
# Recommendation from the Scientific Committee on Occupational Exposure Limits for man made-mineral fibres (MMMF) with no indication for carcinogenicity and not specified elsewhere

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| | |
|---|---|
| 8 hour TWA: | 1 fibre/ml |
| STEL (15 minutes): | - |
| Notation: | - |

Background

In 2000, SCOEL evaluated the health significance of workers exposed to MMVF10 fibres and proposed an OEL of 1 mg/m$^3$ or 10 f/ml (10x10$^6$f/m$^3$). This considered the well-defined NOAEL of 30 fibres/ml, a LOAEL at fivefold higher concentration, and the absence of a carcinogenic potential in long term inhalation studies. Recently, SCOEL proposed an OEL for refractory ceramic fibres (RFCs) of 0.3 f/ml (SCOEL 2010), which was set from epidemiological studies and adjusted for hazards, i.e. mesothelioma and lung cancer, in animal studies.

A general evaluation of available data on MMMF has been started to develop a procedure to regulate MMMF exposure at the workplace. When evaluating the literature it became apparent that although a great amount of publications on MMMF are available only few have been designed to identify dose-response of the adverse effects including identification of NOAELs that can be used as a starting point to derive OELs. Since the number of MMMF is abundant and steadily increasing, SCOEL does not expect that appropriate inhalation studies will be made available for each of the fibre materials to identify a NOAEL. SCOEL concluded therefore that it is not appropriate to propose an OEL for each of such fibres, but to set a value that is applicable for all respirable fibre materials for which no appropriate inhalation studies to set a specific OEL are available. This only applies for fibres without indication of carcinogenicity, according to the criteria for fibre classification of the Annex II to Council Directive 67/548/EEC (see Appendix I). This "general MMMF-OEL"is derived from the available life time inhalation studies in rats, which allowed derivation of a NOAEL or LOAEL. Considering the uncertainties to extrapolate from LOAEL to NOAEL, the uncertainties of interspecies-extrapolation and possible intrinsic differences in fibre toxicity the conservative assessment factors of 20, and 10, respectively have been applied. The resulting values range between 1.3 and 3 (see Table 3). From this the value of 1 fibre/ml is derived. This rather conservative value is supported from the range bracketed by the OEL (10 f/ml) for the low offending MMMF10 and the OEL (0.3 f/ml) for the more offending RFCs. A deviation from the 1 f/ml level is only possible when appropriate studies of the specific material is made available which allow identification of a NOAEL. Accordingly, SCOEL will derive specific OELs for the fibre materials listed in Tables 2 and 3. The main documentations used by the SCOEL in the evaluation of MMMF were MAK (DFG 1993), DECOS (1995) and IARC (2002).

Substance

Man-made mineral fibre (MMMF) is a generic name used to describe an inorganic fibrous material manufactured primarily from glass, rock, minerals, slag and processed inorganic oxides. The MMMF produced are non-crystalline (glassy, vitreous, amorphous).

MMMF are manufactured by a variety of processes based on the attenuation of a thin stream of molten inorganic oxides at high temperatures. All commercially important MMMF are silica-based and contain various amounts of other inorganic oxides. The non-silica components typically include, but are not limited to, oxides of alkaline earth, alkalis, aluminium, boron, iron and zirconium. The MMMF have a broad variety of chemical compositions (IARC 2002). Physical structure influences leaching of the fibres and their reactions to mechanical stress. Leaching favours dissolution and disintegration of the fibre and it changes the surface characteristics of the fibre, such as specific surface area, surface charge, the presence of Fe ions and the fibre dimensions. Fibre surface and fibre dimensions affect interactions with biological structures and the generation of reactive oxygen species (ROS) (Wagner *et al* 1984; Davis 1986; LeBouffant *et al* 1987; Hammad 1988; Jaurand 1997; Fubini 1996; 1997; Greim 1997; Greim *et al* 2000, 2001).

Fibre dimensions are of crucial importance regarding biopersistence and the toxic potential of fibres (Hammad 1984; Bernstein *et al* 1996; Hart *et al* 1994). For regulatory purposes, particles are counted as fibres when they have the following dimensional characteristics: length L > 5 µm, diameter D < 3 µm and an aspect ratio L:D> 3:1, meeting the fibre definition criteria of WHO. They correspond to the respirable fraction of the fibrous dust limited to those being able to enter the alveolar region of humans (D< 3 µm).

In 1988, IARC grouped MMMF into five categories: glass filament, glass wool, rock wool, slag wool and ceramic. To reflect developments in the industry, IARC (2002) expanded the categories into: continuous glass filament, glass wool (insulation wool and special purpose wool), rock wool, slag wool, refractory ceramic and other.

# 1. Occurrence and Use

MMMF do not occur in nature. Significant commercial production of man-made mineral fibres began in the early twentieth century. MMMF products can release airborne respirable fibres during their production, use and removal.

According to IARC (2002) it was estimated that in 2001 over 9 million tonnes of man-made mineral fibres were produced annually in over 100 factories around the world. Most of these are used as thermal or acoustical insulation. Usage for this purpose is divided about equally between glass wool (about 3 million tonnes, used predominantly in North America) and rock (stone) and slag wool (about 3 million tonnes, used predominantly in Europe and the rest of the world). In recent years, high-alumina, low-silica wools (about 1 million tonnes) have been increasingly replacing rock and slag wools in this application. Special-purpose glass fibres are of limited-production, small-diameter fibre products are typically used for purposes other than insulation as in filtration media and batteries. Continuous glass filaments (2 million tonnes) are generally used in the reinforcement of plastics and in textiles but are usually of larger diameter and hence not subject to classification according to EU criteria. Refractory ceramic fibres (RFCs), first produced commercially in the 1950's are widely used (about 150 thousand tonnes) in high-temperature applications such as furnace insulation. The more recently developed alkaline earth silicate (AES) wools (about 10 thousand tonnes) are replacing refractory ceramic in some applications.

# 2. Health significance

## 2.1. Toxokinetics

The uptake of fibres into the body takes place via the respiratory tract. Transport and deposition of the fibres in the airways are determined by their aerodynamic behaviour. The fibre size, their chemical composition and the deposited dose in the lung define their retention kinetics. Fibres may be deposited in the respiratory airways by: impaction, sedimentation, interception and diffusion. The fate of deposited fibres within the respiratory system depends on both the site of deposition and the characteristics of the fibre. The main mechanisms of fibre clearance include mucociliary movement in the nasopharyngeal and tracheobronchial regions and alveolar macrophage phagocytosis in the alveolar region with subsequent removal towards the mucoliary escalator. In addition to these mechanisms, chemical dissolution and leaching, swelling and breakage, can occur.

Biopersistence is defined as the total of all physical and chemical processes leading to clearance of fibres from the respiratory tract *in vivo*. The biopersistence of fibres deposited in the respiratory tract results from a combination of physiological clearance processes (mechanical translocation/removal) and physico-chemical processes (chemical dissolution and leaching, mechanical breaking). Breakage of fibres may lead to temporary increase of fibre numbers in the lung. Dissolution and leaching are processes influenced by fibre composition and the pH of the surrounding milieu (Hesterberg *et al* 1996b; Christensen *et al* 1994; HVBG 1998; Guldberg *et al* 1998, 2002; Kamstrup *et al* 2001, 2002; Knudsen *et al* 1996). Moreover, biodurability depends on whether or not fibres are phagocytised by macrophages (intracellular pH about 5) or not (Luoto *et al* 1995, 1998). Only fibres with lengths up to about 10 µm can be efficiently phagocytosed by rat alveolar macrophages, whereas long fibres (L> 20 µm) lead to "frustrated phagocytosis" (Oberdöster 1991; Oberdöster and Lehnert 1991; Tran *et al* 1996). With regard to fibres >20 µm, Nota Q of EU Directive outlines specific criteria in relation to biopersistence that determine whether or not

classification for carcinogenicity should be applied (Annex I). In addition, Nota R states that "classification as a carcinogen need not apply to fibres with length weighted geometric mean diameter less two standard geometric errors greater than 6 µm". SCOEL further notes that mineral fibres with high $Al_2O_3$ content are more biosoluble than those with high $SiO_2$ contents (Guldberg *et al* 2002; Kamstrup *et al* 2001, 2002).

### 2.2. Mechanism of action

Inhalation of man-made vitreous fibres (MMVF) leads to both inflammatory and fibrotic processes, as well as expression of genes linked to cell proliferation and antioxidant defense in a dose-related fashion. These processes are associated with the activation of alveolar macrophages, lymphocytes, polymorphonuclear cells, mast cells, and fibroblasts and the release of a number of cellular mediators, e.g. tumour necrosis factor $\alpha$ (TNF$\alpha$), interleukin-1$\alpha$ (IL-1$\alpha$), interleukin-6 (IL-6), and basic fibroblast growth factor (bFGF) and the upregulation of protooncogenes. Injury to alveolar epithelial cells is followed by hyperplasia and hypertrophy and occasionally by neoplastic transformation resulting in tumourigenesis. Fibre activated macrophages and other inflammatory cells generate reactive oxygen species (ROS), e.g. $O_2^{-\bullet}$, $H_2O_2$, and NO (Wang *et al* 1999 a). The hydroxyl radical ($OH^{\bullet}$), peroxynitrite, and nitronium ions may also be formed. ROS can also originate from redox reactions occurring at the fibre surface, e.g. by fibre iron catalysis, leading finally to generation of $OH^{\bullet}$. These oxidants induce oxidative stress in the target cells (Baan and Grosse 2004; Driscoll 1996; Fubini 1996; Kamp *et al* 1992; Martin *et al* 1998; Mossman and Churg 1998; Oberdörster and Lehnert 1991; Saffiotti 1998; Staruchova *et al* 2008; Tsuda 1997; Wang *et al* 1999a, b; Zhu *et al* 1998).

These processes, being the underlying mechanism of fibre carcinogenicity, are considered to have a threshold. Cellular antioxidative systems including superoxide dismutase (SOD), catalase, and glutathione-*S*-transferase-dependent systems, protect against cellular injury and DNA damage as long as the release of ROS is not sufficient to overwhelm this defence (Howden and Faux 1996; Marks-Konzcalik *et al* 1998; Oberdörster 1997). Consequently, the lung is able to deal with a considerable number of fibres without detectable molecular or pathogenic events, which has been shown in epidemiologic and experimental studies (Mossman and Churg 1998).

### 2.3. Genotoxicity

Several types of fibres have been shown to induce chromosomal aberrations, deletions, micronuclei, and aneuploidy in both rodent and human cells in culture (overview in Greim 1997; Jaurand 1997). Aneuploidy and polyploidy can result either by sterically blocking cytokinesis, by mitotic disturbances or by physical interaction with chromosomes and the spindle apparatus (Dopp *et al* 1995, 1997; Jensen *et al* 1996; Ong *et al* 1997). Some limited *in vitro* data are available on the formation of oxidised DNA bases (e.g. 8-hydroxydeoxyguanosine, 8-OHdG) (Jaurand 1997, Schurkes *et al* 2004). ROS (see section 3) also play a role in DNA and chromosomal breakage (Dopp and Schiffmann 1998). The induction of DNA strandbreaks, DNA-DNA crosslinks and of DNA repair has been demonstrated (Wang *et al* 1999 b). But these *in vitro* data have not been sufficiently validated in *in vivo* studies, with the exception of few *in vivo* studies (Unfried *et al* 2002; Schürkes *et al* 2004).

The extent of genotoxicity may depend on a cell's ability to adapt to oxidant stress. It has been suggested that a threshold fibre concentration should be exceeded in order to initiate a significant enhancement of abnormal anaphases/telophases and subsequent cell transformation (Okayasu *et al* 1999; Yegles *et al* 1995).

## 2.4. Carcinogenicity

The life time studies in rats on rock wool and slag wool as well as insulation fibre glass (and of TISMO) did not reveal carcinogenic effects. Recent evaluations of the epidemiological studies of workers exposed to respirable rock wool and glass wool fibres (Lipworth *et a*l 2010) and glass wool fibres (NTP 2010) support these data. Lipworth *et al* (2010) who conducted a systemic review and meta-analysis of lung and neck cancers in epidemiological studies of workers exposed to rock wool and glass wool concluded: "Despite a small elevation of the RR for lung cancer among MMVF production workers, the lack of excess risk among end users, the absence of any dose-risk relation, the likelihood of detection bias, and the potential for residual confounding by smoking and asbestos exposure argue against a carcinogenic effect of MMVF, rock wool, or glass wool at this time. Similar conclusions apply to head and neck cancer."

NTP (2010) came to a similar conclusion: "There is inadequate evidence of the carcinogenicity of glass wool fibres as a class from the available studies in humans. Although studies of occupational exposure found excess lung-cancer mortality or incidence, there was no convincing evidence that the excess lung cancer was due to exposure specifically to glass wool fibres, because (1) no clear positive exposure-response relationships were observed, and (2) the magnitude of the risk estimates were small enough to potentially be explained by co-exposure to tobacco smoking."

## 2.5. Derivation of an OEL for Man-Made Mineral Fibres

### 2.5.1. OEL for MMMF proposed by DECOS

The Dutch Expert Committee on Occupational Standards (DECOS) evaluated the available information and proposed occupational exposure limits (OELs) for MMMF (DECOS 1995).

The expert committee evaluated the carcinogenic potency of MMMF at the OEL (Table 1). For glass wool fibres, DECOS used the rat study of LeBouffant *et al* (1987), which showed that a 12- to 24-month exposure of respirable glass wool fibres at a concentration of 5 mg/m$^3$ induced an alveolar macrophage reaction with a slight septal fibrosis. The effect was related to the duration of the exposure and tended to diminish after the exposure stopped. Applying a safety factor of 10 for the extrapolation of animal data to man, an OEL of 0.5 mg/m$^3$ (4.8 fibres/ml) for respirable glass wool fibres has been proposed (Table 1).

There are many physical and chemical similarities between special-purpose glass fibres and glass wool fibres. No human data are available. Animal data showed that 332 respirable special-purpose glass fibres/ml induces an effect (irritation and inflammation of the nasal mucous membranes) level. For this reason, DECOS proposed a safety factor of 50 for special-purpose fibres, 10 for the interspecies variation, and 5 for taking an effect level as the starting point, that means to compensate for the use of a LOAEL (Table 1).

Because DECOS considered the nature of the critical effects of the MMMF of rock wool, slag wool, glass wool, and special-purpose fibres to be very similar, it recommended an equal OEL of 3 respirable fibres/ml for these fibres. This was based on the NOAEL for rock wool of 33 fibres/ml being the lowest NOAEL of these fibres.

DECOS considered refractory ceramic fibres, which do not exclude fibres of silicon carbide and silicon nitride, to be carcinogenic on the basis of positive long-term inhalation studies in rodents. Two approaches were used to set an OEL. Assuming a non-genotoxic mechanism, an OEL of 1 respirable fibre/ml was proposed, based on

the NOAEL of 25 fibres/ml. A safety factor of 25 was used to take into account the seriousness of the critical carcinogenic effect. Assuming a genotoxic effect, the acceptable excess cancer risk of 7 x $10^{-4}$ corresponds to an occupational exposure of 1 respirable fibre/ml for 8 hr/day for 40 years.

**Table 1**. Occupational exposure limits for man-made mineral fibres (MMMF), as proposed by the Dutch Expert Committee on Occupational Standards (DECOS 1995).

| Fibres | NOAEL Resp. fibres/ml | LOAEL Resp. fibres/ml | Suggested OEL Resp. fibres/ml | Safety factor |
|---|---|---|---|---|
| Glass wool | | 48 | 4.8 | 10 |
| Rock wool | 33 | | 3.3 | 10 |
| Slag wool | 210 | | 21 | 10 |
| Special purpose glass | | 332 | 6.6 | 50 |
| **Common OEL** | | | **3 (0.3 mg/m$^3$)** | |
| Refractory ceramic | 25 | | 1 | 25 |

### 2.5.2. Chronic inhalation studies

Between 1970 and 1987 several chronic rodent inhalation studies were conducted. Seven studies of fibreglass and three studies of mineral wool were negative for fibrosis and tumourigenesis (Gross *et al* 1970; Lee *et al* 1981; McConnell *et al* 1984; Wagner *et al* 1984; Davis 1986; Le Bouffant *et al* 1987; Muhle *et al* 1987; Smith *et al* 1987). In two studies of refractory ceramic fibres (Davis *et al* 1984), 5% fibrosis and 17% lung tumours following a 12-month exposure of rats were observed, whereas Smith *et al* (1987) neither observed fibrosis nor tumours and only 2% mesotheliomas in hamsters after 24 months of exposure. However, these studies had one or more technical limitations (Hesterberg and Hart 2001). In two studies (Wagner *et al* 1984; McConnell 1984), relatively short test fibres were used. More than 70% of test fibres were shorter than 10 µm. In other studies fibres tended to be too thick for rat respirability, or data on fibre numbers and dimensions in aerosols and/or lung burdens were incomplete or not reported. Due to the less respirable fibres, lung burdens were relatively small. In the Smith *et al* (1987) study, lung burden were roughly 3 x $10^6$ and 2 x $10^6$ for RCFs and JM 475 fibreglass-fibres, respectively, as compared to 150-2 000 x $10^6$ fibres/lung in studies conducted after 1988.

In more recent studies, the fibres were rat respirable (geometric mean diameter about 1 µm or less) with a large portion of long fibres (50% of the fibres had an arithmetic mean length of 20 µm) (Hesterberg *et al* 1993). Moreover, aerosolisation and exposure by nose only inhalation have been improved (Hesterberg and Hart 2001). Using these techniques several inhalation studies on different MMMF have been performed.

## 2.6. Recent long term dose response inhalation studies (Table 2)

### 2.6.1. Rock wool and slag wool

To study dose-related chronic inhalation toxicity and carcinogenic effects rats were exposed to rock wool at concentrations of 3, 16 and 30 mg/m$^3$ (~ 30, 150 or 240 WHO fibres/ml) for 24 months or slag wool at 3, 16 and 30 mg/m$^3$ (~ 30, 130 or 210 WHO fibres/ml) for 24 months. Both type of fibres were size separated to be largely rat respirable (mean diameter < 1 µm) and enriched with long fibres (mean length > 15 µm). Exposure to these fibres induced a dose-related inflammatory response, while

rock wool produced minimal focal pulmonary fibrosis in addition to inflammatory response. Both rock wool and slag wool exposure did not show any neoplastic activity in the lungs or the pleura. In both studies, the NOAEL was 30 fibres/ml (McConnell *et al* 1994).

### 2.6.2. Insulation fibreglass

This type of fibres includes MMVF10 (JM 901) and MMVF11 (Hesterberg *et al* 1993). Rats were exposed to three fibres concentrations of 3, 16 and 30 mg/m$^3$ (approximately 250 WHO fibres/ml, including 73 to 90 fibres/ml longer than 20 μm). The 2 types of fibre-glass did not induce fibrosis nor tumours except transient lung inflammation that disappeared after a post-exposure recovery period, which was disputed however by Infante *et al* (1994). Hamsters exposed to MMVF10a (JM 901 fibre-glass) did not develop fibrosis or thoracic neoplasms at 30 mg/m$^3$ (McConnell *et al* 1999).

In the chronic inhalation study (Hesterberg *et al* 1995) rats were exposed to fibrous glass (MMVF10 and 11) rock wool or slag wool and to RCF1 and chrysotile as positive control. A significant increase in pulmonary fibrosis, lung tumours and mesotheliomas was observed in rats exposed to RCF1, while these tumour incidences were within normal limits after exposure to rock wool, slag wool and fibrous glass. A slight pulmonary fibrosis was observed in rats exposed to rock wool and RCF1.

### 2.6.3. Potassium octatitanate fibres (TISMO)

Ikegami *et al* (2004) investigated potassium octatitanate fibres (TISMO) in a 2-year inhalation study in rats, combined with determination of lung burden and fibre clearance. Groups of 135 rats were exposed to 0, 20, 60 or 200 WHO fibres/ml 6h/day, 5 days/week for 24 months. Lung burdens were determined by sacrificing subgroups after 3, 6, 12, 18 and 24 months. The results indicated that at 20 fibres/ml the steady state of lung burden (equilibrium between lung burden and clearance) was reached after approximately 18 months of exposure. At all times investigated, 200 fibres/ml resulted in a disproportional increase in lung burden indicating saturation of lung clearance as a result of overloading, while a graduate increase was seen at 20 or 60 fibres/ml. To determine lung clearance, subgroups were removed after 6 months of exposure and were killed 3, 6, 12 and 18 months later. Following the 6-month exposure, the amount of fibres in the lung decreased with a half-life of approximately 6 months at all exposures and was decreased by approximately 72%, 74%, and 79% in the 200, 60 and 20 WHO fibres/ml.

Based on the results of the lung burden study and histopathological observations, the exposure concentration of 20 WHO fibres/ml was considered a NOAEL. 60 fibres/ml induced lesions of a borderline level. At the highest fibre concentration, some alveolar walls enclosing aggregates of TISMO laden alveolar macrophages were slightly thickened after 12 months of exposure and revealed slight alveolar fibrosis after 18 and 24 months of exposure. No exposure related pulmonary neoplasm or mesothelioma was observed after 24 months of exposure.

The publication also describes the results of a health hazard evaluation on 27 current employees and 18 former employees at 14 designed production workplaces. The employment period of the current workers ranged from 7 months to 19.1 years, that of the former employees from 3 months to 14.8 years. The health hazard was evaluated by chest x-ray, lung function tests, utilising forced spirometry and expiratory flow volume curves. The geometric means of airborne TISMO fibre concentration ranged from 0.2 to 1.6 WHO fibres/ml in 1994 and decreased to 0.10-0.14 WHO fibres/ml in 1999. No exposure related adverse effects were observed.

Since Ikegami *et al* (2004) described a half-life of about 180 days the high biopersistence does not exclude carcinogenic potential of this fibre although the study supports the NOAEL of 20 WHO fibres/ml.

**Table 2.** Long term dose response inhalation studies not considered by DECOS (1995).

| Fibre | Species/ duration | Exposure | NOAEL | LOAEL | Reference |
|---|---|---|---|---|---|
| MMVF10 | Rats, 24 mo, 6h/d, 5d/w | 3, 16, 30 mg/m$^3$ | 3 mg/m$^3$ (25 f/ml) | | Hesterberg *et al* 1993 |
| MMVF11 | Rats, 24 mo, 6h/d, 5d/w | 3, 16, 30 mg/m$^3$ | 3 mg/m$^3$ (25 f/ml) | | Hesterberg *et al* 1993 |
| MMVF10 | Rats, 78 w, 6h/d, 5d/w | 3, 16, 30, 45, 60 mg/m$^3$ | | 3 mg/m$^3$ 25 f/ml | Hesterberg *et al* 1996 |
| MMVF10.1 | Hamster, 13 w, 6h/d, 5d/w | 3, 16, 30, 45, 60 mg/m$^3$ | | 3 mg/m$^3$ (25 f/ml) | Hesterberg *et al* 1999 |
| MMVF10a, MMVF33 | Hamster, 78 w, 6h/d, 5d/w | 30 mg/m$^3$ | Not determined | | McConnell *et al* 1999 |
| MMVF21 | Rats, 104 w, 6h/d, 5d/w | 3, 16, 30 mg/m$^3$ | 3 mg/m$^3$ | | McConnell *et al* 1994 |
| MMVF22 | Rats, 104 w, 6h/d, 5d/w | 3, 16, 30 mg/m$^3$ | 3 mg/m$^3$ (30 f/ml) | | McConnell *et al* 1994 |
| MMVF21 | Rats, 13-104 w, 6h/d, 5d/w | 16, 30 mg/m$^3$ | Not determined | | Kamstrup *et al* 2001 |
| MMVF34/HT | Rats, 13-104 w, 6h/d, 5d/w | 30 mg/m$^3$ | Not determined | | Kamstrup *et al* 2001 |
| TISMO | Rats, 24 mo 6h/d, 5 d/w | 20, 60, or 200 f/ml | 20 f/ml | | Ikegami *et al* (2004) |
| X607 | Rats, 24 mo 6h/d, 5 d/w | 200 f/ml (≈16 mg/m$^3$) | | 200 f/ml | Hesterberg *et al* 1998 |

MVF10: 901 glass wool

*MMVF10.1: 901 glass wool*

MMVF10a: Typical building insulation fibre glass

MMVF11: Certain Teed glass wool

MMVF21: Traditional (rock) stone wool. HL 65 and 92 days (WHO, long fibres)

MMVF22: Slag wool

MMVF33: Special application fibre glass

MMVF34/HT: Biosoluble rock wool fibre. HL 25 and 6 days (WHO, long fibres)

TISMO: Potassium octatitanate fibres, HL ~ 6 months

X607: Calcium-magnesium-silicate fibre (similar to CMS)

MMVF10, MMVF10a and MMVF10.1 are essentially the same (Hesterberg *et al* 1999). Due to production changes they slightly differ in their fluorine content. They have similar *in vitro* dissolution rates.

**Table 3.** NOAELs/LOAELs and levels of man-made mineral fibres derived by applying assessment factors (AF) according to DECOS (1995).

| Fibres | NOAEL Resp. fibres/ml | LOAEL Resp. fibres/ml | Values derived by applying AFs Resp. fibres/ml | AF |
|---|---|---|---|---|
| MMVF10 (glass wool) Rat, 2 years | 25 | | 2.5 | 10 |
| MMVF10 (glass wool) Rat, 78 w | | 25 | 1.25 | 20* |
| MMVF10.1 (glass wool) Hamster, 13 w | | 25 | 1.25 | 20* |
| MMVF11 (glass wool) Rat, 2 years | 25 | | 2.5 | 10 |
| MMMF21 (rock wool) Rat 2 years | 30 | | 3 | 10 |
| MMMF22 (slag wool) Rat, 2 years | 30 | | 3 | 10 |
| X607[1] Rat, 2 years | | 200 f/ml | 10 | 20* |

[1] X607: Calcium-magnesium-silicate fibre. * Factor 20 to consider LOAEL.

# 3. Recommendation

SCOEL considers properly conducted inhalation studies, preferentially in rats, using fibres of rat respirable size which upon long term exposure did not induce carcinogenic effects as the best basis for setting an OEL. Fibres longer than 5 µm, shorter than 100 to 200 µm of a diameter less than 3 µm with a length/diameter ratio of at least 3:1 are considered respirable. Such studies have been performed with fibres of glass wool, rock wool, slag wool and calcium-magnesium-silicate (Table 3). In all these studies, inflammation and subsequent fibrosis of the lung have been the critical effects. In the two-year exposure studies in rats, NOAELs within the narrow range of 25 to 30 fibres/ml of inhaled air have been determined.

For fibres with insufficient data to derive a specific OEL, SCOEL proposes a general OEL of 1 fibre/ml. This value is derived as decribed before: Considering the uncertainties to extrapolate from LOAEL to NOAEL, the uncertainties of interspecies-extrapolation and possible intrinsic differences in fibre toxicity, the conservative assessment factors of 20 and 10, respectively, have been applied. The resulting values range between 1.3 and 3 (see Table 3). Based upon this information the lowest value of 1.3 fibres/ml for glass wool fibres is adjusted to a general OEL of 1 fibre/ml, which corresponds to about 0.1 mg/m$^3$ (Schneider 1987). This OEL is applicable to MMMF without indication of carcinogenicity (see Annex I) and the characteristics: length >5 µm, diameter D <3 µm and a ratio L:D >3:1 (WHO fibres). For the fibres listed in Tables 2 and 3, for which NOAELs can be derived, SCOEL will propose specific OELs (see e.g. MMVF10, SCOEL 2000).

No fibre counting difficulties are foreseen at the recommended OELs. Fibre counting shall be carried out in accordance with the 1997 World Health Organisation (WHO) recommended method "Determination of airborne fibre number concentrations by phase-contrast optical microscopy (membrane filter method)". Theoretically, the process of counting randomly distributed (Poisson) fibres yields a coefficient of variation (CV) of 10% for 100 fibres and 32% for 10 fibres, taking into account only statistical variation. In practice, however, the actual CV will be greater because of the additional component of variation associated with subjective differences within and between microscopists.

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# ANNEX I

## Fibre classification

Classification of a fibre into the various categories is made according to the following criteria: (Annex II to Council Directive 67/548/EEC):

Category 1, known to be carcinogenic to man

### Positive results from epidemiological studies

Category 2, should be regarded as if they are carcinogenic to man

### Positive results from animal studies

Category 3, cause concern for man owing to possible carcinogenic effects, but in respect of which the available information is not adequate for making a satisfactory assessment

### Based primarily on animal results

All inorganic with critical dimensions are suspected of having a carcinogenic potential and therefore are classified a priori as category 3 carcinogens. This classification need not apply if it can be shown that the fibre fulfills one of the following conditions (Nota Q):

a short-term biopersistence test by inhalation showing that the longer than 20 µm have a weighted half-life of less than 10 days;

or

a short-term biopersistence test by intratracheal instillation showing that the longer than 20 µm have a weighted half-life of less than 40 days;

or

an appropriate intraperitoneal test showing no evidence of excess carcinogenicity;

*or*

absence of relevant pathogenicity or neoplastic changes in a suitable long-term inhalation test.