

## **NTP NANOTECHNOLOGY SAFETY INITIATIVE**

*Year 2006*

### **What are Nanoscale Materials?**

Nanotechnology is defined by the National Nanotechnology Initiative (NNI) as “the understanding and control of matter at dimensions of roughly 1 to 100 nanometers, where unique phenomena enable novel applications.” In theory, these materials can be engineered from nearly any chemical substance; semiconductor nanocrystals, organic dendrimers, and carbon fullerenes (“buckyballs”) 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” compared with “bulk” materials.

Nanoscale materials are a broadly defined set of substances that have at least one critical dimension less than 100 nanometers and possess unique optical, magnetic, or electrical properties. Ultrafine particulate matter is a well-known example of nanoscale particles found in the environment. The NTP’s research program focuses on manufactured nanoscale materials of current or projected commercial importance. The program includes studies to evaluate the biological disposition of nanoscale crystalline fluorescent semiconductors (“quantum dots), long-term toxicology studies of carbon-based nanoscale materials (e.g., single- or multi-walled nanotubes, fullerenes), and phototoxicology studies of representative nanoscale metal oxide particles used in industrial settings and consumer products (e.g. titanium dioxide).

### **Why is the NTP Studying Nanoscale Materials?**

There is very little research focus on the potential toxicity of manufactured nanoscale materials. The unique and diverse physicochemical properties of nanoscale materials suggest that toxicological properties may differ from materials of similar composition but different size. Published studies on the inhalation of ultrafine particles suggest that particle size can impact toxicity equally, if not more so, than chemical composition and hints at the complexity of the topic. 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. There are indications in the literature that manufactured nanoscale materials may distribute in the body in unpredictable ways. Certain nanoscale materials have been observed to accumulate preferentially in particular cellular organelles.

The NTP is engaged in 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. The goal of this research program is to evaluate the toxicological properties of major nanoscale materials classes which represent a cross-section of composition, size, surface coatings, and physicochemical properties, and use these as model systems to investigate fundamental questions concerning if and how nanoscale materials can interact with biological systems.

### **What Studies is the NTP Conducting?**

The NTP intends to conduct studies that test hypotheses focused on the relationship of key physicochemical parameters of selected manufactured nanomaterials to their potential toxicity. Initial parameters of greatest concern are size, shape, surface chemistry, and composition. This strategy will be

accomplished by developing a suite of analytical approaches to evaluate and characterize the physiochemical properties of nanoscale materials in their raw form and as formulated when given to animals or exposed to cells in culture. In addition, we will conduct animal toxicity studies of varying durations with specific nanomaterials using routes of administration that mimic possible human exposure. These studies will include evaluations of the absorption and handling of the materials by rodents. We also intend to develop a battery of *in vitro* models to evaluate the biological and toxicological effects of nanoscale materials. These models would be used to assess whether *in vitro* methods can predict which nanoscale materials might be a hazard for animals or people.

The NTP's nanotechnology safety initiative is focusing on 3 areas of research with respect to specific types or groups of nanoscale materials:

1. Non-medical, commercially relevant/available nanoscale materials to which humans are intentionally being exposed, e.g., cosmetics and sunscreens.
2. Nanoscale materials representing specific classes (e.g., fullerenes and metal oxides) so that information can be extrapolated to other members of those classes.
3. Subsets of nanomaterials to test specific hypotheses about a key physiochemical parameter (e.g., size, composition, shape, or surface chemistry) that might be related to biological activity.

Ongoing research activities are focusing initially on 4 classes of nanoscale materials: (1) metal oxides, (2) fluorescent crystalline semiconductors (quantum dots), (3) fullerenes, and (4) carbon nanotubes.

- NTP scientists at the National Center for Toxicological Research (NCTR) NTP Center for Phototoxicity are examining the potential dermal toxicity of nanoscale materials available in non-medical, commercially available products. For example, nanoscale ceramics (nanoscale titanium dioxide or TiO<sub>2</sub> and zinc oxide or ZnO) are already in use in certain cosmetics and sunscreens. These studies are addressing (1) the fate and distribution of nanoscale ceramics and quantum dots in the body following their dermal application to rodents with attention given to the role of surface coating, size, polarity, vehicle, and skin condition on the ability of nanoscale TiO<sub>2</sub> to penetrate the skin; (2) whether nanoscale TiO<sub>2</sub> and ZnO applied dermally to mice in combination with UVA-containing light affects cell signaling, and (3) the potential for TiO<sub>2</sub> and ZnO applied dermally to haired and hairless mice in combination with UVA-containing light to cause skin cancer.
- NTP scientists at National Institute for Occupational Safety and Health (NIOSH) are planning inhalation studies on single-walled nanotubes. They are interested in the potential toxicity of these nanoscale materials because of potential exposure to workers in occupational settings and because laboratory studies in rodents have reported potential toxicity of nanotubes in the lungs.
- Also in development are systemic studies on fullerenes (buckyballs) and related compounds because of the current, high mass production of these compounds, their increasing use in consumer products, and the use of derivatized fullerenes in drug delivery research. NTP scientists at the National Institute of Environmental Health Sciences (NIEHS) are leading these studies.

Depending on the type of study, results from NTP studies are anticipated to be available in the next 1-5 years. Results from longer-term rodent studies will likely take several years.

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