tailored, ingredient-specific approaches to safety assessment. But as the science advances and the solutions emerge, we need to ensure that alternative (to animal testing) approaches are suitably packaged, evaluated, documented and demonstrated to pave the way for widespread acceptance by regulators, end-users and the consumer.

2537 Histopathological Findings After 12 Months Inhalation to Nano Ceria

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Lung carcinogenicity and putative systemic effects of low-dose lifetime inhalation exposure to biopersistent nanoparticles were examined in a chronic/carcinogenicity inhalation study performed according to OECD test guideline no. 453 with several protocol extensions. Female rats (100/group) were exposed to cerium dioxide (NM-212, 0.1; 0.3; 1; 3 mg/m^3) for two years; a control group was exposed to clean air. After one year exposure, 42 µg cerium dioxide/lung was found in animals exposed to 0.1 mg/m^3 and 2.6 mg/lung in animals exposed to 3 mg/m^3. Histological examination of lungs revealed several adverse and non-adverse effects in the lung. The non-adverse effects comprised accumulation of particle-laden macrophages in alveolar/interstitial areas and in the BALT, particle-laden syncytial giant cells in the BALT and bronchiolo-alveolar hyperplasia (alveolar bronchiolization). The adverse effects included (mixed) alveolar/interstitial inflammatory cell infiltration, alveolar/interstitial granulomatous inflammation, interstitial fibrosis and alveolar lipoproteinosis. The incidence and severity of the effects were concentration-related. Alveolar lipoproteinosis was not observed at lower concentrations of 0.1 and 0.3 mg/m^3 CeO2. Neither pre-neoplastic nor neoplastic changes were observed after 12-months exposure. A no observed adverse effect concentration could not be established in this study. The comprehensive histopathological examinations of lungs and other tissues, after 24 months of exposure will be finalized in 2017. References: Keller, Jana, et al. "Time course of lung retention and toxicity of inhaled particles: short-term exposure to nano-Ceria." Archives of toxicology 88.11 (2014): 2033-2059.

2538 Coo and La2O3 Nanoparticle-Induced Pulmonary Response in Mice After Whole-Body Inhalation Exposure

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Metal oxide nanoparticles have the unique property of semi-conduction and can serve as conduits for electron transfer between aqueous reactants. These semi-conducting properties are implicated in adverse health effects. Two metal oxide nanoparticles with different semi-conductor properties, cobalt monoxoide (CoO) and lanthanum oxide (La2O3) may pose different toxicological potentials *in vivo* and *in vitro*. Our previous *in vitro* study showed that CoO nanoparticles induce a more potent toxicological response in human small airway epithelial cells than La2O3 nanoparticles. The current study determined CoO and La2O3 nanoparticles-induced pulmonary response in mice after whole-body inhalation exposure. Mice were exposed to 10 or 30 mg/m3, for 6 h per day over 4 days and were examined at 1, 7 and 56 days post-exposure. Both CoO and La2O3 nanoparticles were present in the lung at 1, 7 and 56 days post exposure. CoO caused greater lactate dehydrogenase in the bronchoalveolar fluid compared to La2O3 at 1 day post exposure at both doses. La2O3 had elevated numbers of macrophages, lymphocytes, neutrophils and eosinophils in the bronchoalveolar fluid compared to CoO nanoparticles at both doses and all post-exposure time points. Histopathological results show that there was acute pulmonary inflammation at 1 day post-exposure for CoO and an inflammation at 7 day post exposure for La2O3 Fibrosis was not observed at 56 day post-exposure at 10 and 30 mg/m3. Mice exposed to CoO and La2O3 have different expression patterns of pro-inflammatory cytokines at all post exposure time points and doses. Taken together, the results demonstrate that CoO nanoparticles induce more overall acute pulmonary toxicity where as La2O3 nanoparticles caused chronic inflammation. Moreover, this study may fill the gap between *in vivo* and *in vitro* nanoparticle-induced toxicity studies and risk assessment.

2539 Repeated Inhalation Exposure to Amorphous Silica Nanoparticle-Containing Slurries: Derivation of Workplace Exposure Limits for the Electronics Industry

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Background: Chemical mechanical planarization using amorphous silica nanoparticle (NP)-containing slurries is done in the semiconductor industry, creating the potential for the aerosolization of the slurry constituents and subsequent exposures. Based on previous acute rat inhalation exposure studies, we hypothesized that repeated inhalation exposure to silica NP (31 nm) slurry would result in dose-dependent and persistent pulmonary inflammatory reactions in rats. Methods: The slurry was diluted in water, ultrasonically nebulized, and male F-344 rats (200-300 g) were exposed via whole-body inhalation to the dry aerosol for 4 hrs/day, 5 days/week for 4 weeks (total of 19 exposure days) at airborne SiO2 concentrations of 0.2, 1.0, or 4.7 mg/m3 (MMAD, 0.38-0.5 µm; GSD, 1.8-2.4). Controls were exposed to filtered air. Results: Retained lung burdens at 1 day post-exposure (PE) were 14±3, 47±9, and 196±7 µg of SiO2 for the low, mid, and high doses, respectively. These values are lower than what is predicted, suggesting high biosolubility of the SiO2 particles. Lung tissue was harvested from separate groups of rats at 1, 7, and 27 days PE to evaluate inflammatory responses. At 1 day PE, the mid and high concentrations produced statistically significant elevations in lavage neutrophils (5.8%±1.7; 33.9%±1.8) and other inflammatory parameters; although the magnitude of the responses decreased during recovery, they were still higher than controls at 27 days PE. In contrast, the lowest concentration did not produce any significant changes in inflammatory parameters and is, thus, a no-observed-adverse-effect concentration for this study. Conclusions: Using dosimetric extrapolation modeling based on alveolar surface areas and lung weights, human-equivalent exposure concentrations that should be protective for workplace exposures ranging from 0.2 mg/m3 (lung weight basis) to 0.8 mg/m3 (alveolar surface area basis), measured as SiO2, were determined. This research was funded by NIH P30 ES01247 and SUNY Research Foundation subaward 13-15.

2540 Investigating *In Vivo* Bioprocessing of Engineered Nanoparticles (NP): A Novel Approach in Nanotoxicology

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Background: By using advanced imaging technologies (1 nm spatial resolution) and simultaneous elemental analysis with acquisition of material phase changes and analysis of oxidation states of retained NP in tissue, we define "*in vivo* processing" as the dynamic chemical and/or physical breakdown of the NP at the cellular and subcellular level. The goal of our studies is to investigate cellular interactions of NP in target tissues associated with their retention and biological/toxicological effects. Methods: Groups of rats were exposed to amorphous SiO2 NP aerosols for 4 hrs/day, 5 days/week for 4 weeks with a 27 day post-exposure observation period at three concentrations. Dose-dependent pulmonary inflammation was found in the rats. Prior analysis of the clearance kinetics using modeling of retained lung burden showed significant *in vivo* solubility which raises the question about underlying cellular mechanisms that result in the instability of the particles and toxicity. Lung tissue was fixed and thin sections were prepared for high resolution imaging. Results: Examination of phagocytosed SiO2 NP in phagolysosomes of alveolar macrophages showed significant *in vivo* breakdown and transformation of the NP after inhalation. A comparison with the pristine precursor SiO2 NP showed that the original spherical morphology of ~20-40 nm size was not retained in the lung. Instead, the NP exhibited dissolution patterns and secondary reaction zones which formed around partially dissolving SiO2 NP. We discovered that the *in vivo* processing led to second generation NP of ultra-small sizes (<4 nm) which resulted in a much greater surface area. Elemental mapping of the *in vivo* processed SiO2 NP showed an association of sulfur and phosphor-rich zones in the immediate vicinity of the bioprocessed NP. Moreover, ultra-high resolution analysis of the reaction zones around most SiO2 NP in phagolysosomes show breakdown patterns, void spaces and significant pore formation, suggesting that there are continuing processes that release and relocate the SiO2 NP which results in the observed reaction zones. Conclusion: Further detailing the physico-chemical changes during bioprocessing of NP may be an effective tool in understanding their subcellular and temporal fate that controls toxicity.

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Preface

This issue is devoted to the abstracts of the presentations for the Continuing Education courses and scientific sessions of the 55th Annual Meeting of the Society of Toxicology, held at the New Orleans Ernest N. Morial Convention Center, March 13–17, 2016.

An alphabetical Author Index, cross referencing the corresponding abstract number(s), begins on page 603.

The issue also contains a Keyword Index (by subject or chemical) of all the presentations, beginning on page 629.

The abstracts are reproduced as accepted by the Scientific Program Committee of the Society of Toxicology and appear in numerical sequence. Author names which are underlined in the author block indicate the author is a member of the Society of Toxicology. For example, J. Smith.

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- EC Education-Career Development Sessions
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- HH Historical Highlights Sessions
- IS Informational Sessions
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