

Particles and Health 2021

Inflammation as a key adverse outcome pathway in particle-induced effects

Moderator: Paul Borm, PhD

Presentation Summary

Title: “Particle-Induced Inflammation and Lung Cancer – Conclusions from The Edinburgh Workshop”

Kevin E. Driscoll PhD

“Lung particle overload” refers to the impaired lung particle clearance and increased particle retention occurring with high lung doses of poorly soluble low toxicity particles (PSLT). In rats, lung particle overload is associated with inflammation; epithelial hyperplasia; and, in extreme cases, lung cancer. Considerable scientific evidence indicates inflammation is an early and mechanistically necessary contributor to overload-associated rat lung cancer. While the relevance of overload-associated rat lung cancer to human hazard has been questioned, ECHA, NIOSH, and IARC have used such outcomes as the basis to classify materials as possible human carcinogens. Such classifications have important implications for the use and handling of such materials.

To document the state-of-the-science on PSLT toxicology, an expert workshop was held in 2019 to discuss the hazards and risks of PSLT inhalation. Significant among the outcomes of the expert workshop was the consensus reached on rat lung cancer. Regarding hazard, the expert panel agreed, in the absence of supporting data from other species, overload-associated lung tumors in rats do not imply a human hazard. From a risk perspective, there was expert agreement that rat lung tumors occurring only under conditions of lung particle overload are not relevant to non-overloading PSLT exposure conditions in humans. Regarding PSLT OEL setting, the Expert Panel agreed prevention of inflammation should be a driving principle in setting exposure limits for PSLTs as inflammation was considered to precede and contribute to other adverse lung responses e.g., fibrosis. The expert consensus on the relevance of overload associated rat lung tumors supports reconsidering human hazard classifications based primarily on these outcomes.