

Lung Toxicity and Genotoxicity of Multi-Wall Carbon Nanotubes, and a Proposal for Risk Assessment

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New chemicals make our life remarkable progress. Fundamentally chemicals have benefit and risk. Concerning nanomaterials, there are remarkable benefits but information on risk assessment is very scanty at present. Recently carbon nanotubes, particularly multi-wall carbon nanotubes (MWCNTs) shaped like fibers have raised serious concerns for their toxicities. In this international workshop, two subjects on MWCNT toxicities are presented: 1) lung toxicity by intratracheal instillation of MWCNT in rats and 2) its *in vitro* and *in vivo* genotoxicity.

Male, F344 rats were intratracheally treated once with MWCNT at doses of 0, 40, and 160 $\mu\text{g}/\text{rat}$ and observed until day 91. Phagocytosed MWCNTs were found in alveolar spaces and walls, and bronchus-associated lymphoid tissue. Type II cell hyperplasia, microgranuloma and fibrosis were observed in dose-dependent and time-dependent manner. These results indicate that MWCNT shows fiber toxicity *in vivo*. Further long-term study should be conducted for the lung carcinogenicity. *In vitro* genotoxicity of MWCNT using Chinese hamster lung cells was characterized by formation of polyploidy without structural chromosome aberration, increased number of bi- and multi-nucleated cells without micronucleus induction, and negative hgprt mutagenicity. The mutagenicity was also negative in the lung of gpt-delta rats. These results indicate that genotoxicity of MWCNT may be related to indirect interaction inducing genomic instability such as aneuploidic events.

In addition, our experimental data on low dose carcinogenicity of genotoxic carcinogens in rats, implying existence of carcinogenic threshold are also presented here for understanding a novel carcinogenic risk assessment.