GENERAL REMARKS ON MAN-MADE MINERAL FIBRES

Previous working groups have evaluated the carcinogenicity of asbestos (IARC, 1977, 1982, 1987a), silica, wollastonite, attapulgite, talc, erionite (IARC, 1987a,b) and sepiolite (1987b).

Characterization of man-made mineral fibres

Physicochemical characterization of a sample is essential when testing fibrous particulates for biological activity, for two reasons: (i) to ensure that the sample to be tested is representative of the materials to which humans are exposed; and (ii) to permit evaluation of specific physical and chemical characteristics of the fibres which may be important in the induction of cancer. It is important that sufficient numbers of fibres from each sample to be tested for carcinogenicity be measured using methods that allow detection of both submicroscopic and microscopic fibres, so that the number of fibres of specific dimensional categories per unit mass can be calculated.

When characterizing exposures to man-made mineral fibres, it is necessary to specify the distributions of fibre diameters and lengths, as well as the total number of fibres per unit volume of air in order to lay a foundation for dose-response relationships. The most desirable reporting mode for research purposes is in numbers of fibres per unit volume in size classes of diameter and length. In the studies reported in this monograph, such information was not always available. For the purposes of occupational safety, the number of fibres per unit volume in a given size and length class is usually specified.

The composition of bulk material and the fibre sizes vary widely among and within each fibre category, i.e., glass, rock, slag and ceramic. Therefore, specifications of bulk material should accompany data on exposure whenever possible. Trade names broadly classify bulk material with regard to composition and to distribution of fibre diameter and length; but airborne fibres released by bulk materials vary greatly in diameter and length, even within a single trade designation.

Man-made mineral fibres break predominantly across the fibre axis. They do not form fibrils, as does chrysotile. These differences in breakage characteristics explain why chrysotile in air is associated with a large number of submicron-size fibres, while airborne man-made mineral fibres are not. Optical microscopy can be used for routine assessment of man-made mineral fibres (length, >5 μm) in work places. Detailed analysis of size and determination of the elemental composition of all man-made mineral fibres except very fine fibres can be performed with a scanning electron microscope. Analysis of very fine fibres requires transmission electron microscopy.

Routes of exposure to mineral fibres

Inhalation is the major route of exposure to mineral fibres that have been shown to cause cancer in humans (e.g., asbestos). Therefore, it is desirable to use the inhalation route, if possible, when testing such fibres for their carcinogenicity in animals; however, the qualitative and quantitative aspects of particle deposition and retention in rodents are considerably different from those in humans. As a result, particles that may be important in the induction of disease in humans may never reach the target tissues in sufficient quantities in rodents. This problem cannot be overcome by generating higher concentrations of particulate aerosols because of technical complications, e.g., particle aggregation. The consequence is that inhalation tests may be less sensitive than tests by other routes for evaluating the carcinogenicity of particulate and fibrous materials. In addition, the high cost of and the shortage of adequate facilities for such studies severely limit the number that can be performed.

It is thus often necessary that other routes of administration be used for testing the carcinogenic potential of mineral fibres. The methods that have been most frequently employed are intratracheal instillation and intrapleural and intraperitoneal administration. With the first, various lung tissues as well as the pleural mesothelium are the major targets for the administered test fibres; in the latter two, the pleural and the peritoneal mesothelium, respectively, are the target tissues. These routes of administration can be used to test the carcinogenicity of mineral fibres to laboratory animals because they bring the test fibres into intimate contact with the same target tissues as in humans.

Mechanisms of fibre carcinogenicity

In this monograph, man-made mineral fibres are divided into five groups, according to the materials from which they are produced or to the manufacturing process. The groups are: glasswool, glass filament, rockwool, slagwool and ceramic fibres. The major fibre characteristics, based on current knowledge, that are likely to be determinants of the adverse biological effects of fibres are: (i) fibre length, (ii) fibre diameter, and (iii) in-vivo durability and persistence, i.e., the ability of a fibre to remain fixed in a given location in the target tissue for an extended period. It should be noted that the number of fibres in a given mass can vary over at least two orders of magnitude depending on variations in the distribution of fibre size.

Wide differences in the durability of man-made mineral fibres have been demonstrated both *in vivo* and *in vitro*, which depend on the chemical composition. The most durable man-made mineral fibres are also likely to be more hazardous to man than relatively soluble fibres. It would appear that, in order to predict health hazards from man-made mineral fibres, their dissolution rates in tissues would have to be determined for each fibre product. Other factors, such as surface properties and, for some man-made fibres, chemical leaching from fibres may also play a role, but these are much less well understood.

The precise mechanisms by which fibres exert a carcinogenic effect are unknown; however, in studies of experimental animals exposed to mineral fibres by inhalation in which significant tumour levels are seen, a high frequency of fibrosis is also usually found. A possible causal relationship has been suggested.

Present scientific knowledge indicates that the major determinants of the carcinogenic potential of fibres are biological durability, dimensions (length and diameter) and, as for any other carcinogen, dose to the target organ. In this monograph, specific evidence is evaluated concerning the carcinogenicity of glass fibre, rockwool, slagwool and ceramic fibres as groups. It is conceivable, however, that the fibre characteristics, durability and physical dimensions span the categories of all mineral fibres, including the man-made mineral fibres evaluated here, and that these are the characteristics that are most important in relation to the possible carcinogenicity of a material.

Considerations regarding epidemiological studies

In this monograph, standardized mortality ratios (SMRs) for lung cancer found in the cohorts differ depending on whether national or local reference comparisons were made. This is a potential problem in studying countries where lung cancer rates vary markedly from area to area, and particularly in the absence of extremely high SMRs. Interpretation of a study may be difficult if one of these ratios deviates significantly from unity while the other does not or deviates in the opposite direction.

Characteristics of the occupational cohort under study may suggest which type of ratio is more appropriate. For example, if a cohort has been assembled from a number of factories in various representative (rather than all urban) parts of a country, a nationally-based SMR may be more appropriate. The same might be the case if a particular factory has attracted a work force from representative areas of a country, including different ethnic groups. However, if a cohort has been drawn from only one factory with a locally-recruited work force, a locally-based SMR would be more appropriate. The population base from which the local rate is derived should be large enough that it is not dominated by the work force under study and that it permits (reasonably) stable estimates to be made. The latter requirement may not always be fulfilled for rare diseases, although statistical imprecision in the reference rates can be taken into account in the analysis. The presence of an increased risk caused by another local industrial exposure may also have considerable impact on local rates with regard to rare disorders; this situation would suggest that national (or regional) rates be applied.

These and other arguments have been proposed by various authors, as summarized and elaborated by Gardner (1986), in relation to the use of national and local rates with regard to other factors, such as social class. Internal comparisons within the cohort, rather than with an external reference population, may be preferred in instances where the cohort can be subdivided and where the numbers are large enough to prevent the introduction of appreciable random error.

Reference

Gardner, M.J. (1986) Considerations in the choice of expected numbers for appropriate comparisons in occupational cohort studies. *Med. Lav.*, *77*, 23-47