

Title *

Long-term Inhalation Study with Nano Ceria – Histopathology of the Lung

Abstract *

To investigate possible chronic toxicity and/or carcinogenicity of long-term nano Ceria inhalation, a 24-month inhalation carcinogenicity study (according to OECD guideline no.453) with an additional 6 month post exposure observation subgroup was performed in female Wistar rats [CrI:WI(Han)] at BASF SE, Ludwigshafen, Germany (EU-Project NanoReg, FP 7/2007-2013, grant agreement no.310584). Four different dose groups (0.1; 0.3; 1; 3mg/m³) of cerium oxide (CeO₂, NM-212) were used with 100 animals per test group. Clean air inhalation served as negative control. The lungs of all animals were histologically evaluated at Fraunhofer ITEM, Hannover, Germany (German Environment Agency [UBA]: FKZ371261206; German Federal Institute for Occupational Safety and Health [BAuA]: F2325).

An extended histopathological examination of the lung was performed in order to detect very small tumors and pre-neoplastic lesions. The lungs were step-sectioned at intervals of 500 µm resulting in 60-70 sections per lung. The lung lesions were diagnosed in accordance with the International Harmonization of Nomenclature and Diagnostic Criteria for Lesions in Rats and Mice (INHAND). Preliminary results show a dose-dependent accumulation of particle-laden macrophages, occurrence of syncytial giant cells, interstitial fibrosis and alveolar-interstitial granulomatous inflammation. Interestingly, the inflammatory changes were visible already in the lowest dose group (0.1mg/m³). In addition, alveolar lipoproteinosis and osseous metaplasia were increased only in both high dose groups (1 and 3mg/m³). Furthermore, bronchiolo-alveolar hyperplasias were elevated in all particle exposure groups. However, 12- and 24-month inhalation of CeO₂ showed no increased tumor incidence in the lungs in any group.

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