Informing Selection of Nanomaterial Concentrations for ToxCast In Vitro Testing using the Multi-Path Particle Dosimetry Model

Sumit Gangwal[1], James S. Brown[2], Amy Wang[1], Keith A. Houck[1], David J. Dix[1], Robert J. Kavlock[1], Elaine A. Cohen Hubal[1]

[1]National Center for Computational Toxicology, U.S. EPA, RTP, NC, USA; [2]National Center for Environmental Assessment, U.S. EPA, RTP, NC, USA

Currently, little justification is provided for nanomaterial testing concentrations in *in vitro* assays. The *in vitro* concentrations typically used may be higher than those experienced in exposed humans. Selection of concentration levels for hazard evaluation based on real-world exposure scenarios is desirable. Nanomaterial concentrations in air (particle mass or count per air volume) are being measured in manufacturing and R&D lab settings. We reviewed nanomaterial levels reported across facility types for different nanomaterial classes. Using particle number concentration data from these studies, we calculated nanomaterial mass retained in the trachobronchial and alveolar regions of the human lung using the open-source Multiple-Path Particle Dosimetry (MPPD) model. These estimates of inhalation dosimetry were performed for carbon nanotubes (CNTs), titanium dioxide (TiO_2) and silver nanoparticles. The key model input parameters that affect the alveolar mass retained after 24 hours of nanoparticle exposure were particle size and size geometric standard deviation, aspect ratio, breathing conditions (resting, light or heavy exercise), and aerosol concentration. These key parameters were varied to further calculate alveolar mass retained per alveolar surface area ($\mu g/cm^2$) for different particle sizes (ranging from 5 to 100 nm), aerosol concentrations (0.1 and 1 mg/m^3), and exposure times (24 hours and a full working lifetime of 45 years at 8 hours per day, 5 days per week of aerosol inhalation). The alveolar mass retained per surface area for silver and TiO_2 nanoparticles for *a full working lifetime* exposure duration was similar to the high-end concentrations (~ 100-200 μg/mL) typical of *in vitro* testing for silver and TiO_2 nanoparticles. The amount retained per surface area after 24 hours of exposure equated to approximately 0.5 μg/mL. *This abstract may not necessarily reflect U.S. EPA policy*.