to the average aerosol dimensions at all time point between 3 and 24 months exposure.

A three month exposure period, followed by 21 months recovery showed a significant shift toward smaller fibre with (≤0.5 µm) as compared to exposed animals with no recovery period. A significant reduction in fibres ≥10 µm in length was also seen. These findings are very similar to those of Hammad (31) who found that ceramic fibre clearance was dependent mostly on length and that they were not altered chemically in vivo. In both studies the size distribution of the aerosol does not reflect the size distribution of fibres deposited and retained in the pulmonary compartment of the lung. Retention rates were also similar, 20% for fibres after 21 months recovery and 24% fibres after 9 months recovery, respectively. In the Geneva study, with hamsters longer fibres tended to persist, compared to the rat lung, in which half-time of approximately 200 days was calculated for the kaolin-RCF (64). In these studies the interference of the non-fibrous dust component on the clearance rate was not fully evaluated.

7.4. Dosimetry models of RCF

In a mathematical model based on size distributions of retained fibres in the accessory lobe of rats after inhalation exposure, it was found that the clearance rate of RCFs was inversely dependent on lung burden; as lung burden increased, the clearance rate was found to decrease (120). There was no single dependence on fibre size, as has been shown for some asbestos fibres. Hamsters were also used in the same experiment, but tumour responses were not alike in the two species. A dosimetry model was then developed for hamster upon the same expo-

sure data (119). These data may help to understand the species difference of tumour induction. The greater number of long thin fibres observed in hamster lung may be related to the higher mesothelioma occurrence rate observed in hamsters.

8. Relevant kinetic interactions

No data available.

9. Biological monitoring

Biological monitoring techniques are not applicable for exposure to RCFs. Other MMVF than RCF have been analysed in mucous thread and clumps from the inner corner of the eye to estimate particle deposition in the eyes (93).

There are no data on the indication of exposure by examination of sputum. Sebastien (96) observed both native and highly transformed RCFs in bronchoalveolar lavage (BAL) fluids of voluntary current workers in a ceramic plant. This technique is not applicable for biological monitoring.

10. Mechanisms of Toxicity

10.1. Fibre properties of importance for toxic effects

10.1.1. Dimensions

For mineral those in general, only those having widths of 3.0-3.5 µm or less and a length of 200-300 µm or less are respirable (101). The fraction of airborne RCF in this size range is the most important for pulmonary effects. As seen in Section 3, RCF may be broader or narrower than 3.5 µm.

In general, durable mineral fibres become increasingly toxic in vivo and in vitro when they become finer, notably in the submicron range, and with increasing length, notably above 5 µm (86).

In implantation experiments, based on the injection of the same mass of sized fibres into the pleura, the optimum length of durable fibres for the production of malignant mesothelioma in rats was greater than 8 µm and the optimum width was less than 0.25 µm (98). Refractory fibres, but not RCFs were included in this study.

In a study of 13 fibrous mineral dusts in vitro, which included a mainly respirable fibrous alumino-silicate (not further specified), a significant association between fibre length and biological activity occurred in two assays (8).

Recovery of fibres from the lungs after inhalation exposure of rats to two glass-fibres and one kaolin-based RCF for 3-4 months, revealed no major differences in

fibre lengths or widths that could be assigned to the differences in tumour rates for these fibres (38).

10.1.2. Surface chemistry

RCFs do not readily form reactive oxygen radicals, as shown by Leandersson (53), see Section 11.5. There are no data available on RCF-surface chemistry and biological interactions.

10.1.3. Durability

The durability of fibres is an important factor for elimination (see Section 7.3), and for biopersistence as well as toxic effects. Biopersistence may be influenced by fibre size, but there are no data available on in vivo half-life values by size categories. Factors of importance for durability are outlined in Section 3.6.2.

In vitro, the biological activity of RCFs heated to above 1200°C decreased (11). See Section 11.3

10.1.4. Interaction with pulmonary cells.

Pulmonary alveolar macrophages (AMs) are activated by asbestos and other mineral fibres presenting biological activity. Male Wistar rats inhalation-exposed to 20.1 mg/m^3 RCFs (mass median aerodynamic width 4.4 µm) prepared from bulk ceramic insulation material, for 6 h/d, 5 d/week, for up to 3 weeks had AM recovered from the BAL fluid 1, 2 and 3 weeks after exposure. After one week total cellularity was increased, but differential counts were not affected. Alveolar macrophages phagocytic ability as shown by quantification of yeast particle uptake, was significantly increased after only two weeks of exposure, but not the first or third week. It is concluded that inhalation exposure to ceramic fibres leads to activation of alveolar macrophages (118). When these fibres were incubated in vitro with AM, there was an increase in solubility as determined by levels of aluminium in the culture supernatant.

10.2. Carcinogenesis

The mechanisms for animal carcinogenesis of RCFs are not well understood. The appearance of kaolin-RCFs induced tumours in animals corresponds to those induced by other mineral fibres, although RCFs in general is associated with higher tumour rates. Important factors for carcinogenicity of RCFs in animals have been summarised in Sections 10.1.1, 10.1.3 and 3.6, 11.5 and 7.3.

Dimensions of airborne RCFs are within the critical fibre size range for induction of tumours by mineral fibres (57, 98).

In vitro no synergistic effects were shown on DNA damage, by ceramic fibres (not further specified) and tobacco smoke condensate (54), in contrast to Rockwool, which showed a synergistic increase in formation of 8-OHdG as an index of DNA damage, suggesting iron-mediated damage caused by hydroxyl radicals. By contrast with RCFs, iron is a constituent of Rockwool. See also Section 11.7.

The relationship between fibrosis and cancer in experimental animals exposed to asbestos and other fibres were reviewed by Davis (20). A close overall relationship between mean levels of fibrosis and tumour production has been demonstrated for many asbestos samples and one sample of ceramic fibre (alumino-silicate 1327362). This may suggest a relationship between inflammation, subsequent fibrosis, and carcinogenesis. Contrary, intrapleural injection of four different RCFs did not reveal any correlation between the mesothelial proliferation and the occurrence of mesothelioma (85). It has also been observed that fibrosis is not a prerequisite for mesothelioma induction following injection of chrysotile asbestos (88).

RCF-carcinogenesis by an overload effect in experimental animals, which involves other factories than those described for mineral fibre tumorigenesis (48), has also been discussed (28, 76). It could thus be argued that the lung tumours at the maximum tolerated dose (MTD) level (67) were produced by an epigenetic mechanism mediated by cytotoxicity followed by regenerative cell proliferation (9).

10.3. Fibrosis

Section 10.1 outlines the toxic mechanisms related to fibre characteristics. Mineral fibre induced lung fibrosis is related to the ability of these fibres to interact with macrophages and the subsequent release of inflammatory mediators. Persistence of fibres in the lung sustains the low grade inflammatory reaction, with more or less prominent deposition of collagen and other connective tissue fibres. Persistence of these reactions for more than 3-6 months in experimental animals may cause irreversible fibrosis in the walls of peripheral airways and finally into the adjacent lung parenchyma. Higher concentrations of RCFs in lung tissue of animals due to overload may cause fibrosis not solely related to the fibrous form of the particles (76).

Exposure to "after-service" RCFs may also cause lung fibrosis (silicotic nodules) mediated through cristobalite (67).

11. Effects in Animals and in Vitro studies

11.1. Irritation and sensitisation

No data available. It is generally accepted however that mineral fibres broader than 4-6 µm may cause irritation of the skin and mucous membranes, mainly unrelated to chemical composition.

11.2. Effects of single exposures

A fraction extracted from the HSA (high specific area) grade of Fiberfrax (length 8.3 µm, width 0.3 µm, aspect ratio 38.5), containing 60% non fibrous particles were not active in the in vitro haemolytic test, in contrast to other mineral fibres tested. It was highly toxic towards rat pulmonary macrophages in vitro (77).

11.3. Effects of short term exposures

In a comparison of two in vitro assays, a mainly respirable man-made fibrous alumino-silicate not further specified, was inactive in the V79-4 cell colony inhibition assay but active in the A459 cell assay which determines the ability of dusts to induce an increase in width of the cells (8).

Three grades of ceramic fibres, one "as-manufactured" and two others heated to 1,200 and 1,400°C, have been examined in for their biological effect in-vitro. After thermal decomposition, the fibres had lower affinity for the surface of V79-4 cells. Toxicity was reduced in the V79-4 cell assay and the A459 cell assay (11).

The activation of macrophages by RCF after short term inhalation exposure (118) is described in Section 10.2.

11.4. Effects of long-term exposures

The use of animal models in toxicity testing of RCFs and other MMVFs is well established (6, 7, 19, 112). Many techniques are available. In the seventies intrapleural injection in rodents was shown useful to demonstrate that the potential of durable mineral fibres to produce pleural tumours, and their relationship to lengths and widths (98). For human risk assessment inhalation studies are recommended (7, 68).

11.5. Carcinogenicity

11.5.1. Inhalation studies

Results from published animals experiments are summarised in Table 4. The alumino-silicate RCFs have received most attention; results of inhalation studies published up to the nineties are equivocal. Interpretation is difficult due to the high proportion of non-fibrous particles in the dust-cloud.

One inhalation study with rats and hamsters (39, 65, 67, 69) has fulfilled the recommendations on adequate inhalation models for hazard assessment of mineral fibres, set forth by a WHO meeting (112). In this study specially sized fibres (approximate average dimensions, 1 x 20 µm) were used to generate a fibre aerosol that was respirable by the rat. Care was taken in advance to define the MTD. In this study exposures were generated corresponding to approximately 30 mg/m^3 (approximately 200-250 fibres). The rats were exposed to four different RCF for

24 months: i) kaolin-RCF; ii) Zirconia-RCF; iii) high purity RCF of different chemical compositions; and iv) "After service" RCF (kaolin-based RCF previously exposed to high temperatures, containing 27% cristobalite). Hamsters were only exposed to kaolin RCF. For comparison the animals were also exposed to a reference dust from the National Institute of Environmental Health; the NIEHS-Chrysotile. Negative controls inhaled filtered air. As shown in Table 4, kaolin-based RCFs induce pulmonary tumours and fibrosis as well as mesotheliomas in hamsters and rats (68, 71). This shows that the four types of RCF presents carcinogenic activity in rats and hamsters. An evaluation of the high number of mesotheliomas in hamsters (42%) compared to rats (1.7%) for the kaolin-RCF is difficult since there are very few hamster data available for mineral fibres and other materials. It was also observed that the mesotheliomas were small and did in general not cause the death of the exposed animals. The multidose chronic inhalation study in rats (67) is described in Section 13.2.2.

11.5.2. Administration by other routes than inhalation

Results from published animals experiments are summarised in Table 5.

In the fifties, submicron particles prepared from Fiberfrax (an alumino-silicate) administered intratracheally weekly for 5 weeks to rats, had considerably less effect on lung tissue than feldspar particles. The reaction more closely resembled that produced by limestone, which is another inert dust (31). This and other early studies were not reliable since the dusts were not well characterised and there were problems with latent infection in the animals.

Pigott (85) tested for carcinogenic effects of four RCF: Saffil refractory alumina, a new sample and one which had been thermally aged. The two other samples were alumino-silicate fibres. Suspensions (0.2 ml) of the test materials with different diameter distributions were injected intrapleurally into 48 rats in each group. At the end of the life-span there was minimal chronic pleurisy/fibrosis with adhesion formation, and proliferation of the mesothelial linings of pleura, pericardium and peritoneum in the Saffil groups. In the alumino-silicate groups the reaction was similar but somewhat more severe. Malignant mesothelioma was seen in three rats in one of the groups dosed with alumino-silicate, and not in the Saffil treated groups. The fibres injected into rats which had mesotheliomas, differed mainly from the other alumino-silicate group by the numbers of thin fibres: 30% had d≤ 1 µm, compared to 10% in the other group. The numbers of fibres with diameters 1-1.5 µm were alike. Also Saffil fibres were few in the 1-1.5 µm width range, suggesting in this study a higher potency for submicron fibres to produce mesothelioma. Seven mesotheliomas were observed in the positive control group injected with UICC Chrysotile A asbestos.

Pott et al (88) in a series of intraperitoneal injections to female Wistar-rats, reported a higher tumour incidence than expected for ceramic fibres.

11.6. Fibrogenicity

11.6.1. Inhalation studies

See Table 4 for details. Pulmonary fibrosis was shown in one inhalation study with rats, exposed to ceramic alumino-silicate glass (ceramic fibre) on average 95 fibres/ml for 12 months (18), but not in another inhalation study for 24 months where rats and hamsters were exposed to "Fiberfrax" at an average concentration of 200 fibres/ml (97). In this study 12/55 hamsters had fibrosis. The proportions of non-fibrous dust particles were 4:1 and 33:1, respectively.

No significant treatment related histopathological changes were observed in the lungs of male Wistar rats 6 months after inhalation exposure (average concentration of 27.2 mg/m^3, 6 h/d, 5 d/week for two weeks) of ceramic fibres with a geometric mean (GM) length 20 µm and GM aerodynamic diameter of 0.65 µm (117). Table 4.

In the RCC (Research and Consulting Company, Geneva, Switzerland) inhalation study, pulmonary fibrosis was recorded in rat exposed to kaolin-RCF in all exposure levels from 3 mg/m^3 to 30 mg/m^3 and for all for RCFs tested at the MTD level. The same grade (Wagner grade 4) for fibrosis was observed in rats and hamsters exposed to MTD of kaolin-RCF (67, 69).

11.6.2. Administration by other routes than inhalation

These studies are detailed in Table 5. The studies are important for the evaluation of the fibrogenic potential related to fibre characteristics, but do not replace inhalation studies for risk assessment.

Fiberfrax, an alumino-silicate (length 50% <5 µm, average length 8.3 µm, width 0.2 µm, aspect ratio 38.5) administered by intratracheal instillation of 1.5 and 10 mg in saline to rats, caused granulomatous reaction and the appearance of early fibrosis, after one month (55). The observation period was not extended further .

Twenty milligrams of Saffil type A and type B injected intraperitoneally produced a mild chronic inflammatory response with only small amounts of collagen, whereas chrysotile asbestos caused advanced peritoneal fibrosis. The difference in surface properties of the two RCFs had thus no effect on their fibrogenic potential (84).

Table 4. Animal Studies. Chronic Inhalation Toxicity studies with RCFs.

Species Number of animals	Fibre dimention (µm) length (L), diameter (D)	Exposure	Observation time (months)	Effects and rate	Comments	Ref.
Rat: 40 "young", not further specified. 50% males and females.	*Saffil R* median D: 3.3 µm >95% aluminium 3-4% silica. *Thermally aged Saffil R* *UICC Chrysotile Asbestos*	Mean respirable dust concentrations (mrdc): 2.18 mg/m^3 mrdc: 2.45 mg/m^3 mrdc: 4.57 mg/m^3 6 h/day, 5 days/week 86 weeks exposure	Interim killing of 2 animals per group at week 14, 27 and 53. Other animals were observed until 85% mortality.	*Saffil R* 0/48 tumours, no fibrosis *Thermally aged Saffil R* 0/38 tumours, no fibrosis *UICC Chrysotile Asbestos* 5 adenoma, 4 carcinoma,	Only a small proportion of the original dust cloud (20-120 mg/m^3) was respirable . The fibres are crystalline.	83
Rat (three months old): SPF Wistar, AF/HAN strain 48 exposed animals and 40 controls.	Airborne dose: 95 fibres/ml D <3 µm L >5 µm:	Ceramic alumino-silicate glass 95 fibres/ml, (8.4 mg/m^3) 7 h/day, 5 days/week for 224 days.	Pulmonary tumours: 8 (3 carcinomas, 4 malignant histiocytomas). One peritoneal mesothelioma. Pulmonary fibrosis (5%) Control group; 0/40 tumours, 2 very mild pulmonary fibrosis.		High content of shot Approx. 90% of fibres: L <3 µm D <0.3 µm No concurrent positive control group.	18
Hamster: male Syrian Hamster (70) Female Osborne Mendel rats (55) Sham exposed rats (59) and hamsters (58)	Mean D: 1.8 D <2.0: 86% L >10	Fiberfrax 200 fibres/ml (12 mg/m^3), 6 h/day, 5 days /week for 24 months.	Lifetime	Rat: No tumours, 22% fibrosis. Hamster: mesothelioma in 1/70 animals. No fibrosis. Sham exposed hamsters: bronchoalveolar tumour 1/58 Sham exposed rats: 0/59	Also tumours observed by Crocidolit, but no other MMMFs.	97

Table 4. Cont.

Species Number of animals	Fibre dimention(µm) length (L), diameter (D)	Exposure	Observation time (months)	Effects and rate	Comments	Ref.
Rat: male Fischer 344, 140 animals Hamster: Syrian, 112 animlas	Aerosol fiber dimentions Geometric mean (GSD): *RCF-1* D: 0.82 (1.89) L: 15.9 (2.4) *RCF-2*: D: 0.88 (1.92) L: 12.8 (2.5) *RCF-3*: D: 0.85 (1.91) L: 17.4 (2.4) *RCF-4*: D: 1.22 (1.68) L: 9.8 (3.8)	Nose only inhalation of four RCFs:, *RCF-1*: Kaolin *RCF-2*: Zirconia *RCF-3*: High purity Kaolin *RCF-4:* "After service" (kaolin-based ceramic fiber containing 27% cristalline silica) Exposure: 30 mg/m^3 (approximatley 200-250 f/ml) 6 h/day, 5 days/wk, for 24 months. Hamsters were exposed to only *RCF-1*	At death or planned interim sacrifices at 13, 26, 39, 52, 65, 78 and 104 weeks of exposure. Terminal sacrifice when survival was 20% (29 months).	Rat: *RCF-1:* 13% lung tumours Two (1.7%) mesotheliomas *RCF-2*: 7.4% lung tumours and 2.5% mesotheliomas *RCF-3:* 15.7% lung tumours and 1.7% mesotheliomas *RCF-4*: 3.4% lung tumours and 0.8% mesotheliomas *Chrysotile*: 19% lung tumours 1.4% mesotheliomas Hamster: *RCF-1:* Pulmonary fibrosis beginning at 6 months. 41% mesotheliomas.	Lung fibrosis in rats: progression from 3-6 months, followed by no further progression up to 24 months. RCF produces more tumours and fibrosis than 2 samples of MMVFs	65,69
Rat: Fischer 344	RCF-1: AMD: 0.98 µm (0.12-4.53) AML: 22.3 µm (1.3-76.6)	Kaoline-RCFs: 16 mg/m^3 (120 fibres/ml), 9 mg/m^3 (75 fibres/ml), 3 mg/m^3 (25 fibres/ml). Exposures for up to 24 months. Terminal sacrifice at 29 months (at 20% survival)	3, 6, 12, 18 and 24 months. Groups of 3-6 rats from each exposure group were killed at each time point.	*At 3 months:* dose-dependent increase in lung fibrosis. *At 6 months:* minimal progression *At 12, 18 and 24 months*: Further progression with a dose-response-relationship, except for the lowest exposure level . *Lung tumours:* 3.9% and 1.6% in groups exposed to 9 and 16 mg/m^3 respectively. (0.8% in controls).	This study is additional to the maximum tolerated dose study cited above.	67

Table 5. Animal Studies. Administration of RCFs by others routes than inhalation.

Fibre dimention (µm) length (L), diameter (D)	Exposure	Observation time (months)	Effects and rate Comments	Ref.
Intraperitoneal (i.p.) administration of ceramic fibres				
I.p. injection of ceramic wool (Fiberfrax) in female Wistar rats (8 weeks old)				88
L: 51 µm : <90% L: 13 µm : <50% L: 3.6 µm : <10% D: 2.2 µm : <90% D: 0.89 µm: <50% D: 0.36 µm: <10% 61% of total injected mass were fibres	5 weekly injections of 9 mg of fibres in two ml saline. The total amount of injected fibres (L <5 µm D <3 µm, aspect ratio <5:1): 150 millions.	Animals sacrificed after 130 weeks, or earlier when in bad health.	33 of 47 (70%) tumour bearing animals. UICC Chrysotile (1 mg): 30/36 (83%) tumours Saline: 2/102 (2%) tumours	
I.p. injection of ceramic fibres in AF/Han Wistar rats (3 months old)				18
90% of fibres D <0.3 µm L <3 µm 20% of injected particles were fibres longer than 5 µm.	25 mg in 2 ml saline one application to each of 32 animals 2 ml saline to 39 control animals	The first tumour appeared after 850 days	3/32 pulmonary tumours. Sex of animals not stated. Few fibres longer than 5 µm. Much particulate material. No concurrent positive control group.	
I.p. injection of ceramic wool (Manville Corporation) in female Wistar rats (8 weeks old)				88
L: 81 µm : <90% L: 16 µm : <50% L: 4.2 µm : <10% D: 4.1 µm : <90% D: 1.4 µm: <50% D: 0.50 µm: <10% 6% of total injected mass were fibres.	5 weekly injections of 15 mg of fibres in two ml saline. The total amount of injected fibres (L <5 µm, D <3 µm, aspect ratio <5:1): 21 millions.	animals sacrificed after 130 weeks, or earlier when in bad health.	12 of 54 (22%) tumour bearing animals. Average life span of these animals: 54 weeks. UICC Chrysotile (1 mg): 30/36 (83%) tumours. Saline: 2/102 (2%) tumours.	

Table 5. Cont.

Fibre dimention (µm) length (L), diameter (D)	Exposure	Observation time (months)	Effects and rate Comments	Ref.
I.p. injection of ceramic fibres in female Osborne -Mendel rats (100 days old)				97
L: geometric mean 25 µm D: geometric mean 0.9 µm 83% of the fibres L >10 µm 86% of the fibres D <2 µm Ratio non-fibres/fibres in the dust: 33.1	25 mg in 0.5 ml saline to experimental rats and 0.5 ml saline to control rats	Lifetime	19/23 mesotheliomas in the experimental group. No tumours in 25 control animals. UICC Crocidolite group: 20/25 mesotheliomas. Median survival 169, 105, and 83 weeks, respectively.	
I.p. injection of ceramic fibres in male Syrian Golden hamsters (100 days old)				97
L geometric mean 25 µm D geometric mean 0.9 µm 83% of the fibres L >10 µm 86% of the fibres D <2 µm Ratio non-fibres/fibres in the dust: 33.1	25 mg in 0.5 ml saline to two experimental groups and 0.5 ml saline to control group	Lifetime	2/15 and 5/21 mesotheliomas in the experimental groups. No tumours in control animals. UICC Crocidolite group: 8/25 mestheliomas. Median survival 66, 70, 72 and 73 weeks, respectively. Local tissue reaction/fibrosis in all non-tumour bearing animals.	

Table 5. Cont.

Fibre dimention (µm) length (L), diameter (D)	Exposure	Observation time (months)	Effects and rate Comments	Ref.
Intrapleural (i.pl.) administration of ceramic fibres				
I.pl. injections of aluminium and alumino-silicate (ceramic) fibres in Albino rats (Alpk:AP).				85
I) Saffril as manufactered. D: <3 µm: 86.3% L: <10 µm: 8.0%	24 rats of each sex in dose groups and control groups Age at start 8 weeks.	Animals were observed until 85% mortality was reached.	Malignant Mesothelioma 3 in group IV, 7 in group UICC Chrysotile. No mesotheliomas in other groups.	
II) Saffril after thermal aging D: <3 µm: 82.3% L: <10 µm: 0.2%	20 mg suspended solid in 0.2 ml saline as a single intrapleural injection.		No mesotheliomas in other groups. % fibres with diameters <1µm for fibres shorter than 10 µm: Group I: 2% II: 0.2% III: 8.7% IV: 30.3%.	
III) Alumino-silicate made from kaolin clay D: <3 µm: 66.3% L: <10 µm: 19.8%	Saline or UICC Chrysotile were given to the control groups.		In all groups there was local reaction to the injected fibres: minimal to moderat focal fibrosis and mesothelila proliferation, similar for I) and II) and for III) and IV), the two latter somewhat more severe.	
IV) Alumino-silicate made from aluminium and silica D: <3 µm: 92.3% L: <10 µm: 54.5%				
UICC Chrysotile A				
I.pl injection of ceramic alumino-silicate fibres in SPF Wistar rats in groups of 31-36 animals.				107
Alumino-silicate fibres, unknown source. D: 0.5-1 µm	20 mg in 0.4 ml saline in a single intrapleural injection.	Life long observation	3/31 mesotheliomas. In groups with two types of Canadian SFA chrysotil, the tumour incidence was 23/36 and 21/32.	

Table 5. Cont.

Fibre dimention (µm) length (L), diameter (D)	Exposure	Observation time (months)	Effects and rate Comments	Ref.
Intratracheal administration of ceramic fibres				
Intratracheal instillation of Fibrefrax in rats.				30
Coarser dust: D: 0.1-10 µm L: 2.5 µm-25 mm *Finer dust:* mean D: 0.04 µm	*Coarser dust:* amount injected: 50 mg in corn oil. (19 animals) Up to 5 intratracheal instillations weekly. Single instillations of total doses from 3.3-72 mgs. 10 animals were given single injections, 1 had two injections, 1 had three and 13 had four injections.	Three rats killed at 2 and 6 months; Survivors killed at 12 months.	*Coarser dust:* 13/19 spontaneous deaths. Pulmonary infections, but no definite traitment-related pathology. *Finer dust:* 100% mortality rate when single injections were made regardless of dose. A total amount of 13.2 mg injected in four fractionated injections produced the lowest lethality: 3/13. Interpretation difficult due to the high incidence of infections and spontaneous deaths.	
Intratracheal instillation of RCFs in experimental animals.				97
Refractory ceramic fiber GML: 25 µm GMD: 0.9 µm L: 83% >10 µm D: 86% < 2 µm	Rat: Osborne Mendel 100 days old, 22 females in the group. Hamster: Syrian golden, 100 days old, 25 males in the group given 2 mg in 0.2 ml saline once a weeek for 5 weeks.	Life-long observation of the animals	No pulmonary tumours in hamster or rats exposed to either fibre. Both groups had reduced life span compared with controls. UICC Cricidolite group: 2/22 broncho-alveolar tumours in rats and 20/27 bronchoalveolar tumours in hamsters. Fibrosis: rat 2/22 (9%) hamster 4/25 (16%)	

11.7. Mutagenicity and genotoxicity

Data on interactions with DNA are conflicting. Ceramic fibres (not further described) caused very slight DNA damage as determined by hydroxylation of deoxyguanosine (dG) to form 8-hydroxydeoxyguanosine (8-OHdG). The hydroxylation capacity is poor compared to iron-containing MMVFs (53). The combined effect of MMMFs and tobacco smoke increased the levels of 8-OHdG synergistically, but marginally for ceramic fibres compared with Rockwool (54).

Another study demonstrates that ceramic fibres do not form 8-OHdG at all, in contrast to other fibres where iron is a constituent (80).

Four RCFs induced micronuclei in Chinese hamster ovary cells in a length dependent manner, together with other mineral fibres, regardless of fibre widths ranging from 0.3 µm to 7 µm (34, 35)

Four RCFs, induced aneuploidy in oocytes of Drosophila melanogaster. The effects were modest but statistically significant, in the range found for chrysotile and amosite asbestos (82).

Activation of certain oncogens as determined by the levels of mRNA of c-fos and c-jun, shows a slight elevation, but less than for asbestos in kaolin-RCF exposed rat pleural mesothelial cells in vitro. There are no elevations of these gene expressions in the kaolin-RCF exposed hamster tracheal epithelial cells (47).

11.8. Reproductive and developmental effects

No data available.

12. Observations in Man

12.1. Acute effects by contact and systematic distribution

No data available on irritative effects on skin and mucous membranes or on other effects.

12.2. Effects of repeated exposure on organ systems: skin, eye, respiratory system, gastrointestinal tract, liver, kidneys, blood forming organs & peripheral blood, cardiovascular system, nervous system, endocrine system, immune system, other)

Information on man is limited. Data is available to some extent only for the respiratory system among production workers. In some studies caution in interpretation of results must be exercised because some workers may have been previously exposed to asbestos.

In the European Ceramic Fibre Insulation Association ceramic fibre morbidity study (1986-1989), over 650 employees involved in RCF manufacturing showed no evidence of lung disease among workers who never smoked. Smokers had a decline in lung function consistent with their smoking habits. Symptoms of dry cough and breathlessness were also found but could not be attributed to RCF exposure (102).

Chest X-rays of 214 current employees in two RCF manufacturing plants were examined by Horvath (44) as cited by Glass et al (28) had findings consistent with those observed in surveys of non-RCF exposed factory workers (45).

A longitudinal study of pulmonary morbidity among US RCF-manufacture workers production, cited by Glass et al (28), is currently underway. The cohort (n = 742) represents 98.5% of the exposed population. Thirty per cent of the cohort had 10 to 20 years of exposure and 4% had more than 20 years exposure. Workers were classified as exposed (measure of exposure: duration and latency) or not. A decrease (2-3%) was observed in forced vital capacity (FVC) and forced expiratory volume in one second (FEV_1). These effects appeared to correlate with smoking history and the duration of exposure to RCFs (58, 60).

Pleural plaques were found in 2.4% of the production employees. There was no evidence of interstitial fibrosis and no excess of lung cancer and mesotheliomas were not reported (58, 59).

A more detailed study of employees in two of the plants was conducted by Lockey et al (61) and cited by Glass et al (28). Oblique and posterior-anterior chest X-rays demonstrated pleural plaques in 2/214 (0.9%) of non-production workers, in 1/117 production workers with less than 10 years of RCF exposure, in 7/248 (2.8%) of workers with 10-20 years of RCF exposure, and in 9/72 (12.5%) of workers with greater than 20 years. Corrections for age and previous asbestos exposure has not been done. Chest X-rays from 3/652 (0.46%) workers showed borderline parenchyma changes. For the whole cohort, the number and causes of death was consistent with that in the general population, with no excess risk of lung and pleural tumours (59).

Marked chemical modification have been shown for mineral vitreous fibres when extracted human lung (73) and in RCFs recovered from BAL fluids (95, 96) in a limited number of exposed workers. These findings have not been shown in experimental animals, possibly related to their shorter life span and hence time for leaching of the minerals.

12.3. Genotoxic effects

No data available.

12.4. Carcinogenic effects

No data available.

12.5. Reproductive and developmental effects

No data available.

13. Dose-Effect and Dose-Response Relationships

13.1. Single/short term exposure

The inflammatory response in rat lung one month after intratracheal exposure to Fiberfrax, HSA, (1.5 and 10 mg), suggests a dose-related response (55).

13.2. Long term exposures

13.2.1. General

A comparison of the dose-response relationship of asbestos fibres and MMMFs is difficult, because the number of fibres in each size category, their durability and possibly unknown surface properties must be taken into account, and information on these characteristics is still inadequate.

The dose of mineral fibres required to obtain effect in the tissues is also related to their persistence at the site of action. Care should be taken not to expose animals to concentrations leading to overload-induced tumours (see 119).

13.2.2. Animals studies

The RCC inhalation study showed that in hamsters a high dose (30 mg/m^3, 24 months) of kaolin RCFs produced many mesotheliomas (42%), but chrysotile did not (69). In rats there were significant excesses of lung cancer (14.7% total lung tumours (carcinomas and adenomas) (65). Mesotheliomas were also observed (2%). In rats exposed to the other RCFs the percentage of lung-tumour bearing animals was: zirconia-RCFs: 9%, high purity-RCFs: 16%, "after service-RCFs": 3.2%. There were also some mesotheliomas, which appears to be biologically significant, but the incidence was not statistically significant.

Three lower doses (3, 9, 16 mg/m^3) of the kaolin RCF did not produce excess lung cancers (lung tumour incidences 2.7%, 4.3%, and 1.8%, respectively), but there was one mesothelioma (67). There were 1.6% tumours in the sham-exposed group. Among rats exposed to 11 mg/m^3 of Chrysotile there were 21% lung tumours and 1% mesothelioma. This indicates that the exposure response curve for kaolin-RCF-related tumours was very steep. From this study Rossiter, cited by bignon et al (7) concluded that there is no significant exposure-response relationship for the development of pulmonary or pleural tumours by kaolin RCF. This is consistent with the possibility of a threshold close to the MTD (91).

In the same study pulmonary fibrosis was reported for all RCFs and for kaolin-RCF at all exposure levels. All were allocated Wagner-grade approximately 4 except kaolin-RCF at 3 mg/m^3 (grade 3.2). In rats exposed to Chrysotile, the fibrosis

was qualitatively different compared with the fibrosis observed in the rats exposed to RCFs. Although both fibres produced alterations in the same locations and had grade 4, the deposition of collagen was more severe in the Chrysotile-group than in any of the groups exposed to RCF. When information from the multidose study is pooled with the RCF maximum tolerated dose study, there is a demonstration of a dose-response relationship with minimal irreversible histopathological changes at the lowest exposure level (3 mg/m^3), a fibrotic response in the mid level and fibrosis at the highest (MTD) airborne exposure level (12).

13.2.3. Observations in humans

Analysis of mineral fibres in BAL fluid and cells of only seven current workers in a ceramic fibre plant, revealed a positive relationship between the native fibre content and the cellularity of the BAL fluids. There was no relationship between the concentration of fibres and the duration of exposure (95).

Pleural plaques are registered in workers exposed to RCFs, increasingly with time of employment (61), but no correction has been made for previous asbestos exposure and age. See also Section 12.2.

14. Previous Evaluations by (Inter)National Bodies

In 1988, an evaluation of the carcinogenicity of RCFs as a subgroup of MMMF has been conducted by the International Agency for Research on Cancer (IARC). Few animal inhalation experiments involving RCFs were available at that time (19, 83, 97). There was some evidence of fibrosis and some evidence of a carcinogenic effect. When all animals studies, including intracavitary injections, were evaluated together, the IARC working group considered that there was sufficient evidence for the carcinogenicity of ceramic fibres in experimental animals. No data were available at that time regarding the carcinogenicity of ceramic fibres to humans. The overall IARC evaluation classified ceramic fibres as possibly carcinogenic to humans (III B).

These fibres have also been reviewed by the US Environmental Protection Agency (103), and the International Programme on Chemical Safety and Health (46).

15. Evaluation of human health Risks

15.1. Assessment of health risks

Data available from epidemiological studies in RCF-workers have up to now been scarce and non conclusive on carcinogenesis and fibrogenesis. There are no data available on the irritation of skin and mucous membranes as has been shown for most mineral fibres with widths exceeding 4-6 µm. The shortcomings of epidemi-

ological investigations of RCFs to date, necessitates laboratory investigations of RCF toxicity. Some of the limitations of animal experiment are commented in the following.

Animal exposure of mineral fibres, RCFs included, have been performed by various routes; Intracavitary and intratracheal installations are easier and less expensive to accomplish compared to chronic inhalation studies. It has been argued by many authors that the latter provides the best model for assessing potential risk to humans (6, 7, 39, 112). Others claim that the sensitivity of the inhalation model is too low for the identification of the carcinogenic potential of mineral fibres (87, 88).

The dose used in the kaolin-based RCF-inhalation study (65, 69), is much higher (200-fold) than the exposures encountered in the workplace. High exposures to dusts in general may delay clearance due to particle "overload effect", which also has been observed with "nuissance dust" (24). In chronic inhalation studies, when lung burden of nuisance dust reached 1-3 mg/g, a significant retardation of particle clearance was found (76). Such mechanisms may be involved in the reduction of clearance rates after inhalation of RCF-1 at 30 mg/m^3 compared to clearance after lower exposure concentrations (120). This may cause prolonged interaction between dusts and cells at the site of action leading to biological effects that otherwise would not have been observed. This may be of importance when assessing the form of the dose-response curve for lung tumours induced by kaolin-RCF, exhibiting a jump at the high dose level, see Section 13.2.2.

Nonphysiologically high concentrations of fibres at the critical site must also be considered when applying the intraperitoneal injection technique (88). The use of this technique in carcinogenicity testing of mineral fibres has been debated (6, 7).

Alveolar deposition efficiency in rat and man are sufficiently similar for particles and fibres with aerodynamic widths less than 5 µm for rats to be a relevant model for airborne dusts in this size range. Pulmonary toxic effects of fibres with widths larger than 1-2 µm may not be sufficiently evaluated in rodents, however, since the alveolar deposition rate for fibres up to 3 µm is lower compared to man.

The rat is a good model for experimental induction of cancer and fibrosis (18, 20, 107). The interspecies difference in tumour rates shown in the RCC-study (65, 69) is high. This may be due to the differences between rats and hamsters in uptake, deposition and elimination of the inhaled fibres (119).

The durability of the fibres in the lung tissue may however be more important over the longer life-span of humans (49).

15.2. Scientific basis for occupational exposure limit

Alumino-silicate RCFs and others are inducers of pulmonary neoplasms in rats and other rodents in inhalation and injection studies. Epidemiological studies are currently underway. Biological effects of RCFs in workers has not definitely been shown, but non neoplastic pulmonary response cannot be excluded on the basis of findings in chest X-rays and lung function tests. Altogether the RCFs that have been investigated are more biologically active than the MMVF-wools. Human

data until now cannot disclose fibrogenic effects of RCFs. Both carcinogenicity and fibrogenicity of these fibres should be the subject of monitoring and further scientific investigations.

For tumourgenesis and fibrogenesis the potential of RCF toxicity has been shown in many experiments to be between the isolation wools and asbestos.

The critical effect for setting Occupational Exposure Limits for MMVF today is respiratory cancer, and irritative effects of the skin and mucous membranes. When examining RCFs, fibrogenesis should also be taken into account, since both tumours and fibrosis are produced at similar exposure levels in some experiments.

16. Research needs

16.1. Better characterisation of bulk fibre materials and exposure levels

There are few data on airborne levels of RCFs in the manufacturing industry (90). Dustiness associated with the use of RCFs should be evaluated further (23).

Airborne RCFs contains a relative high proportion of non fibrous particles. Since health risk is mainly related to the fibrous particles, efforts should be made to report scientific data on the basis of fibre number, as is currently done in the Nordic and many other countries. Consequently Occupational Exposure Limits may be expressed in fibre numbers per unit volume of air (22).

Industry must identify new fibres of commercial interest so that their biological effects can be studied.

16.2. Biological issues not resolved

More inhalation studies on carcinogenicity are needed. Animals should be exposed to well characterised fibres without shot. Also inhalation studies are needed to fill the data gap for the concentration range between 16-30 mg/m^3 in the dose-response curve for RCF-induced lung tumours (67).

Issues related to fibre durability should be addressed, such as: What is the relationship between persistence time in the tissues and biological effect? Must the persistence time in humans be longer than in rodents for an adverse effect to take place?

The role of surface properties is still unclear. It is not known what the properties of a durable fibre have to be to initiate the carcinogenic process. It is also not known for what duration fibres have to remain in the bronchial wall or serosa tissue to cause an alteration that can lead to the development of a tumour without the further presence of fibres.

The role of fibre widths and lengths to cause biological effects should be further elucidated. Data on fibre translocation, composition, and solubility are also needed.

16.3. Extrapolation of experimental models to human data.

For human health risk assessment experimental models and standard sized reference fibres may help to predict human risk.

More information on interspecies differences is necessary

16.4. Human studies

Better characterisation of exposure at the workplace for a better correlation with dose in the lung tissues. Mineralogical analysis of BAL fluids, and tissues whenever possible, should be encouraged.

16.5. Epidemiological investigations.

Ongoing studies and further epidemiological investigations of exposed RCF-workers and users should be encouraged (72).

Exposures at the workplace should be characterised by fibre types and fibre size distribution in the airborne dust cloud. Groups of workers must be examined for tumours of the lung and pleura, pulmonary fibrosis, pathology of the pleura and lung function. Irritation of the skin and mucous membranes should also be examined.

17. Summary

Skaug V. 121. Refractory ceramic fibres. Nordic Expert Group for Documentation of Occupational Exposure Limits. *Arbete och Hälsa* 1996:30.

Refractory ceramic fibres (RCFs) are highly temperature resistant materials. The main group is alumino-silicate RCFs is commented in the present document. Airborne fibres generally have dimensions in the respirable range. They are carcinogenic and fibrogenic in animal assays. Extrapolation to the human situation is somewhat difficult due to the high concentrations used in animal inhalation experiments as compared with the measured levels in the air of the work environment.

Human data on carcinogenic effects are currently unavailable. Limited data suggests that they may be associated with pleural plaques in humans. Based on a limited number of animal studies and the characteristics of RCFs, an assumption can be made that these fibres may pose a definite risk to the limited number of workers who are highly exposed, and that exposures should be regulated and monitored accordingly.

Key words: refractory ceramic fibres, ceramic fibres, refractory fibres, man-made-vitreous fibres, occupational exposure, rodent inhalation exposure, carcinogenicity, non-neoplastic pulmonary effects, risk assessment.

18. Summary in Norwegian

Skaug V. 121. Ildfaste keramiska fibrer. Nordic Expert Group for Documentation of Occupational Exposure Limits. *Arbete och Hälsa* 1996:30.

Keramiske fibrer er ildfaste materialer. Den største gruppen, aluminiumsilikat - fibrer, omtales i dette kriteriedokumentet. Fibrer i arbeidsatmosfæren har dimensjoner slik at de også kan innåndes Fibrene er karsinogene og fibrogene hos forsøksdyr etter innånding av relativt høye fiberkonsentrasjoner. Slike forsøksbetingelser gjør det vanskelig å direkte ekstrapolere til arbeidssituasjonen for mennesker.
Basert på epidemiologiske undersøkelser har vi frem til i dag ingen kunnskap om at eksponeringen for slike fibrer kan føre til kreft hos mennesker. Det er begrenset informasjon i litteraturen om at de kan være assosiert med pleura plaques hos mennesker. Basert på noen få dyreforsøk og fibrenes karakteristika er det grunn til å anta at gruppen keramiske utgjør en sikker helserisiko for et begrenset antall arbeidere i yrkesgruppene som er høyest eksponert. Eksponeringene bør derfor reguleres og overvåkes tilsvarende.

Nøkkelord: ildfaste fibrer, keramiske fibrer, uorganiske syntetiske fibrer, syntetiske mineralfibrer, yrkeseksponering, inhalasjonsforsøk hos forsøksdyr, kreftuvikling, kronisk lungeskade, risikovurdering.

19. Comments

This document includes literature up until April 1995. The following data bases have been consulted: NIOSHTIC, Chemical abstracts, Medline, Toxline, M-base (excerpta medica).

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2. Borg G. Psychophysical scaling with applications in physical work and the perception of exertion. *Scand J Work Environ Health* 1990;16, Suppl. 1: 55-58.

3. Bergkvist M, Hedberg G, Rahm M. Utvärdering av test för bedömning av styrka, rörlighet och koordination. *Arbete och Hälsa* 1992;5.

b. Chapter in book

1. Birmingham DJ. Occupational dermatoses. In: Clayton GD, Clayton FE, eds. *Patty's industrial hygiene and toxicology Vol.1.* 3rd ed. New York: John Wiley, 1978: 203–235.

c. Book

1. Griffin MJ. *Handbook of human vibration.* London: Academic, 1990.

2. Klaassen CD, Amdur MO, Doull J, eds. *Casarett and Doull's toxicology.* 3rd ed. New York: Macmillan, 1986.

d. Report

1. Landström U, Törnros J, Nilsson L, Morén B, Söderberg L. *Samband mellan vakenhetsmått och prestationsmått erhållna vid körsimulatorstudie av-seende effekter av buller och temperatur.* Arbetsmiljöinstitutet, 1988 (Undersökningsrappport 1988:27).

e. Articles written in langueges other than English, French, German or one of the Nordic languages

1. Pramatarov A, Balev L. Menstrual anomalies and the influence of motor vehicle vibrations on the conductors from the city transport. *Akushersto Ginekol* 1969;8:31-37 (in Russian, English abstract).

f. Article in conference proceedings

1. Mathiassen SE, Winkel J, Parenmark G, Malmkvist AK. Effects of rest pauses and work pace on shoulder-neck fatigue in assembly work. *Work and Health Conference.* Copenhagen 22–25 February 1993: 62–63 (Abstract).

2. van Dijk F, Souman A, deVries F. Industrial noise, annoyance and blood pressure. In: Rossi G, ed. *Proceedings of the Fourth International Congress on Noise as a Public Health Problem.* Milano: Centro Ricerche e Studi Amplifon, 1983: 615-627.

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