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INTERNATIONAL AGENCY FOR RESEARCH ON CANCER

IARC Monographs on the Evaluation of Carcinogenic Risks to Humans

Volume 43
Man-made Mineral Fibres and Radon

Summary of Data Reported and Evaluation

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MAN-MADE MINERAL FIBRES
Glasswool (Group 2B)
Glass filaments (Group 3)
Rockwool (Group 2B)
Slagwool (Group 2B)
Ceramic fibres (Group 2B)

For definition of Groups, see Preamble Evaluation.

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Subsequent evaluation: Vol. 81 (2002)

5. Summary of Data Reported and Evaluation

5.1 Exposure data

More than 5 million tonnes of man-made mineral fibres are produced annually in more than 100 factories located throughout the world. Glass fibre products comprise over 50% of the total. Most glasswool, rockwool and slagwool is used for thermal and acoustical insulation in the construction industry. Glass filaments are used mainly as textiles and as reinforcement materials in plastics. Ceramic fibres are being produced in increasingly large quantities for high-temperature insulation and in specialty products.

Man-made mineral fibre products release airborne respirable fibres during their production and use. In general, as the nominal diameter of man-made mineral fibre products decreases, both the concentration of respirable fibres and the ratio of respirable to total fibres increase. Exposure levels in glasswool production have generally been 0.1 respirable fibre/cm^3 or less; in rockwool and slagwool production, exposures have been somewhat higher. Higher occupational exposures may occur when man-made mineral fibre products are used in confined spaces, such as in the application of loose insulation. Concentrations of man-made mineral fibres have been measured in outdoor air and in nonoccupational settings indoors and found to be much lower than those associated with occupational settings.

5.2 Experimental carcinogenicity data

Glasswool

Several samples of glasswool with different particle size distributions in the respirable range were tested by inhalation in five experiments in rats, in one experiment in hamsters, and in one limited experiment in baboons. There was no statistically significant increase in the incidence of tumours of the lung or pleura; however, a few respiratory-tract tumours occurred in most experiments in rats. It should be noted that in the intended positive control groups, crocidolite produced no statistically significant increase in lung tumour incidence, while chrysotile usually did.

Glasswool was adequately tested in two experiments in rats and in one experiment in hamsters by intratracheal instillation. Lung tumours were observed in one experiment in rats, and lung tumours and mesotheliomas were observed in the experiment in hamsters, after repeated instillations of samples of glasswool with median fibre diameter less than 0.3 µm. No lung tumour or mesothelioma was induced by glasswool in the other experiment by intratracheal instillation in rats; however, in the positive control group treated with crocidolite, there was a low incidence of lung tumours.

Various samples of glasswool were tested by intrapleural implantation or injection in five studies in rats and in one in mice. Pleural tumours were induced in four of five studies in rats, the incidence varying with the size of the instilled fibres. No pleural tumour was observed in treated mice.

Samples ofglasswool were injected into the peritoneal cavity in eight studies in rats and in one in hamsters. Mesotheliomas or sarcomas were induced (the incidence depending on dose and fibre size) in the peritoneal cavity in all studies in rats, but prior 'leaching' of the fibres with hydrochloric acid in two studies reduced or eliminated the incidence of these tumours. Treatment of the fibres with sodium hydroxide did not reduce the carcinogenicity. No tumour was induced in hamsters.

Glass filament

In experiments in which three types of glass filaments of relatively large diameter (> 3 µm) were administered intraperitoneally to rats, no statistically significant tumour response was found.

Rockwool

In two studies in which rats were exposed to rockwool by inhalation, no statistically significant increase in lung tumour incidence was observed in one study and no lung tumour in the other. Chrysotile was used as the positive control in both studies and led to high pulmonary tumour incidence.

Rockwool was tested by intrapleural injection in one experiment in rats, producing a low, statistically nonsignificant increase in the incidence of pleural mesotheliomas. After intraperitoneal injection of two samples of rockwool in two experiments in one laboratory, a high incidence of tumours was observed in the abdominal cavity; however, in one study, the histopathology had not been completed.

Slagwool

Slagwool was tested in one experiment by inhalation in rats and hamsters; no increase in the incidence of respiratory-tract tumours was reported. In the intended positive control groups, crocidolite induced no or few tumours. In two experiments in rats, intrapleural injection of slagwool produced no thoracic tumour in one study and one pleural sarcoma in the other. In one study in rats by intraperitoneal injection, equivocal findings were obtained.

Ceramic fibres

In an experiment in which rats were exposed to ceramic fibres by inhalation, a statistically significant increase in the incidence of benign and malignant tumours of the lung was observed. Two further studies, one in rats and one in hamsters, by inhalation showed no increased tumour incidence in groups exposed to ceramic fibres, whereas, in the intended positive control group, crocidolite produced a few lung tumours in rats but not in hamsters. No pulmonary tumour was found in an experiment in which rats were exposed by inhalation to relatively thick ceramic fibres.

Intratracheal instillation of ceramic fibres did not produce lung tumours in one study in rats and in one study in hamsters, while, in the intended positive control group, crocidolite produced a high percentage of benign and malignant lung tumours in hamsters but only a few in rats.

In one study, intrapleural implantation in rats of several kinds of ceramic fibres produced variable incidences of pleural mesotheliomas or sarcomas. Another study of ceramic fibres injected into the pleural cavity of rats produced equivocal results.

After intraperitoneal injection of ceramic fibres into rats in three experiments, mesotheliomas were found in the abdominal cavity in two studies. Only a few mesotheliomas were found in the abdominal cavity of hamsters after intraperitoneal injection in one experiment; however, the ceramic fibres tested were of relatively large diameter.

In interpreting all these experiments, the Group had in mind considerations outlined in the 'General Remarks on Man-made Mineral Fibres' (see monographs volume).

5.3 Human carcinogenicity data

No increase in the occurrence of mesothelioma has been observed in man-made mineral fibre production workers.

Glasswool

The main study of glasswool workers in the USA showed a slightly raised mortality from respiratory cancer compared to local rates. Mortality from respiratory cancer increased with time since first exposure, but was not related to duration of exposure nor to an estimated time-weighted measure of fibre exposure. A subcohort of these workers who were exposed to small-diameter fibres had a higher standardized mortality ratio for respiratory cancer than those not exposed, which increased with time since first exposure. Neither the overall increase nor any of these trends was statistically significant.

In the multinational European study, there was no overall excess mortality from lung cancer compared to regional rates. Mortality from lung cancer showed a statistically nonsignificant increase with time since first exposure but was not related to duration of exposure or to different technological phases reflecting differences in the intensity and quality of exposure.

A study of Canadian glasswool workers showed a substantially raised mortality from lung cancer, which was statistically significant, but this was not related to time since first exposure or to duration of exposure.

Glass filament

Among glass filament workers in the US study, there was no excess of respiratory cancer, and in the European study no excess of lung cancer, and no upward trend with time since first exposure or with duration of exposure in either study. In the US study, there was also no trend with an estimated time-weighted measure of exposure.

Rockwool and slagwool

Effects of exposures in rockwool and slagwool industries could not be distinguished in the studies reported. The two are therefore referred to together as 'rock-/slagwool'.

The study of rock-/slagwool workers in the USA indicated a statistically significant raised mortality from respiratory cancer compared to local rates. In this cohort, however, there was no relationship with time since first exposure, duration of exposure or an estimated time-weighted measure of fibre exposure.

In the European study, there was an overall, statistically nonsignificant excess of lung cancer among rock-/slagwool workers compared to regional rates, as well as a statistically nonsignificant increasing mortality with time since first exposure. There was no relationship between lung cancer mortality and duration of exposure. The highest and statistically significant lung cancer rates were found after more than 20 years' follow-up among persons first exposed during the early technological phase (i.e., before the introduction of oil binders and during the use of batch processing methods). Slag was used as a raw material particularly during this phase of the industry. There was a statistically significant decreasing trend in lung cancer mortality with the introduction of oil binders and modern mechanized methods of production. The presence of asbestos, bitumen, pitch and formaldehyde as work place contaminants could not explain the' lung cancer excess.

In the US and European studies combined, there was a statistically significant excess of mortality from lung cancer for rock-/slagwool workers.

The raised lung cancer mortality rates were considered unlikely to be the result of confounding due to cigarette smoking, although this was not directly measured in the cohort studies.

5.4 Other relevant data

Many samples of man-made mineral fibres with large fibre diameter have low respirability.

The solubility of man-made mineral fibres *in vitro* and their durability *in vivo* vary with chemical composition. While, in general, glasswool fibres appear to be relatively nondurable, one sample was shown to be very insoluble *in vitro*. Conversely, while in one study ceramic fibres were very durable, one sample proved to be as soluble as glasswool used for comparison in the same experiment *in vitro*. Insufficient samples of slagwool and rockwool have been tested to allow a prediction of their overall range of solubility in tissues. On the available evidence, no generalization can be made regarding the durability of any single class of man-made mineral fibres.

There is little evidence for acute toxicity after the inhalation of man-made mineral fibres. Glasswool, rockwool and slagwool administered by inhalation produced little pulmonary fibrosis in experimental animals. Glasswool was fibrogenic following intratracheal instillation in some but not all studies. In one study in rats, inhaled ceramic fibres were fibrogenic.

Glasswool induced numerical and structural chromosomal alterations but not sister chromatid exchanges in mammalian cells *in vitro*. It caused morphological transformation in rodent cells *in vitro*; transformation was found to be dependent on fibre length and diameter. Glasswool did not induce mutation in bacteria.

Ceramic fibres caused a weak response in an assay for morphological transformation but did not induce DNA damage in mouse cells *in vitro*.

No adequate data on genetic and related effects of rockwool and slagwool were available.

5.5 Evaluation

There is *sufficient evidence* for the carcinogenicity of glasswool and of ceramic fibres in experimental animals.

There is *limited evidence* for the carcinogenicity of rockwool in experimental animals.

There is *inadequate evidence* for the carcinogenicity of glass filaments and of slagwool in experimental animals.

There is *inadequate evidence* for the carcinogenicity of glasswool and of glass filaments in humans.

There is *limited evidence* for the carcinogenicity of rock-/slagwool in humans.

No data were available on the carcinogenicity of ceramic fibres to humans.

Overall evaluation

Glasswool is *possibly carcinogenic to humans (Group 2B)*.

Glass filaments are *not classifiable as to their carcinogenicity to humans (Group 3)*.

Rockwool is *possibly carcinogenic to humans (Group 2B)*.

Slagwool is *possibly carcinogenic to humans (Group 2B)*.

Ceramic fibres are *possibly carcinogenic to humans (Group 2B)*.

For definition of the italicized terms, see Preamble Evaluation.

Synonyms for Glasswool

- JM 100 [Johns Manville]
- JM 102
- JM 104
- JM 110

Synonyms for Glass filament

- ES 3
- ES 5
- ES 7

Synonyms for Rockwool

- G + H

Synonym for Slagwool

- RH
- ZI

Synonyms for Ceramic fibre

- Fiberfrax
- Fibermax
- Fireline Ceramic
- Fybex
- MAN
- PKT
- Saffil

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RADON
(Group 1)

For definition of Groups, see Preamble Evaluation.

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CAS No.: 10043-92-2
Chem. Abstr. Name: Radon

CAS No.: 14859-67-7
Chem. Abstr. Name: Radon-222

CAS No.: 15422-74-9
Chem. Abstr. Name: Polonium-218

CAS No.: 15735-67-8
Chem. Abstr. Name: Polonium-214

CAS No.: 13981-52-7
Chem. Abstr. Name: Polonium-210

CAS No.: 14733-79-4
Chem. Abstr. Name: Bismuth-210

CAS No.: 14733-03-0
Chem. Abstr. Name: Bismuth-214

CAS No.: 15067-28-4
Chem. Abstr. Name: Lead-214

CAS No.: 14255-04-0
Chem. Abstr. Name: Lead-210

5. Summary of Data Reported and Evaluation

5.1 Exposure data

Radon and its decay products are ubiquitous in soil, water and air. Radon in the ground, groundwater or building materials enters working and living spaces and disintegrates into its decay products. In comparison with levels in outdoor air, the concentrations of radon and its short-lived decay products to which humans are exposed in confined air spaces, particularly in underground work areas, such as mines and in buildings, are elevated. In those houses where the concentrations of radon are high, the primary source is usually the ground under the structure. Although high concentrations of radon in groundwater may contribute to human exposure through ingestion, the radiation dose to the body due to inhalation of radon released from the water is usually more important.

Concentrations of radon decay products measured in the air of underground mines throughout the world vary by several orders of magnitude. In countries for which data were available, concentrations of radon decay products in underground mines are now typically less than 1000 Bq/m^3 EEC_{Rn}. The concentration of radon and its decay products in houses also varies widely - by as much as four orders of magnitude. The average radon concentrations in houses are generally much lower than the average radon concentrations in underground ore mines; however, in many countries where surveys have been performed, the concentrations of radon and its decay products in a small percentage of houses are comparable to the concentrations observed in many underground mines.

5.2 Experimental carcinogenicity data

Radon and its decay products were tested for carcinogenicity in inhalation experiments in male rats and hamsters and in dogs of both sexes. In rats and dogs, a significant increase in the incidence of respiratory-tract tumours was observed in comparison with unexposed animals. A dose-response relationship was noted in those experiments in rats in which it was tested. In most instances, tumours at sites other than the lung were not reported, but, in one study, mention was made of tumours of the upper lip and urinary tract in rats.

Three treatments (inhalation of cigarette smoke, inhalation of cerium hydroxide particles and repeated intraperitoneal injections of benzo-5,6-flavone) increased the incidence of respiratory-tract tumours in rats exposed to radon and its decay products.

5.3 Human carcinogenicity data

Raised lung cancer rates have been reported from a number of cohort and case-control studies of underground miners exposed to radon and its decay products. These include particularly uranium miners, but also groups of iron-ore and other metal miners, and one group of fluorspar miners. Strong evidence for exposure-response relationships has been obtained from several of these studies, in spite of uncertainties that affect estimates of the exposure of the study populations to radon decay products. Several small case-control studies of lung cancer have suggested a higher risk among individuals living in houses known or presumed to have higher levels of radon and its decay products than among individuals with lower presumed exposure in houses.

The evidence on the interaction of radon and its decay products with cigarette smoking with regard to lung cancer does not lead to a simple conclusion. The data from the largest study are consistent with a multiplicative or submultiplicative model and reject an additive model. Some other studies with smaller numbers do not clearly support this finding.

In many studies of miners and in one of 'presumed' domestic exposure, small-cell cancers accounted for a greater proportion than expected of the lung cancer cases. In one population of uranium miners, this proportion has been declining with the passage of time.

5.4 Other relevant data

The effects of radon are largely attributable to the inhalation of its decay products. The pattern of their deposition in the respiratory tract is dependent on whether they are attached to particles or not. Deposition of the attached fraction is determined by the size of the particles in the associated aerosol. Following inhalation of radon and its decay products by experimental animals, the highest concentrations of short-lived decay products occur in the tracheobronchial and pulmonary region and in the kidney.

Although exposure of experimental animals to high levels of radon and its decay products can cause death, there is no evidence of any acute toxicity to humans from levels to which humans have been exposed.

In some, but not all, studies of groups of people either occupationally exposed to, or resident in areas of, high natural radiation, including elevated levels of radon and its decay products, an increased incidence of chromosomal aberrations has been observed. Radon and its decay products did not induce chromosomal aberrations *in vivo* in rabbits in one laboratory experiment but did induce chromosomal aberrations in human cells *in vitro* and sex-linked recessive lethal mutations in *Drosophila*.

5.5 Evaluation

There is *sufficient evidence* for the carcinogenicity of radon and its decay products in experimental animals.

There is *sufficient evidence* for the carcinogenicity of radon and its decay products in humans.

Overall evaluation

Radon and its decay products are *carcinogenic to humans (Group 1)*.

For definition of the italicized terms, see Preamble Evaluation.

Synonyms for Radon

- Alphatron
- Niton
- Radium emanation

Synonym for Polonium-218

- Radium A

Synonym for Polonium-214

- Radium C'

Synonym for Polonium-210

- Radium F

Synonym for Bismuth-210

- Radium E

Synonym for Bismuth-214

- Radium C

Synonym for Lead-214

- Radium B

Synonym for Lead-210

- Radium D

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