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
