NATIONAL TOXICOLOGY PROGRAM
FACT SHEET
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National Toxicology Program (NTP)
Toxicological Evaluation of Nanoscale Materials

The National Toxicology Program (NTP) is developing a broad-based research program to address potential human health hazards associated with the manufacture and use of nanoscale materials. This initiative is driven by the intense current and anticipated future research and development focus on nanotechnology and a formal nomination from the Rice University Center for Biological and Environmental Nanotechnology requesting that the NTP conduct toxicological studies on representative nanoscale materials. Discussion and formal review of a research program in this area has highlighted the need for studies of nanoscale materials that apply existing toxicology testing methodologies, but also explore the development of appropriate novel toxicological methods to adequately assess potential human health effects.

Background

Nanoscale materials are a broadly defined set of substances where at least one critical dimension is less than 100 nanometers. Ultrafine particulate matter is a well-known example of *ambient* nanoscale particles, however, the NTP's research program will initially focus on *manufactured* nanoscale materials of current or projected commercial importance. Nanoscale materials can in theory be engineered from nearly any chemical substance; semiconductor nanocrystals, organic dendrimers, and carbon fullerenes and carbon nanotubes are a few of the many examples. Nanoscale materials are already appearing in commerce as industrial and consumer products and as novel drug delivery formulations. Commercial applications and resultant opportunities for human exposure may differ substantially for nanoscale vs. "bulk" materials.

Currently there is very little research focus on the potential toxicity of manufactured nanoscale materials. Studies from the ultrafine particle inhalation toxicology literature suggest that particle size can impact toxicity equally if not more so than chemical composition and hints at the complexity of the topic. The unique and diverse physico-chemical properties of nanoscale materials suggests that toxicological properties may differ from materials of similar composition but larger size. There are indications in the literature that manufactured nanoscale materials may distribute in the body in unpredictable ways and certain nanoscale materials have been observed to preferentially accumulate in particular organelles. Surface properties can be changed by coating nanoscale particles with different materials, but surface chemistry also is influenced by the size of the particle. This interaction of surface area and particle composition in eliciting biological responses adds an extra dimension of complexity in evaluating potential adverse events that may result from exposure to these materials.

Approach

The intent of the NTP's research program is to evaluate the toxicological properties of major nanoscale materials classes which represent a cross-section of composition, size, surface coatings, and physico-chemical properties, and use these as model systems to investigate fundamental questions concerning if and how nanoscale materials can interact with biological systems. Some of these fundamental questions include: What are the appropriate methods for detection and quantification of nanoscale particles in tissues? How are nanoscale materials absorbed, distributed in the body and taken up by cells? Are there novel toxicological interactions? As part of this research program, the following specific studies are currently proposed:

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1. Evaluate the size- and composition-dependent biological disposition of nanoscale crystalline fluorescent semiconductors ("quantum dots").
2. Conduct short- and long-term toxicology studies of one or more carbon-based nanoscale materials (e.g. single- or multi-walled nanotubes, fullerenes).
3. Evaluate the role of particle core and surface composition in the immunotoxicity of nanoscale crystalline semiconductor materials and carbon nanoscale materials.
4. Conduct phototoxicology studies of representative nanoscale metal oxide particles used in industrial settings and consumer products (e.g. titanium dioxide).