GENERAL REMARKS

This one-hundred-and-eleventh volume of the *IARC Monographs* contains evaluations of the carcinogenic hazard to humans of fluoro-edenite fibrous amphibole, silicon carbide fibres and whiskers, and carbon nanotubes. None of these agents had been evaluated previously by the Working Group. A summary of the findings of this volume appears in *The Lancet Oncology* (Grosse et al., 2014).

The relevant route of exposure for studies of carcinogenicity with fibres or carbon nanotubes in experimental animals is inhalation, since humans are most likely to be exposed to fibres or carbon nanotubes by this route. Exposure by inhalation to fibres or carbon nanotubes involves distribution, deposition, and clearance from the lung, and potential translocation of fibres to the pleura. However, in most of the studies of carcinogenicity in experimental animals reviewed in the present volume, fibres or carbon nanotubes were administered by intraperitoneal or intrapleural injection of a bolus of fibres or carbon nanotubes directly to the mesothelium, resulting in a high dose. These non-physiological routes of exposure can induce mesothelioma with a relatively short latency, and have been used historically as sensitive methods for the evaluation of carcinogenicity caused by fibres. For the agents evaluated in the present volume, several of the latter types of studies were judged inadequate due to the use of insufficient numbers of animals, the short study duration, or the lack of concurrent controls. However, the Working Group gave some consideration to studies of sufficient duration that included adequate numbers of animals, but lacked concurrent controls, because mesothelioma is a rare spontaneous tumour.

The assessment of the numerous mechanistic studies on carbon nanotubes revealed variability in the physicochemical properties of the carbon nanotubes tested, the toxicological end-points assessed, and the experimental procedures adopted. In addition, data on end-points related to chronic toxicity were lacking for many types of carbon nanotube. As a result, the Working Group considered the overall mechanistic data to be uninformative regarding the carcinogenicity of specific types of carbon nanotube (see also Kuempel et al., 2017).

References

Grosse Y, Loomis D, Guyton KZ, Lauby-Secretan B, El Ghissassi F, Bouvard V, et al.; International Agency for Research on Cancer Monograph Working Group(2014). Carcinogenicity of fluoro-edenite, silicon carbide fibres and whiskers, and carbon nanotubes. *Lancet Oncol*, 15(13):1427–8. doi:10.1016/S1470-2045(14)71109-X PMID:25499275

Kuempel ED, Jaurand MC, Møller P, Morimoto Y, Kobayashi N, Pinkerton KE, et al. (2017). Evaluating the mechanistic evidence and key data gaps in assessing the potential carcinogenicity of carbon nanotubes and nanofibers in humans. *Crit Rev Toxicol*, 47(1):1–58. doi: 10.1080/10408444.2016.1206061 PMID:27537422