C-18. Working With Nanomaterials

I. Purpose And Scope

At this time, there are no published regulations for safe work practices with nanomaterials, nor for controlling release of manufactured nanomaterials into the environment. Manufactured nanomaterials may pose unusual risks to human health due to their unique composition, reactivity, size, and ability to cross cell membranes [Nel 2006]. Preliminary studies indicate that engineered nanomaterials may exhibit markedly higher toxicity compared with macro scale materials of similar chemical composition. Current information about environmental, health, and safety risks associated with exposure to engineered nanomaterials is extremely limited. Until more definitive conclusions are made regarding the occupational and environmental risks of nanomaterials, interim precautionary work practices will be established and followed. Risk assessments and control strategies for nanotechnology research at the NCI-Frederick will be based on the most current toxicological data, exposure assessments, and exposure control information that is available[1].

II. Policy

It is the policy of the National Cancer Institute at Frederick (NCI-F) that all work with nanoparticles and material containing nanoparticles be conducted in a safe and responsible manner that protects NCI-F employees, the public, and the environment.

Safe work practices are generally based on an understanding of the hazards associated with the composition of a material. Since the toxicity and hazards associated with nanomaterials is uncertain, nanomaterials will be handled using the same precautions currently used at NCI-F when handling toxic materials or materials of unknown toxicity (Chemical Hygiene Plan, Chapter C-1, EHS Operations Manual).

III. Definitions

Nanomaterials - Nanomaterials are defined as having at least one dimension less than 100 nanometers (nm; a nanometer is 10^{-9} meters) and typically are engineered to have unique properties which make them desirable for medical or commercial applications. Nanotechnology is a multidisciplinary grouping of

[1] The National Institute for Occupational Health and Safety (NIOSH) is participating in an international effort of research groups, government agencies, and industries to understand the health impact of nanotechnology and how to control potential risks. As new information becomes available, NIOSH disseminates this information. This policy is based upon the most current NIOSH information [NIOSH 2006, NIOSH 2007]. Although recent NIOSH toxicology studies have provided better understanding of the ways in which some types of nanoparticles may enter the body and interact with the body's organ systems, the breadth and depth of such research efforts have been limited to a few nanoparticle types. More types of nanoparticles need to be assessed for characteristics and properties relevant for predicting potential health risk.

physical, chemical, biological, engineering, and electronic processes, materials, applications, and concepts in which the defining characteristic is size. In this policy, nanotechnology is a generic term that encompasses the manipulation of matter at atomic or near atomic scales to produce new materials, structures, or devices.

IV. Procedure

With guidance from the NCI-F Environment Health and Safety Program (EHS), implementation of specific control measures will be carried out on a case-by-case basis. Factors affecting exposure to engineered nanoparticles include the amount of material being used and whether the material can be easily dispersed (in the case of a powder) or form airborne sprays or droplets (in the case of suspensions). Engineering controls, work practices, personal protective equipment (PPE), and administrative controls will each play a role in laboratories involved with nanotechnology.

A. Engineering Controls

The control of airborne exposure to nanoparticles will primarily be accomplished using engineering control techniques similar to those used in reducing exposures to general aerosols. Although aerosol control methods have not been well-characterized for nanoparticles[2], aerosol theory and limited experimental data indicate that conventional ventilation, engineering control and filtration approaches should be effective [Lee and Liu 1982, Hinds 1999, Maynard 2005].

Ventilation systems will be designed, tested, and maintained using approaches in accordance with NCI-F's Lab Ventilation Management Program in the EHS Operations Manual, Chapter C-13. Effective performance of these systems will be highly dependent on appropriate use and maintenance. Additionally, if engineered nanoparticles have the potential to contaminate air exhausted from a containment device, the exhaust air must pass through a HEPA filter whenever the toxicity of the engineered nanomaterial is unknown, and the potential to generate aerosols is medium to high; or, when the toxicity of the engineered nanomaterial is medium to high and the potential to generate aerosols is high (Table 1).

[2] NIOSH is currently conducting research to validate the efficiency of HEPA filter media used in environmental control systems and in respirators in removing nanoparticles. Filters are tested using particles that have the lowest probability of being captured (typically around 300 nm in diameter). Collection efficiencies for smaller particles should exceed the measured collection efficiency at this particle diameter [NIOSH 2006, NIOSH 2007].

Table 1: Requirement for HEPA Filtration for Exhausted Air

Aerosol Generation Potential	Toxicity of Engineered Nanomaterial		
	Low	Medium	High/Unknown
Low			
Medium			HEPA
High		HEPA	HEPA

Any NCI-F investigator who proposes to work with engineered nanomaterials without HEPA-filtered exhaust is responsible for requesting a risk assessment from the NCI-Frederick EHS department. EHS is responsible for determining whether the aerosol generation potential and the toxicity of the engineered nanomaterial are “low”, “medium”, or “high/unknown”.

Examples of potential aerosol generation that would require engineering controls include:

- Working with nanomaterials in liquid media during pouring or mixing operations, or where a high degree of agitation is involved;
- Generating nanoparticles in the gas phase;
- Handling nanostructured powders;
- Maintenance on equipment and processes used to produce or fabricate nanomaterials;
- Cleaning of dust collection systems used to capture nanoparticles.

B. Work Practices

The incorporation of good work practices will help minimize worker exposure to nanomaterials. Good work practices are outlined in the NCI-F Chemical Hygiene Plan (Chapter C-1, EHS Operations and Compliance Manual). Examples include the following:

- Storage and consumption of food or beverages in areas where nanomaterials are handled is prohibited.
- Application of cosmetics, etc. in labs where nanomaterials are used or stored is prohibited.
- Personnel will wash hands before leaving the work area and after removing personal protective gloves.
- Protective lab clothing such as coveralls or lab coats can become contaminated and shall not be worn in administrative areas or outside a lab facility.
- Personnel will avoid touching the face or other exposed skin with contaminated fingers; use of PPE (such as face masks) may help to avoid the potential transfer of nanomaterials. Ingestion exposure in the workplace results primarily from hand-to-mouth contact. It

follows that strategies that tend to reduce dermal exposure in the workplace will also tend to reduce exposure by ingestion.

- All vessels holding nanomaterials and hazardous chemicals, including transfer containers and transfer lines, must be properly labeled in accordance with Chapter C-6 in the EHS Operations and Compliance Manual (Employee Right-to-Know).
- Cleaning work areas using HEPA vacuum pickup and wet wiping methods, as needed and applicable. Dry sweeping or compressed air should not be used to clean work areas. Cleanup and disposal should be conducted in a manner that prevents worker contact with wastes and complies with NCI-Frederick's Waste Management and Waste Disposal Programs, Chapters D-1 and D-2 in the EHS Operations and Compliance Manual.

C. Personal Protective Equipment

Currently, specific guidelines are not available on the selection of personal protective equipment (PPE) for the prevention of dermal exposure to nanoparticles. Yet there is some evidence that dermal exposure to nanoparticles may lead to direct penetration of nanoparticles into the epidermis and possibly beyond into the blood stream [Tinkle 2003, Aitken 2004]. Therefore, protective gloves will be worn when handling dry nanoparticulates, solutions containing nanoparticles, and when using or generating nanoparticles in the gas phase. Proper gloves that have good to excellent resistance to the solvent the particles are suspended in should be used. Two pairs of gloves should be worn if prolonged contact is anticipated.

Glove selection guides are available from EHS. However, glove-resistance to various chemicals materials will vary with the manufacturer, model and thickness. Therefore, review of glove-resistance charts from the manufacturer is recommended.

Using the hierarchy of controls listed above (e.g. engineering controls are primary), it is unlikely that respirators will be necessary for current nanotechnology research at the NCI-F. The decision to institute respiratory protection will be based on a combination of professional judgment and risk assessments. If worker exposure to nanoparticles remains a concern after instituting engineering measures to control exposure, the use of respirators can further reduce worker exposures. If respirators are deemed necessary, use will be in compliance with the EHS Respiratory Protection Program, Chapter C-10, EHS Operations and Compliance Manual.

D. Administrative Controls

Researchers are strongly encouraged to prioritize research so that work with hazardous agents occurs only during core working hours (8 am – 5 pm, Monday through Friday). After-hours work (on nights and weekends) should be restricted to non-hazardous activities. If hazardous materials must be used at nights or on weekends, ensure that at least one other person is available to provide help in an emergency.

Supervisors shall consider the hazards involved in their research, and designate areas, activities, and tasks that require specific types of personal protective equipment as described above.

E. Clean-up of nanomaterial spills

No specific guidance is currently available on cleaning up nanomaterial spills. Until relevant information is available, it is prudent to base strategies for dealing with spills on current good practices, together with available information on exposure risks and the relative importance of different exposure routes. Standard approaches to cleaning up powder and liquid spills include the use of HEPA-filtered vacuum cleaners, wetting powders down, using dampened cloths to wipe up powders and applying absorbent materials/liquid traps. As in the case of any material spill, handling and disposal of the waste material will comply with the EHS Waste Management and Waste Disposal Programs, Chapters D-1 and D-2 in the EHS Operations and Compliance Manual.

When developing procedures for cleaning up nanomaterial spills, consideration will be given to the potential for exposure during cleanup. Inhalation exposure and dermal exposure will likely present the greatest risks. Consideration will therefore need to be given to appropriate levels of personal protective equipment. Inhalation exposure in particular will be influenced by the likelihood of material re-aerosolization. In this context, it is likely that a hierarchy of potential exposures will exist, with dusts presenting a greater inhalation exposure potential than liquids, and liquids in turn presenting a greater potential risk than encapsulated or immobilized nanomaterials and structures.

F. Animal Studies

Dosing and necropsies shall be conducted within an exhausted hood. Determination of HEPA filtration will follow the guidance outlined in Table 1. It is currently unknown how animals dosed with nanoparticles will excrete nanoparticles. Additionally, the composition of the nanoparticles will vary amongst animal study protocols (ASP's), e.g. chemical composition, radiolabelled nanoparticles, nanoparticle structure, etc., so potential toxicity and safety control measures may also vary with each

ASP. To address these complexities, EHS will review ASP's and make specific safety control recommendations for animal care personnel. These recommendations will be "cradle-to-grave" and will address animal waste and animal bedding.

G. Material Safety Data Sheets (MSDSs)

NCI-F investigators and EHS will review MSDSs for nanomaterials as they become available. However, it should be noted that some current MSDSs for nanomaterials may not have accurate information[3]. Particle size may be a component of toxicity of nanomaterials [Nel 2006], and particle size is not currently included in MSDSs. NIOSH has recommended that the current MSDS system be changed to incorporate relevant classification, toxicity data, and safety and health recommendations for working with nanomaterials.

H. EHS Responsibilities

EHS will remain current with the literature that addresses environmental health and safety and regulatory agency requirements. EHS will assure the latest information is applied, and that controls for nanotechnology research are based upon the most recent regulations, directives, guidance, and/or other applicable information.

V. References

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[3] For example, the MSDSs for some commercially available carbon nanotubes (CNTs) refer to the graphite permissible exposure limit (PEL) as a relevant exposure standard. Graphite is composed of coarse particles while CNTs are shaped like fibers and have much different tensile and conductive properties than graphite. Additionally, CNTs may be more toxic than graphite in the short-term, as shown in animal and in-vitro tests [Lam 2004, Oberdörster 2006].

Exchange with NIOSH**.** DEPARTMENT OF HEALTH AND HUMAN SERVICES, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health. http://www.cdc.gov/niosh/topics/nanotech/safenano/pdfs/approaches_to_safe_nanotechnology_28november2006_updated.pdf.

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