Olfactory Transport and Systemic Delivery of Inhaled Nanoparticles

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There is still very limited knowledge of the fate of inhaled nanomaterials. Delivery of inhaled materials can reach the central nervous system (CNS) by systemic delivery or via direct transport of materials from the nasal cavity to the brain via the olfactory nerve (olfactory transport). There is a critical need to determine whether inhaled nanoparticles are delivered to the CNS via either of these routes. Studies with commercially available nanoparticles will examine mechanisms involved in the initial uptake of these materials by the olfactory epithelium. An initial phase of the project will examine the uptake of nanomaterials by cells lining the respiratory tract (e.g., alveolar macrophages, respiratory epithelial cells, olfactory neurons). These studies will use appropriate *in vitro* systems, including primary cells, cell lines, or explant cultures, and a variety of nanomaterials with different diameters. Other experiments will compare and contrast CNS delivery of materials following nasal or intratracheal (pulmonary) instillation or intravenous injection to explore the potential of a select group of nanomaterials to undergo olfactory transport and/or systemic delivery to the CNS (and other tissues). Nanomaterials to be used in this phase of the project will be chosen in part based upon their commercial availability, results of our *in vitro* studies, and our ability to use the materials in inhalation studies. Research products will include a more quantitative understanding of delivery and retention of particles in tissues. In this manner, real data on particle uptake and clearance will displace vague concerns that lead to conservative, default decisions. Data derived from these studies will also be used by CIIT scientists that have developed dosimetry models that describe nasal and lung deposition of particles and olfactory transport of inhaled materials, as well as other models developed to describe the fate of inhaled materials by laboratory animals. Our research will improve our understanding of the dosimetry and toxic potential of nanoparticles.

**Implications:** A limited number of particles can be deposited on tissues within the nose and taken up into the CNS along nerves of the olfactory system. Without a more quantitative measure of uptake rates and sites of accumulation of different particles, it will be difficult to confirm or refute the importance of this pathway for possible toxicity. This study provides approaches to measure CNS uptake from nasal epithelium and place this pathway in perspective compared to other routes of administrations and other possible target tissues.

**Start and end date:** January 2006 – December 2008

**Presentations:**


This abstract was prepared by the principal investigator for the project. Please see [www.americanchemistry.com/lri](http://www.americanchemistry.com/lri) for more information about the LRI.
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\textbf{Peer-reviewed publications:}


\textbf{Other publications:}


\textbf{Sponsors in addition to the LRI:} None.

\textbf{Abstract revision date:} March 2009