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Lung Dosimetry and Risk Assessment for Nanoparticles: Use of *In Vitro* and *In Vivo* Data to Extend Current Models in Rats and Humans

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Risk assessment of nanomaterials is a critical need in occupational safety and health. Human data are limited on exposure-response relationships to nanoparticles in the workplace, but quantitative data are available from a number of studies in rats. These studies have shown a consistent relationship between the particle surface area lung dose of respirable particles, including nanoparticles, and pulmonary inflammation and other responses. To use these data in risk assessment, a scientifically reasonable approach for extrapolating the rodent data to humans is required, including adjustment for species differences in the relationship between airborne exposures and internal dose. Lung dosimetry models provide a biologically-based approach to extrapolating internal doses (e.g., those associated with a given risk of disease) in animals to humans. However, current mass-based lung dosimetry models do not account for recently observed differences in the clearance and translocation of particles by size and composition.

We describe the use of human lung dosimetry models in a risk assessment framework for inhaled particles. Statistical models are used to describe the dose-response relationships in rats and estimate disease risks associated with given particle doses. Human lung dosimetry models are used to estimate the exposures associated with the human-equivalent doses from the rat studies. Examples are provided using rat data for particles of low or high toxicity, and fine or ultrafine sizes. We also describe ongoing research to provide *in vivo* and *in vitro* data to fill gaps in the current lung dosimetry models such as size-specific particle clearance or translocation rates, and provide a basis for extrapolating these parameters to the human models when human data are lacking. These updated models will provide estimates of the retained particle dose by size and composition in the lungs and other organs, and therefore improve risk assessment of occupational exposure to nanoparticles.

FRONTIERS IN AEROSOL DOSIMETRY RESEARCH

PROCEEDINGS OF A CONFERENCE

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Editors

*Robert F. Phalen, Michael J. Oldham, Susan W. Akhavan,
Mark D. Hoover and Kamlesh Asotra*

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Dear Dosimetry Conference Attendee,

Enclosed are copies of the Conference Proceedings and issue of *Inhalation Toxicology* that has our peer-reviewed papers.

A sample format for citing material in the Proceedings is:

Wang, C., and Friedlander, S. K. 2006. Effects of thermophoresis and diffusiophoresis on regional deposition of inhaled nanoparticles. In *Frontiers in Aerosol Dosimetry Research: Proceedings of a Conference*. eds. R. F. Phalen, M. J. Oldham, S. W. Akhavan, M. D. Hoover, and K. Asotra, pp. 5-85 – 5-96. Air Pollution Health Effects Laboratory, APHEL Report No. 06-01, University of California, Irvine, CA, USA.

As before, thank you for supporting the Conference.

Warm regards,

Bob, Mike, and Susan

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