DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

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Thomas J. Goehl, Ph.D.
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Dear Dr. Goehl;

I am writing to you in your capacity as editor of a journal concerning manuscripts submitted for publication that investigate biological/toxicological interactions or effects of nanotechnology derived products. On November 3-4, 2004 a workshop titled "Developing Experimental Approaches for the Evaluation of Toxicological Interactions of Nanoscale Materials" was held in Gainesville, Florida. The purpose of the workshop was to identify and discuss issues associated with the proper conduct of studies to characterize the potential toxicities of manufactured nanoscale materials. The 75 invited participants represented expertise in biology, medicine, toxicology, physics, chemistry, and materials science, and were drawn from government, industry, academic and public interest sectors. Over the course of the two-day workshop several central themes emerged from the presentations and discussions. These themes were summarized in a final workshop report that is available on the web at www.nanotoxicology.ufl.edu.

The purpose of this letter is to accomplish one of the workshop recommendations, which follows:

> *It is essential that the physical and chemical characterization of nanoscale materials be much more complete than has been the case in the sparse toxicology literature appearing to date. State of the art analytical characterization techniques were described (during the conference) and their application to all phases of toxicology studies was considered... The group recommended that scientific journal editors be urged to require proper physical and chemical characterization of nanoscale materials for all publications in the newly emerging field of "nanotoxicology".*

There was a general appreciation that unlike other chemical entities "nanoscale materials" can exist in various forms across molecular, macromolecular, supramolecular and higher order states. Given that the potential biological effects associated with exposure to nanoscale materials may reflect some aspect of any of these states, the workshop participants agreed that nanoscale materials should be characterized to the greatest extent possible, not only as the "bulk" synthesized materials, but as they exist when delivered to a specific biological or test system environment. However, certain characteristics of the materials as received by the manufacturer (for commercially procured materials) and as dosed or otherwise exposed to the biological system under study, should also be catalogued and verified for quality control purposes. A set of example parameters was identified, with the understanding that this set would most likely be both material and application specific. These parameters were categorized by whether they are determined *ex vivo* or *in vivo*, and more specifically categorized according to whether they describe physical or chemical characteristics. The list of parameters is:

Ex vivo

Physical: size, shape, surface area, surface porosity, roughness morphology (agglomerate vs. primary particles, stability of agglomerates), crystallinity, magnetic properties

Chemical: solubility, stability (dissolution), chemical composition and purity, surface chemistry [zeta potential, acidity/basicity, redox potential, functional groups, reactivity (redox, photoactivity, etc)] and information on the aging and or storage conditions for the materials

In vivo

Dispersion of particles, dosage (number density for materials with narrow size distribution; mass dosage for materials with wide size distribution), images that visualize nanomaterials in contact with biological systems

With regard to the *ex vivo* characterization, it was noted that the distributions of particle properties should be considered in addition to statistics of central tendency such as the mean or median. Also, the history of the particles should be considered as a means of determining what is likely to be on the surface, e.g., chemical functional groups. Thus, reference to the core synthesis paper should be included when reporting particle properties.

Because characterization of the material used within a specific experimental situation is so crucial to developing an understanding of which physiochemical parameters are responsible for an observed biological response, the workgroup recommended that the characterization of a nanomaterial in publications should include as much information as possible relating to the properties outlined above, but at a minimum the following information should be provided:

Description of preparation methods and physico-chemical characterization of the material with conventional analytical methods

Assessment of purity (this might be from a NIST certified laboratory, or using a NIST certified method) and identification/quantification of contaminants

Particle size distribution on basis of volume and mass, number of particles per unit volume or mass (mL or g), surface area, and particle shape

Characterization of stability in the dosing medium

a. Description of methodology, e.g., "1 g was suspended in 4 mL of acetonitrile, vortexed, and analyzed using a ..."
b. Estimation of the half-life of chemical stability and aggregation

Shape and crystal structure, if appropriate

Surface chemistry, charge, and type of and integrity of coatings if present

It is imperative that this type of information be included in research papers dealing with manufactured nanoparticles to allow for easier replication of findings by others and to avoid situations where opposite results are reported in repeated studies of seemingly similar materials. Given this, there is a very real possibility that progress in understanding potential hazard of nanocale materials to human health may actually be hindered if such information is not reported. Therefore, on behalf of the workshop organizing committee, I urge that you carefully consider these recommendations during your peer-review process dealing with the effects of manufactured nanomaterials for publication in *Environmental Health Perspectives*. Thanks very much for your attention to this request.

Sincerely Yours

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