High Temperature Insulation Wool toxicology – What have we learned?

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OBJECTIVES

- To show where High Temperature Insulation Wools (HTIW) sit in the family of synthetic mineral fibres.
- To review the principal mechanisms of fibre toxicity.
- To describe the early toxicological investigations on HTIW.
- To present current understanding of the toxicology of HTIW, including that of heated (after-service) fibres.

HTIW AND OTHER MAN-MADE MINERAL FIBRES

A classification of fibres

Natural

- Organic
  - Animal
  - Plant
- Inorganic
  - Vitreous (e.g. volcanic glass)
  - Crystalline (e.g. asbestos, zeolites and fibrous clays)

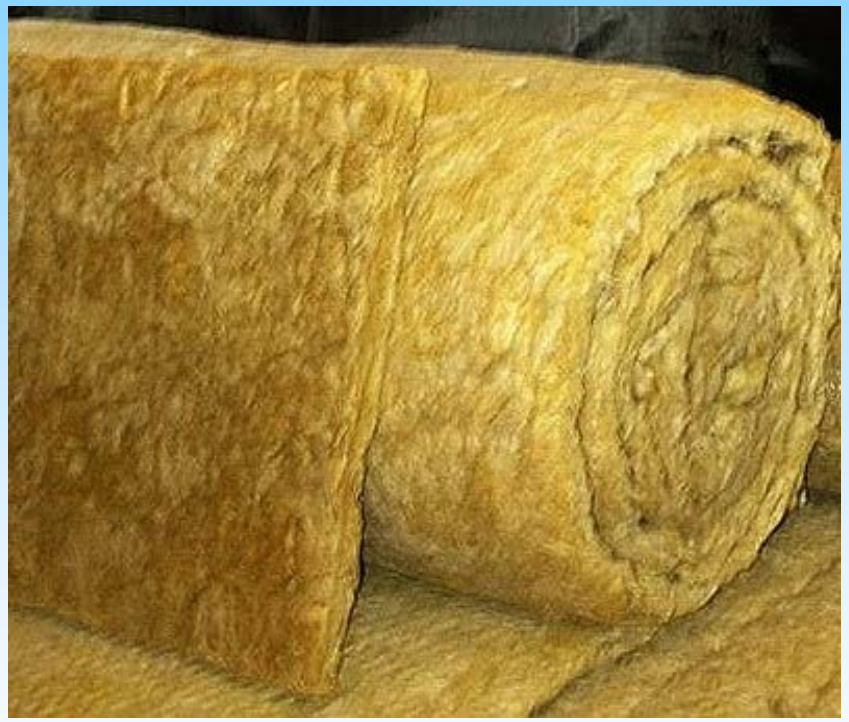
Man-made

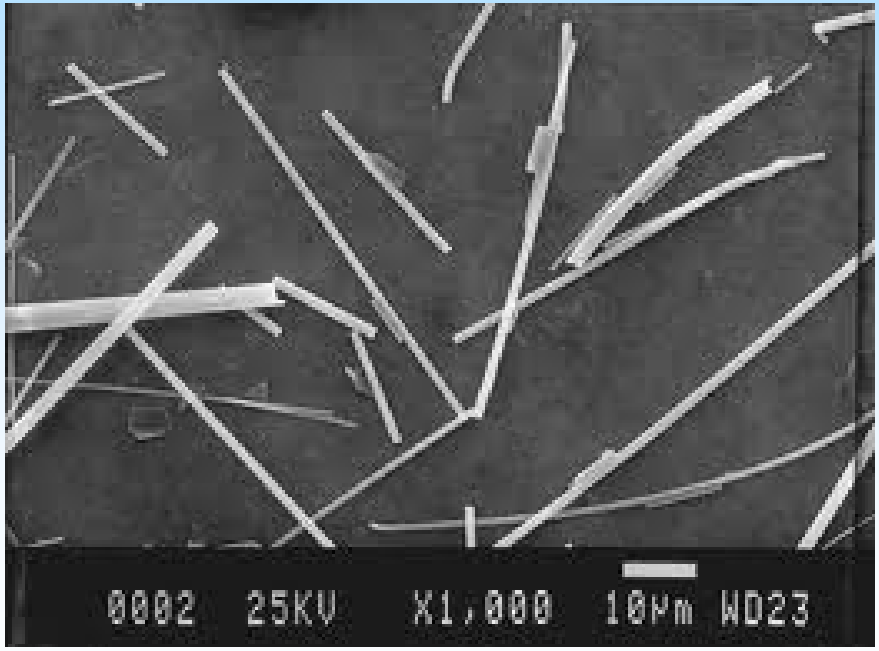
- Organic
  - Textile
  - Aramid
- Inorganic
  - Vitreous (e.g. glass textile, mineral wool, refractory ceramic fibres)
  - Crystalline (e.g. carbon fibre, silicon carbide whiskers, polycrystalline wool)

Some common types of man-made fibre

- Glass wool (continuous filament)
- Rock/Stone wool
- **Aluminosilicate Wools/Refractory ceramic fibres (ASW/RCF)**
- **Alkaline Earth Silicate (AES) wool**
- **Polycrystalline wools (PCW)**
- Metal oxides
- Silicon carbide ‘whiskers’
- Carbon fibres and nanotubes
- Organic fibres (e.g. aramid fibres)

Macro- and microscopic appearance of MMMF

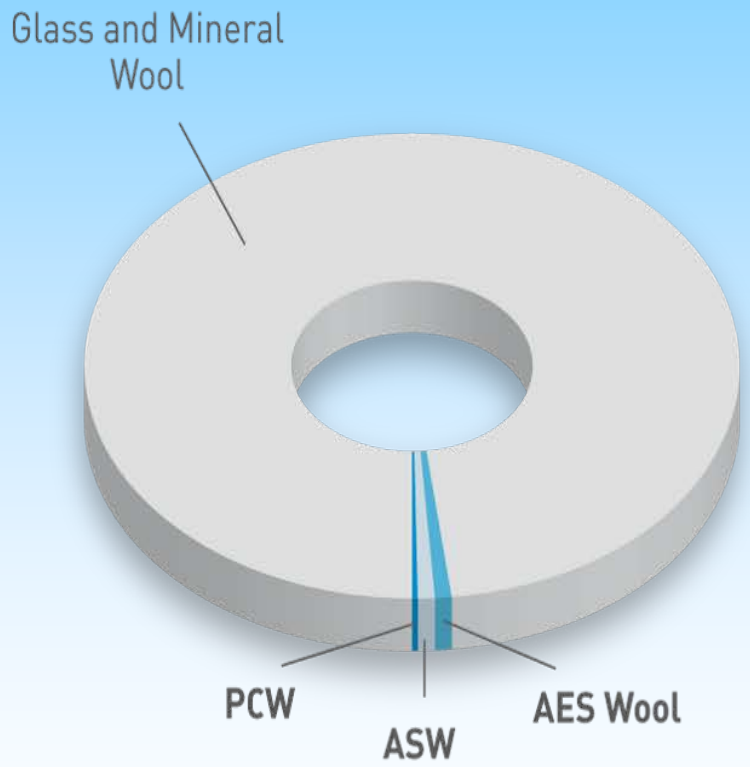




Chemical composition of some MMMFs

- Glasswool: Silica with oxides of sodium, aluminium and calcium in different proportions
- Rockwool and slagwool: As for glasswool, but including magnesium and ferrous (and other) oxides
- **Aluminosilicate wools/Refractory ceramic fibres** (ASW/RCF): Silicon and aluminium oxides, and sometimes zirconium oxide
- **AES wools**: Various combinations of calcium, magnesium and silicon oxides

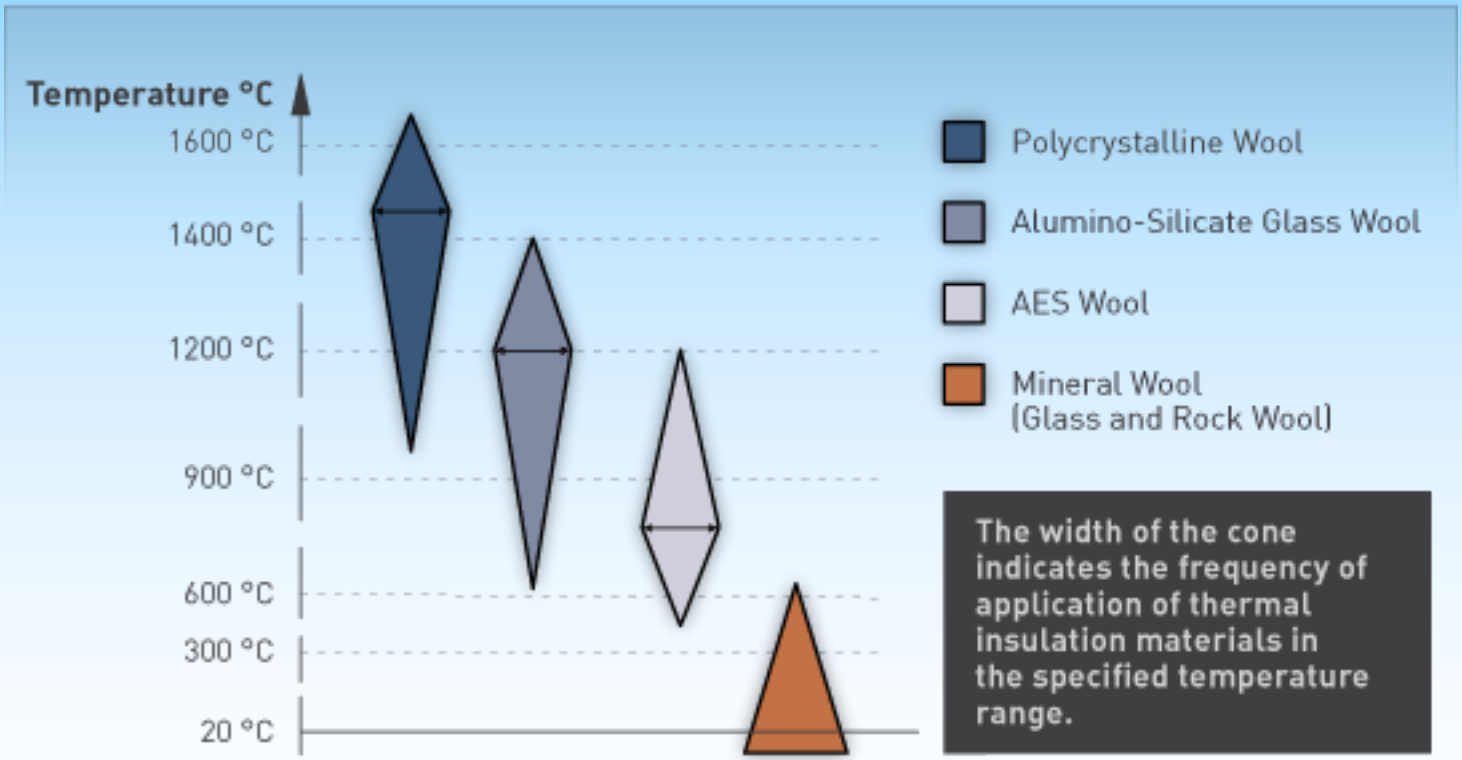
HTIW in the family of MMMF products



HIGH TEMPERATURE INSULATION WOOLS < 2 %

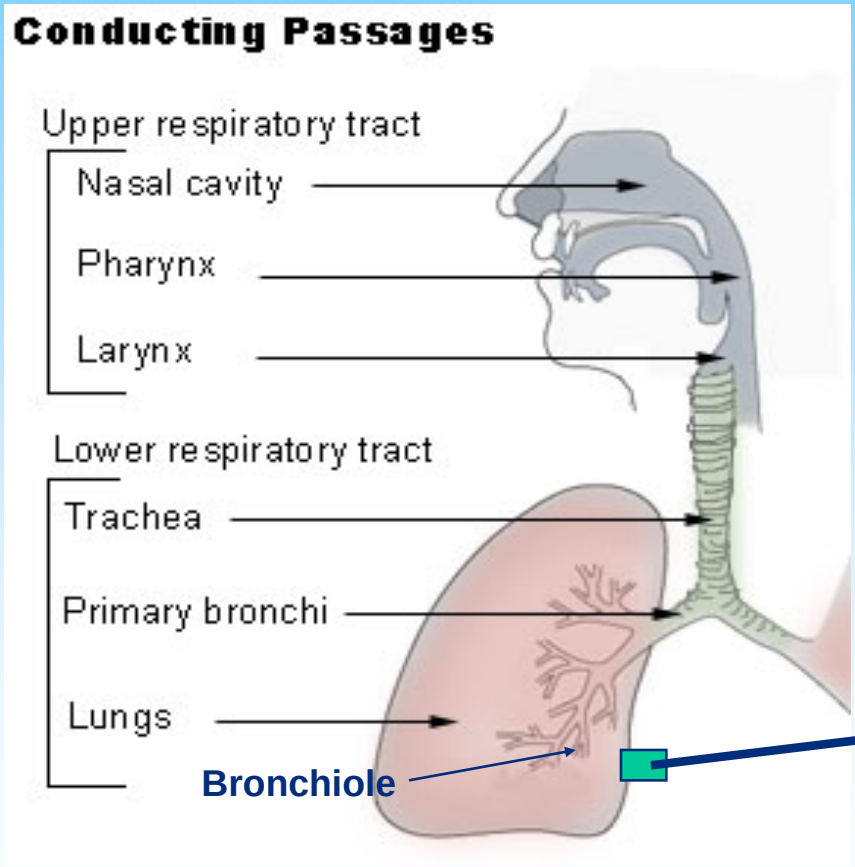
Application temperatures for HTIW

Temperature ranges for the application of inorganic synthetic mineral and High-Temperature Insulation Wools

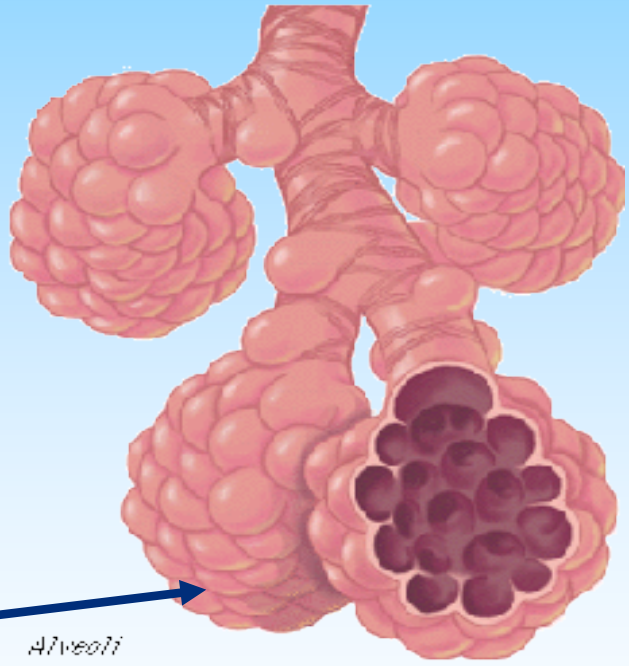


FIBRE TOXICOLOGY

The Respiratory Tract

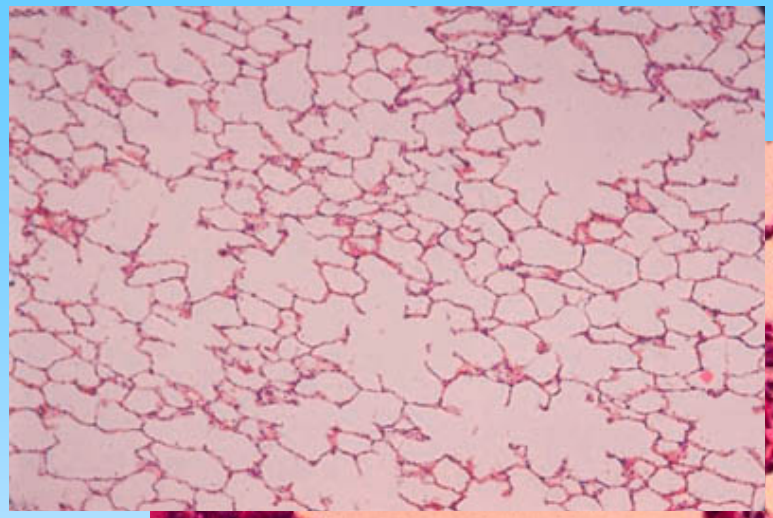


Gas exchange system

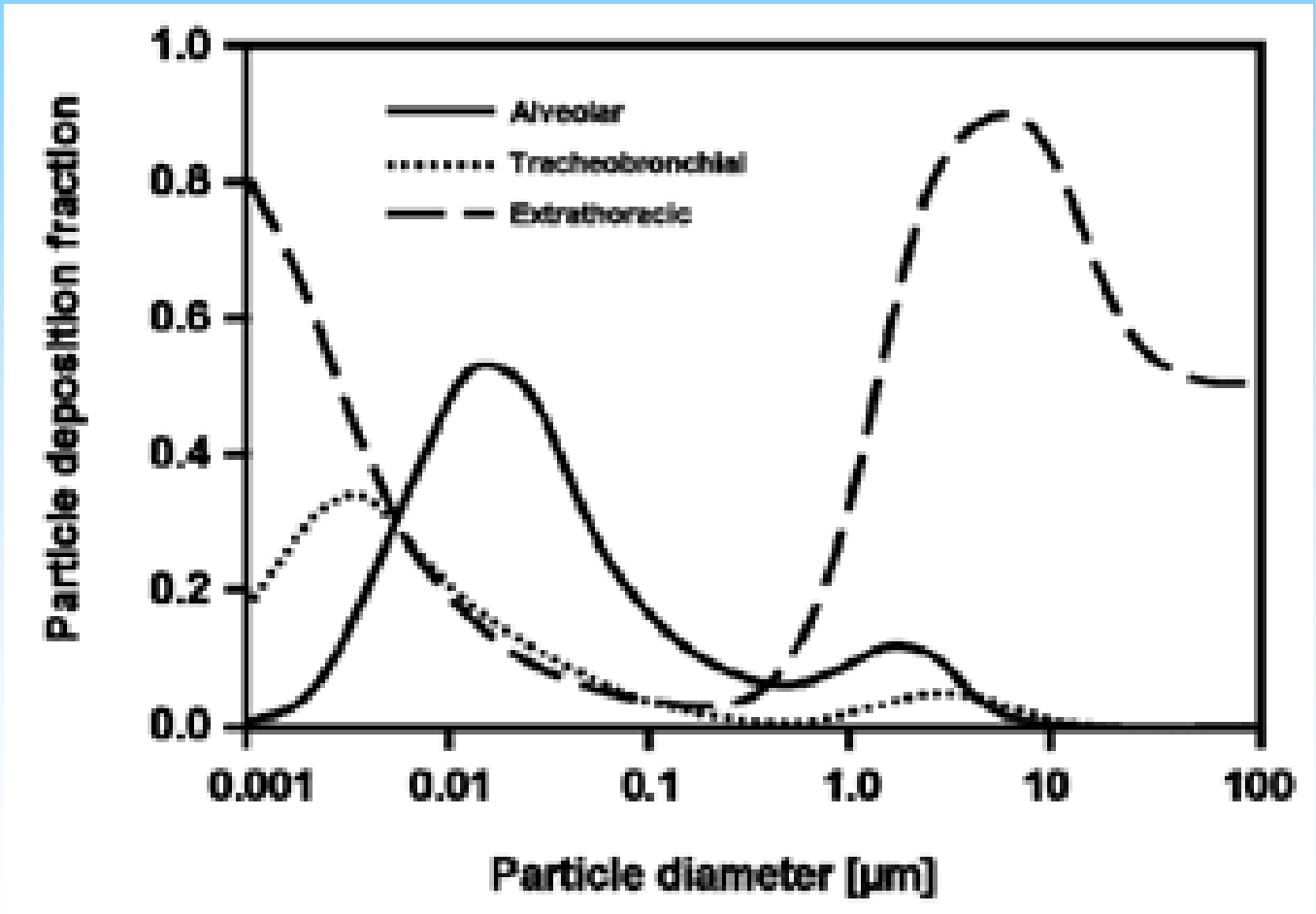


Respiratory unit

Lung histology



Pulmonary deposition of particles



Definition of a ‘Fibre’

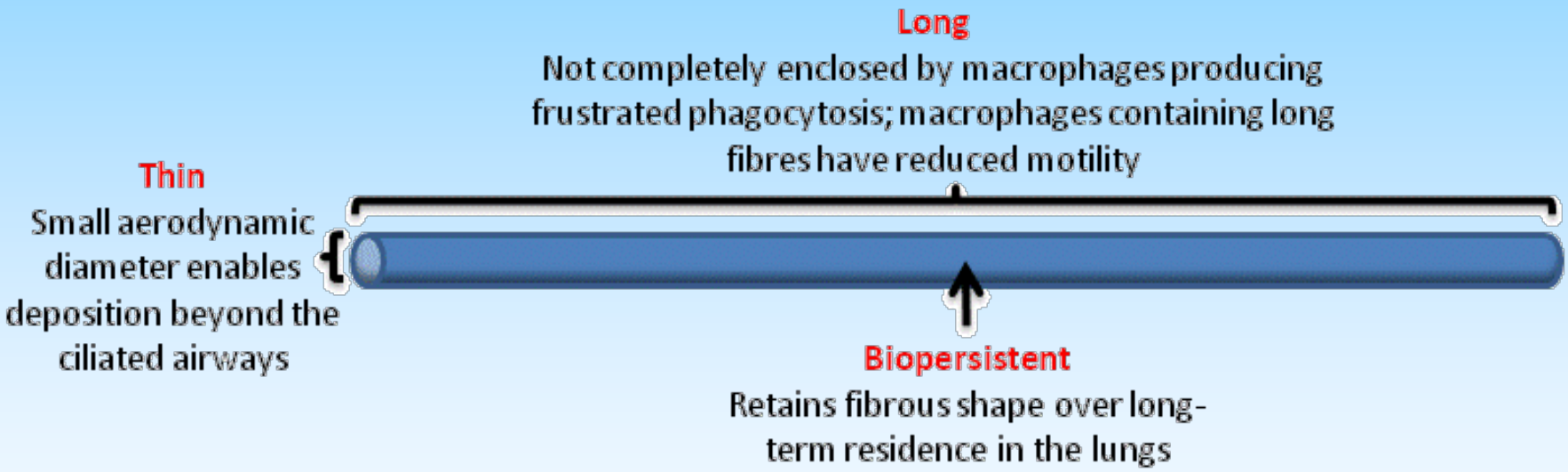
Primarily to achieve consistency and comparability for the analysis of airborne fibre samples, WHO has defined a fibre as **any particle with length greater than 5µm, diameter less than 3µm, and length to diameter ratio greater than 3:1.**

Pulmonary deposition of fibres

‘WHO fibres’ are not all equally likely to enter and remain in the lung.

The probability of deposition in the deep lung (alveolar region) varies from <1% for fibres close to 3µm diameter up to about 40% for thinner fibres of 0.5 -1.0µm diameter.

What makes a fibre toxic?



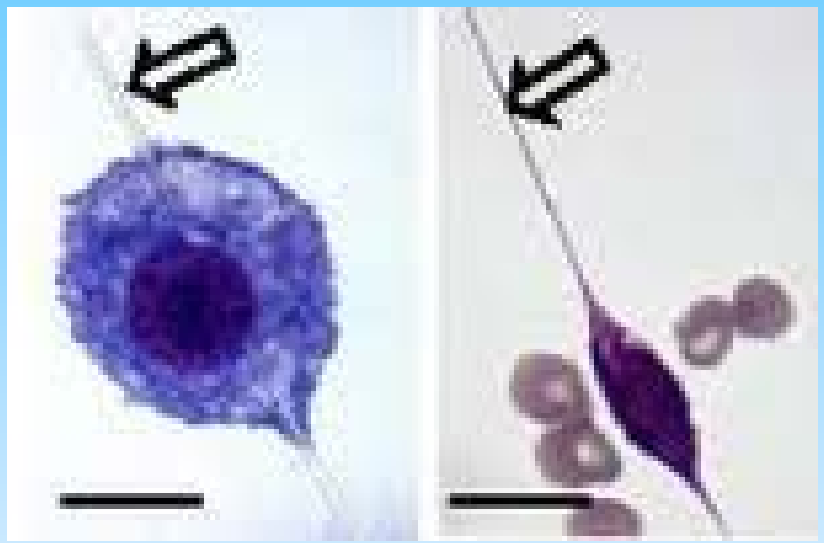
The 3 ‘D’s of fibre toxicity

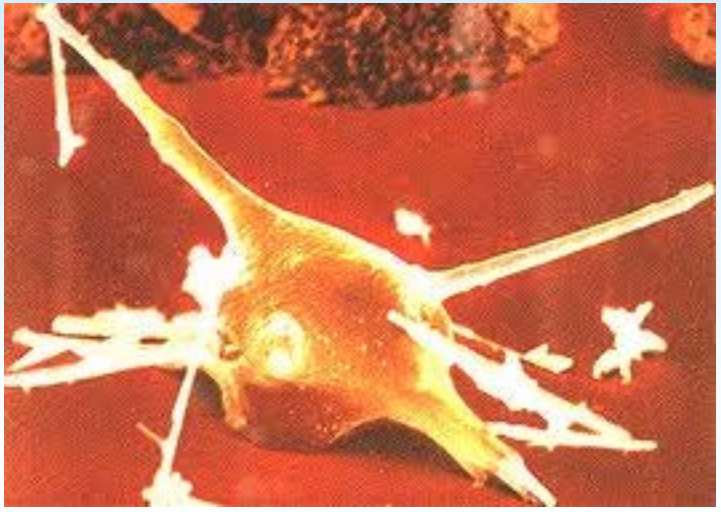
- **Dose** – the amount reaching the lung (normally the deep alveolar region of the lung)
- **Dimensions** (Morphology) – the length and diameter of the fibre, which influence both its respirability and its toxic effects in the lung.
- **Durability** (Biopersistence) – the ability to resist the body’s attempts at removal and thus remain in the lung for an extended period.

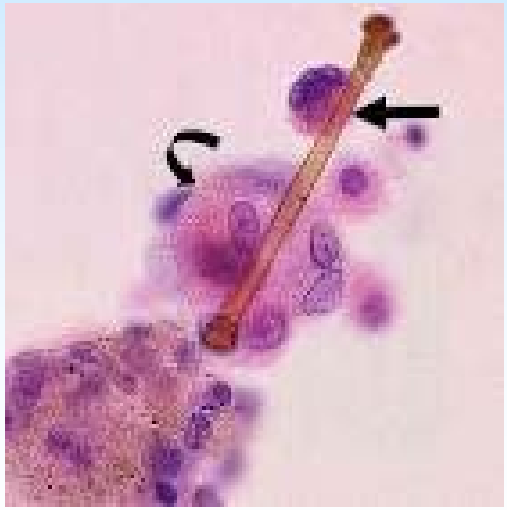
The importance of physical characteristics in determining hazard

- Fibre **size and shape** are of fundamental importance because they determine **respirability** and deposition in the lung.
- Also**, long fibres** are more resistant to removal by lung **macrophages** because they cannot readily be engulfed and digested ➔ 'frustrated phagocytosis'. Experiments have shown that, as a general rule, fibres longer than 20µm are more toxic than shorter fibres.
- Chemical composition appears to be less important, except insofar as it relates to fibre solubility/ **biopersistence**.

‘Frustrated phagocytosis’





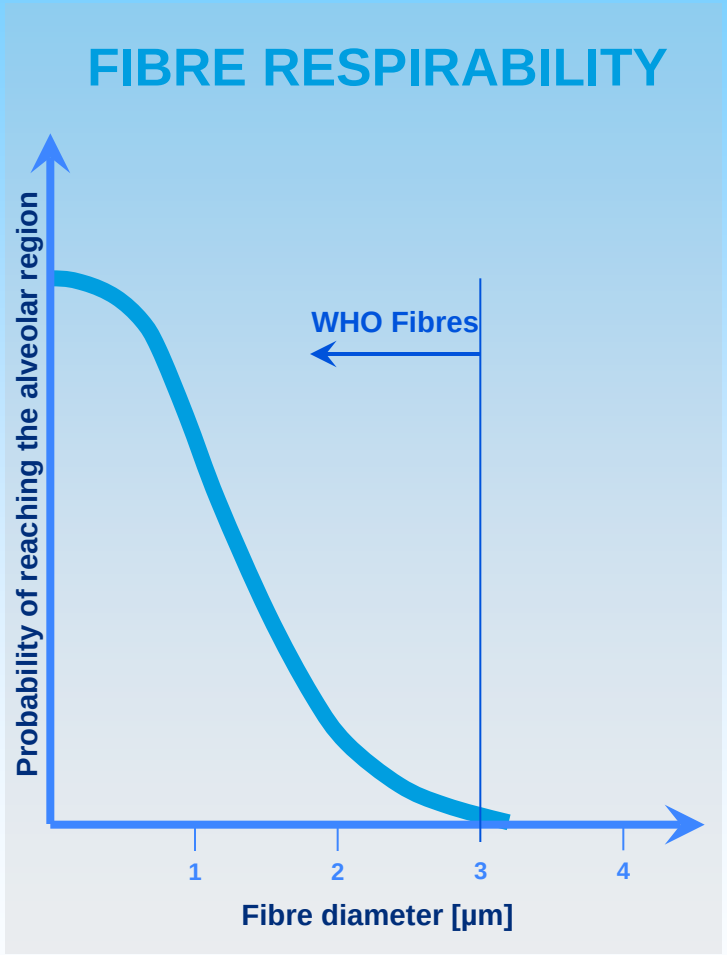


Fibre deposition

The number of fibres reaching the deep (alveolar) region of the lung depends on:

- The number of airborne fibres to which the lung is exposed
- The physical characteristics (dimensions) of the fibres, especially diameter, which determines their respirabiltiy.

'WHO' fibres are not all equally respirable.

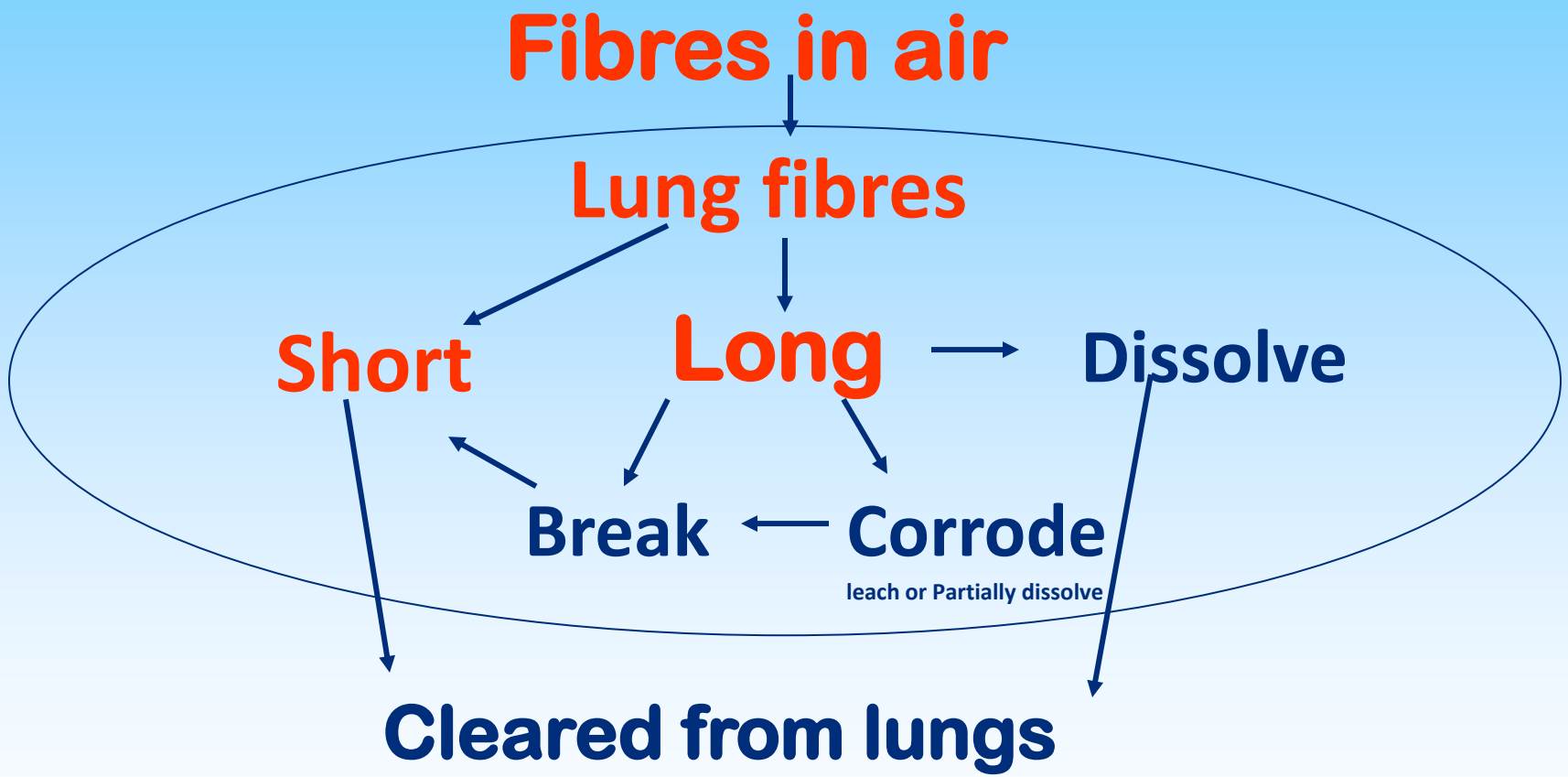


The importance of fibre biopersistence

- The number of fibres remaining in the lung depends the degree to which the inhaled fibres are resistant to the lung's chemical and biological/cellular removal processes – a property known as fibre *biopersistence* or *durability*.
- Both experimental and epidemiological studies (on different types of asbestos) have demonstrated the importance of biopersistence in determining disease outcomes; this key characteristic is now acknowledged in the classification of man-made mineral fibres in the EC.

- Biopersistence is not synonymous with solubility in water. Fibres are exposed to a range of pHs in the lung and fibres that are relatively insoluble in water at neutral pH may actually be cleared rapidly from the lung following inhalation.
- The propensity of fibres to break transversely is also extremely important in determining their persistence in the lung because shorter fibres can be more readily cleared by macrophages.
- Ultimately the toxic effects of fibres are determined by the interplay between biopersistence and dose (rate of exposure).

A consensus model for fibre clearance



As long fibres are those which cause disease, the safest fibrous materials are those which dissolve releasing tiny quantities of harmless mineral salts or corrode and then break. Short fibres and fragments, whether inhaled or produced by breaking long fibres, are cleared from the lungs like other dusts encountered in everyday life.

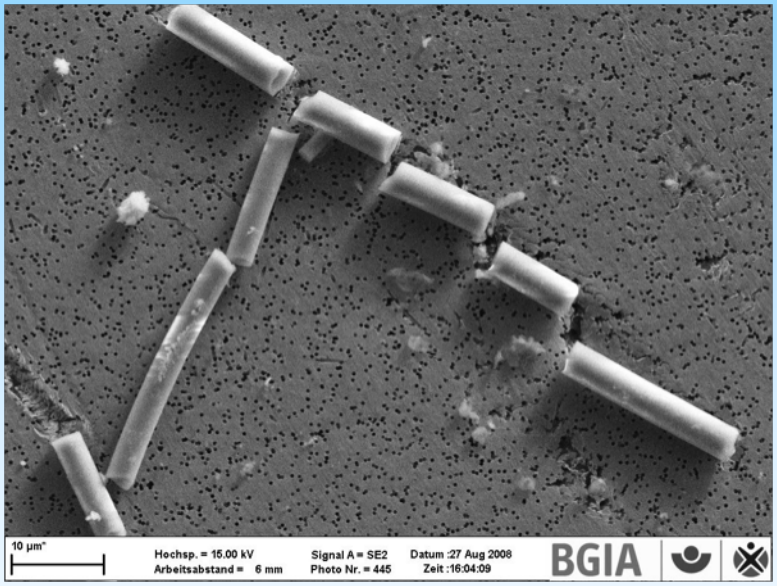
Differences between asbestos and MMMF

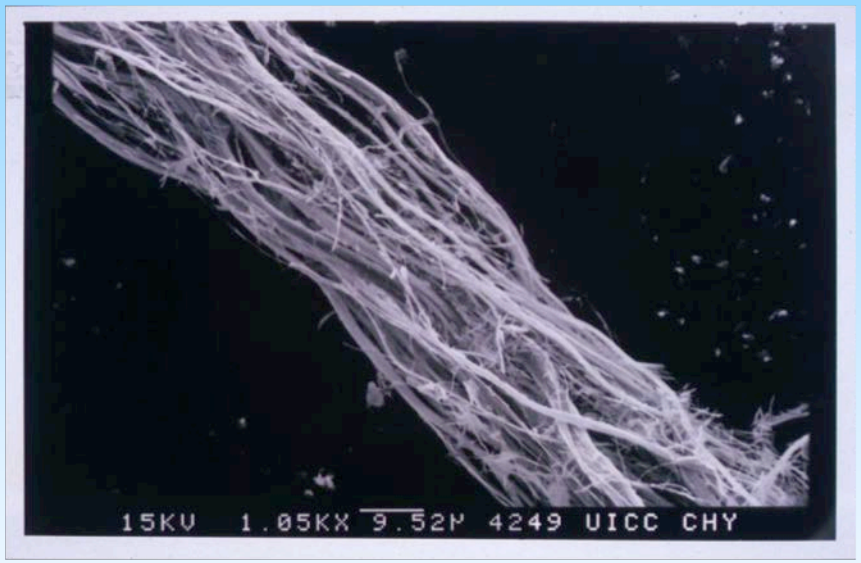
Asbestos and MMMF are very different in their propensity to release airborne fibres (MMMF break transversely whereas asbestos fibres split longitudinally, liberating more and finer fibrils into the air)

Asbestos fibres, being very thin (generally <0.1µm diameter), are more likely to reach the deep lung than MMMF (generally >1µm diameter).

MMMF are generally less biopersistent (partly due to their propensity to be eroded and break transversely in the lung and hence be more readily removed by macrophages).

Differences between asbestos and MMMF





Scanning electron micrographs of MMMF (*L*) and chrysotile asbestos (*R*)

Impacts on the design of HTIWs

Understanding and applying the 3-D's principle of fibre toxicology has led to the design and development of inherently less hazardous HTIW.

- Morphology (Dimensions)

  Knowledge of the connection between fibre diameter and pulmonary deposition has encouraged the development of materials such as PCW that are manufactured to closely controlled diameters of 3µm or more and liberate very few respirable fibres in typical workplace situations.

- Biopersistence (Durability)

  Understanding the importance of biopersistence has led to the development of less biopersistent HTIW, such as the alkaline earth silicate (AES) wools, by manipulating chemical composition.

TOXICOLOGICAL STUDIES ON HTIW

Early investigations on HTIW

ASW/RCF

- Smith *et al* (1987) studied the effects of RCF exposure in rats after nose-only inhalation exposure for 2 years at an aerosol concentration of 12 mg/m^3. No lung tumors were observed.

ASW/RCF (continued)

- A 2-year rat inhalation carcinogenicity study (Mast et al., 1995a) conducted at the 'Maximum Tolerated Dose' (30 mg/m^3) on different types of ASW/RCF found interstitial fibrosis and increased incidence of lung tumours (ranging from 7.4% to 15.7%).

- A subsequent multiple-dose study at exposure levels of 3, 9 or 16 mg/m^3 (Mast 1995b) found tumour incidence to be within the normal range.

AES

- A 2-year carcinogenicity study (Hesterberg, 1998) in which rats were exposed to approximately 200f/ml demonstrated that AES (X607) fibres are neither fibrogenic nor tumorigenic.

PCW

- PCWs are designed to have a median diameter of around 3µm, which means they are inherently resistant to inhalation into the deep lung.
- A range of toxicological studies have been conducted, all of which indicate that PCW is not carcinogenic.

Current understanding of the toxicology of ASW/RCF

- Investigations and analyses published by Brown et al. (2000, 2005) have shown that the results of the MTD study on ASW/RCF were caused by heavy contamination of the sample with non-fibrous particulate and pulmonary overload at the very high dose tested.
- The findings from Mast et al (1995a) led ASW/RCF to be categorised as an EU Category 2 (CLP Cat 1B) suspected human carcinogen, and this still stands today.

The question of crystalline silica in after-service fibres

- When MMVFs are heated the silica they contain may be transformed to different types of crystalline silica (CS), including *Cristobalite.*
- Because some forms of CS are classified as carcinogenic there is concern that otherwise non-hazardous HTIW may become dangerous after use in high temperature installations.
- However, animal and *in vitro* tests have demonstrated that such ‘after-service’ fibres are not more toxic – possibly because the silica so formed is not bioavailable**.**

Summary of toxicological findings on HTIW

AES: No effects observed in chronic inhalation tests. Low biopersistence demonstrated in short term inhalation and intra-tracheal instillation experiments.

ASW/RCF: Effects (fibrosis and lung cancer) in chronic inhalation studies observed at the highest dose level. Questionable result because of likely 'overload' effect.

PCW: No effects observed in various animal tests. (Testing at elevated doses not possible because of fibre dimensions.)

*After-service (heated) AES and ASW/RCF fibres containing CS are **not** more toxic than unheated fibres*

CONCLUSIONS

Key conclusions (1)

- HTIWs belong to the family of MMMF, which includes both vitreous and crystalline fibres.
- Fibre toxicity is critically determined by fibre dimension and biopersistence.
- Fibres can be designed to be inherently less hazardous.
- HTIW are not comparable to asbestos.
- Flawed early studies at extremely high doses led ASW/RCF to be classified as an EU Category 2 (CLP Cat 1B) carcinogen.

Key conclusions (2)

- AES and PCW are of low toxicity and unclassified with respect to carcinogenicity.
- While some after-service (heated) HTIWs have been shown to contain crystalline silica, there is no evidence that such fibres are more toxic as a result – possibly because the silica so formed is not bioavailable.
- Ongoing activities under the PSP have led to much improved understanding of the toxicity of HTIW over the last 20+ years.