UTHealth
The University of Texas
Health Science Center at Houston

NANOPARTICLES SAFETY GUIDE

I. Purpose

This document has been written to offer health and safety guidance to faculty, staff, students, and visitors working with nanotechnology at The University of Texas Health Science Center at Houston. The purpose of the Nanomaterials Safety Program is to provide a framework for anticipating, recognizing, evaluating, and controlling the potential hazards associated with nanotechnology; however, the Program is not intended to provide stand-alone guidance and should be used in conjunction with the UTHealth Chemical Hygiene Plan and in consultation with the office of Safety, Health, Environment, and Risk Management (SHERM). All work involving nanotechnology requires approval from the institutional Chemical Safety Committee before work with nanotechnology is initiated. A site-specific risk assessment will be conducted by SHERM to determine the potential hazards of working with the nanotechnology. In addition, it is the responsibility of each principal investigator to ensure that laboratory-specific safety plans and standard operating procedures are developed for each laboratory where nanomaterials are used and stored.

II. Introduction

Nanotechnology involves the manipulation of matter at nanometer scales to produce new materials, structures, and devices. Nano-objects are materials that have at least one dimension (e.g., length, width, height, and/or diameter) that is between 1 and 100 nanometers. (CDC/NIOSH, 2009) A nanometer, or nm, is 1×10^{-9} meters or one millionth of a millimeter. The term *nanoparticles* typically refer to materials in which all three dimensions are in the nanoscale. In this document, the term *nanoparticles* or *nanomaterials* will refer to purposefully created, engineered particles with at least one dimension between 1 and 100 nanometers. (CDC/NIOSH, 2009) Nanoparticles may be dry particles, suspended in a gas (as a nanoaerosol), suspended in a liquid (as a nanocolloid or nanohydrosol), or embedded in a matrix (as a nanocomposite). Nanoparticles also exist in several structures, such as nanotubes, nanoplates, and nanofibers. (CDC/NIOSH, 2009)

The term *ultrafine particle* has traditionally been used to describe airborne particles smaller than 100 nm in diameter that are byproducts of industry or nature. Ultra-fine particles tend to be generated through processes such as combustion and vaporization. The particles are produced in large quantities from industrial activities such as thermal spraying and welding and from domestic combustion activities like gas cooking. Ultra-fine particles are also found in the atmosphere, where they originate from combustion sources like forest fires and volcanic activity and from atmospheric gas-to-particle conversion processes, such as photo-chemically driven nucleation. (CDC/NIOSH, 2009)

Research with nanomaterials has shown that the physiochemical characteristics of particles can influence their effects in biological systems. Some of these characteristics include:

- Charge;
- Chemical reactivity;
- Degree of agglomeration;
- Shape;

- Size;
- Solubility;
- Surface area; and
- Surface composition.

There are many unknowns as to whether the unique properties of engineered nanomaterials pose health concerns. The potential health risk following exposure to a substance is generally associated with the following (CDC/NIOSH, 2009):

- Magnitude and duration of the exposure;
- Persistence of the material in the body;
- Inherent toxicity of the material; and
- Susceptibility or health status of the person.

Unfortunately, there is limited data regarding the health risks related to nanomaterials. As such, this document is to provide EHS-accepted recommendations for practicing prudent health and safety measures when working with nanomaterials.

III. Regulations

At this time, there are no federal regulations that specifically address the health and safety implications of nanotechnology. There are also no national or international consensus standards on measurement techniques for nanomaterials in the workplace. However, as with conventional chemicals, research with nanomaterials must be conducted in a manner that is safe and responsible. All chemicals, including nanomaterials, must be transported, stored, used, and disposed in accordance with all federal, state, and local requirements.

The Occupational Safety and Health Administration (OSHA) require employers to maintain a safe and healthful workplace, "free from recognized hazards likely to cause death or serious physical harm." (29 USC 654) According to OSHA, laboratory personnel must be informed of the risks associated with workplace hazards. This is generally accomplished through training programs, material safety data sheets, and labeling and signage.

The Resource Conservation and Recovery Act of 1976 (RCRA) regulates the transportation, treatment, disposal, and cleanup of hazardous waste. Nanomaterials that meet the definition of a "hazardous waste" in RCRA are subject to this rule.

Nanomaterials that are defined as "chemical substances" under the Toxic Substances Control Act (TSCA) and which are not on the TSCA Inventory must be reported to U.S. Environmental Protection Agency (EPA). A Pre-manufacture Notice must be submitted to the EPA by anyone intending to manufacture or import a chemical substance that is not on the TSCA Inventory of Chemical Substances.

The Federal Insecticide, Fungicide, and Rodenticide Act requires that the EPA approve all new pesticide products, as well as new uses and changes in the composition of existing pesticide products, before the products may be sold or distributed in commerce. In order to evaluate an application for registration, the EPA requires the applicant to provide a complete characterization of the composition of the product, proposed labeling which describes the intended use of the product, and the results of extensive health and safety testing.

It should be also noted that the U.S. Food and Drug Administration currently regulates a wide range of products including those that utilize nanotechnology or contain nanomaterials (e.g., a drug delivery device).

IV. Hazard Assessments

Prior to beginning work with nanomaterials, a hazard assessment should be performed by safety personnel. The purpose of the assessment will be to identify appropriate work procedures, controls, and personal protective equipment to ensure worker safety. The assessment will evaluate several factors, including but not limited to the physical and chemical properties of the nanomaterial, the process by which the material will be generated and/or used, and existing engineering controls (e.g., fume hood, glove box). In some instances, the safety personnel may recommend collecting occupational exposure measurements (e.g., sampling). This will be performed to further understand potential hazards or to identify specific processes or equipment requiring additional engineering controls. Additionally, any protocol involving the use to nanoparticles is subject to approval by the UTHealth Chemical Safety Committee.

V. Exposure Routes

The most common route of exposure to a nanomaterial is through inhalation (see Table 1). The deposition of discrete nanomaterials in the respiratory tract is determined by the particle's aerodynamic or thermodynamic diameter. Particles that are capable of being deposited in the gas exchange region of the lungs are considered respirable particles. Discrete nanomaterials are deposited in the lungs to a greater extent than larger respirable particles. Deposition increases with exertion (due to an increase in breathing rate and change from nasal to mouth breathing). It also increases among persons with existing lung diseases or conditions. Based on animal studies, discrete nanomaterials may enter the bloodstream from the lungs and translocate to other organs.

Ingestion is another route whereby nanomaterials may enter the body. Ingestion can occur from unintentional hand-to-mouth transfer of materials. This can occur with traditional materials and it is scientifically reasonable to assume that it could happen during handling of materials that contain nanomaterials. Ingestion may also accompany inhalation exposure because particles that are cleared from the respiratory tract via the mucociliary escalator may be swallowed. A few studies suggest that nanomaterials may enter the body through the skin during exposure. At this time, it is not known if skin penetration of nanomaterials would result in adverse health effects. There is also little information about the health effects of injecting nanomaterials into living organisms.

Potential Sources of Occupational Exposure to Nanomaterials for Various Synthesis Methods

Process Synthesis	*Particle Formation*	*Exposure Source or Worker Activity*	*Primary Exposure Route***
Gas Phase	In Air	Direct leakage from reactor, especially if the reactor is operated at positive pressure	Inhalation
		Product recovery from bag filters in reactors.	Inhalation/Dermal
		Processing and packaging of dry powder.	Inhalation/Dermal
		Equipment cleaning/maintenance (including reactor evacuation and spent filters).	Dermal (and inhalation during reactor evacuation)
Vapor Deposition	On Substrate	Product recovery from reactor/dry contamination of workplace.	Inhalation
		Processing and packaging of dry powder.	Inhalation/Dermal
		Equipment cleaning/maintenance (including reactor evacuation).	Dermal (and inhalation during reactor evacuation)
Colloidal	Liquid Suspension	If liquid suspension is processed into a powder, potential exposure during spray drying to create a powder, and the processing and packaging of the dry powder.	Inhalation/Dermal
		Equipment cleaning/maintenance.	Dermal

Attrition	Liquid Suspension	If liquid suspension is processed into a powder, potential exposure during spray drying to create a powder, and the processing and packaging of the dry powder.	Dermal
		Equipment cleaning/maintenance.	Dermal
** Note: Ingestion would be a secondary route of exposure from all sources/activities from deposition of nanomaterials on food or subsequently swallowed (primary exposure route inhalation) and from hand-to-mouth contact (primary exposure route dermal).			

Table 1 – Sources of Exposure to Nanomaterials through Occupational Activities (Aiken et al. 2004)

VI. Factors Affecting Exposure

Every attempt should be made to prevent or minimize exposure to nanomaterials. Factors affecting exposure to nanomaterials include the amount of material being used and whether it can be easily dispersed or form airborne sprays or droplets. The degree of containment and duration of use will also influence exposure. In the case of airborne material, particle or droplet size will determine whether the material can enter the respiratory tract and where it is most likely to deposit. Inhaled particles smaller than 10 micrometers in diameter have some probability of penetrating and being deposited in the gas-exchange (i.e., alveolar) region of the lungs, but there is at least a 50% probability that particles smaller than 4 micrometers in diameter will reach the gas-exchange region.

At present there is insufficient information to predict all of the situations and workplace scenarios that are likely to lead to exposure to nanomaterials. However, there are some workplace factors that will increase the potential for exposure, including (CDC/NIOSH, 2009):

- Working with nanomaterials in liquid media without adequate protection (e.g. gloves) will increase the risk of skin exposure.
- Working with nanomaterials in liquid media during pouring or mixing operations, or where a high degree of agitation is involved, will lead to an increased likelihood of inhalable and respirable droplets being formed.
- Generating nanomaterials in the gas phase in non-enclosed systems will increase the chances of aerosol release to the workplace.
- Handling nanopowders will lead to the possibility of aerosolization.
- Maintenance on equipment and processes used to produce or fabricate nanomaterials will pose a potential exposure risk to workers performing these tasks.
- Cleaning of dust collection systems used to capture nanomaterials will pose a potential for both skin and inhalation exposure.

VII. Engineering Controls

In order to provide a safe work environment for faculty, staff, students and visitors, engineering controls must be maintained wherever nanomaterials are used or stored. At a minimum, engineering controls should include local exhaust ventilation, localized filtration, and personal protective equipment. Respiratory protection is required when working with nanomaterials when local exhaust ventilation and filtration is not available.

The following engineering controls should be used in conjunction with the aforementioned policy when handling nanomaterials (CDC/NIOSH, 2009; VCU, 2007):

- Use of a chemical fume hood is recommended for all tasks with potential of aerosolizing nanomaterials in either liquid or powder form.
- A well-designed local exhaust ventilation system with a local high-efficiency particulate air (HEPA) filter should be used to effectively remove nanomaterials.
- Animals should be appropriately restrained and/or sedated prior to administering injections and other dosing methods.
- If heavy usage of aerosolized nanoparticles is in use, a proper decontamination, or buffer, area should be utilized to ensure the nanomaterials are not transported outside of the working area.
- Frequent hand washing, especially before eating, smoking, applying cosmetics, or leaving the work area should be employed.
- Laboratories and other spaces where nanomaterials are used or stored must be equipped with an eyewash station that meets American National Standards Institute (ANSI) and Occupational Safety and Health Administration (OSHA) requirements.

VIII. Administrative Controls

Although traditional permissible exposure limits (PEL) exist for many of the substances that nanomaterials are made from, the PEL for a nanomaterial of these substances is not yet clear. Thus, it is important to incorporate the following administrative controls into all laboratory operations:

- The laboratory's safety plan should be modified to include health and safety considerations of nanomaterials used in the laboratory.
- Principal investigators should develop and implement standard operating procedures (SOPs) in the preparation and administration of nanomaterials (with minimal exposure).
- Protocols involving the *in vivo* use of nanomaterials must be reviewed and approved by the Animal Welfare Committee.
- Laboratory personnel must receive the appropriate training, including specific nanomaterial-related health and safety risks, standard operating procedures, and steps to be taken in event of an exposure incident, prior to working with nanomaterials.
- Laboratory personnel must be instructed to use extreme caution when performing injections involving nanomaterials since accidental needle stick presents an exposure threat.
- Exposures involving nanomaterials or any other acutely hazardous material must be reported to the office of Safety, Health, Environmental and Risk Management as soon as possible.

IX. Work Practices

The incorporation of good work practices can help to minimize exposure to nanomaterials. Examples of good work practices include the following (CDC/NIOSH, 2009):

- Projects or applications with the potential for producing nanomaterial aerosols must be conducted within an approved chemical fume hood or ducted biological safety cabinet.
- Needles used for nanomaterial injection must be disposed in an approved sharps containers immediately following use. Needles used for nanomaterial injection should never be bent, sheared, or recapped.
- Bench paper utilized during preparation of nanomaterial stock should be lined with an impervious backing to limit potential for contamination of work surfaces in the event of a minor spill.
- Work areas should be cleaned at the end of each work shift (at a minimum) using either a HEPA-filtered vacuum cleaner or wet wiping methods. Dry sweeping or pressurized air should not be used to clean work areas. Bench tops, chemical fume hood interiors, biological safety cabinet interiors, equipment, and laboratory surfaces with potential for nanomaterial contamination should be routinely cleaned. Cleanup

should be conducted in a manner that prevents worker contact with wastes. The disposal of all waste material should comply with all applicable federal, state, and local regulations.

- The storage and consumption of food or beverages in workplaces must be prevented where nanomaterials are handled, processed, or stored, since exposure may occur via ingestion. Wash hands carefully before eating, drinking, applying cosmetics, smoking, or using the restroom.
- Facilities for showering and changing clothes should be provided to prevent the inadvertent contamination of other areas (including take-home) caused by the transfer of nanomaterials on clothing and skin.

X. Personal Protective Equipment

Typical chemistry laboratory apparel should be when working with nanomaterials in accordance with the University's Chemical Hygiene Plan (UTHealth, 2008). Always wear appropriate clothing (e.g., pants, shirts, shoes) and personal protective equipment, including safety glasses, laboratory coats, and gloves, when working with nanomaterials. Open sandals, shorts, and skirts are prohibited. Laboratory personnel involved in any task with a potential to nanomaterials must wear the following personal protective equipment:

- **Protective gloves:** Glove selection is best determined by a risk assessment and the chemicals used for the procedure. Nitrile or rubber gloves, which cover hands and wrists completely through overlapping sleeve of lab coat when working with nanomaterials, may provide adequate protection. Wearing of two sets of gloves ("double gloving") is advised whenever performing tasks involving nanomaterials and other hazardous substances. Laboratory personnel should thoroughly wash hands with soap and water before and immediately upon removal of gloves.

- **Eye protection**: Safety glasses or goggles are considered to be the appropriate level of eye protection for working with nanomaterials. SHERM recommends wearing a full-face shield when conducting tasks posing potential for any generation of aerosol and/or droplets.

- **Protective clothing:** Laboratory coats or disposable gowns that provide complete coverage of skin must be worn when working with nanomaterials. Clothing contaminated with nanomaterials should be removed immediately. Do not take contaminated work clothes home – contaminated clothing may require disposal as hazardous waste.

- **Respiratory protection:** If engineering controls are not adequate or are not available, and a potential aerosol exposure exists, respiratory protection is required. When working with nanomaterials, one of the following types of respirators must be worn:
  - Filtering face piece (N-95 or greater)
  - Elastomeric half- or full-face piece with N-100, R-100, or P-100 filters; or
  - Powered air-purifying respirator with N-100, R-100, or P-100 filters.

Anyone required to utilize respiratory protection for use with nanoparticle research must contact Chemical Safety at 713-500-5832 to be included in the UTHealth Respiratory Protection Plan.

XI. Nanoparticle Use in Animals

Unless data exists for the use of a specific nanoparticle in an animal, the following Exposure Control methods shall be followed.

Standard PPE for handling of dry nanoparticles when work is performed outside of chemical fume hood or ducted biological safety cabinets include: double gloves, gown, safety goggles or safety glasses, and N-95 or equivalent respirators (CDC/NIOSH, 2009). Work areas should be cleaned at the end of the procedure using either a HEPA-filtered vacuum cleaner or wet wiping methods, using a fresh cloth that is dampened with soapy water. Cleaning cloths must be disposed of. Drying and reuse of contaminated cloths may result in re-dispersion of particles.

Use of nanoparticles in animals can be broken down into three segments: administration, husbandry and disposal.

Administration:

- Injection: Nanoparticles in suspension may be injected in to animal on a bench top covered with absorbent paper. Absorbent paper should be changed after each experiment and disposed as nanoparticles waste. Dispose of the syringe in an approved Sharps container.
- Oral: if preparation is being administered via a syringe or other feeding device, a fume hood or ducted BSC (as above) must be used. If administration is by food, use of a microisolator cage is recommended.
- Aerosol: fume hood or ducted BSC. Proper PPE for investigators must include an N-95 or equivalent respirator.

Husbandry:

- Exposed animals must be housed under BSL-2 conditions for the first 72 hours post exposure. After 72 hrs, animals can be housed at BSL-1.
- All bedding and waste must be bagged and incinerated.

Disposal:

- All potentially contaminated carcasses, bedding and other materials must be disposed of through incineration.
- Any surplus nanoparticle stocks must be disposed of as hazardous waste.

As additional information is discovered concerning nanoparticles, the complexity of evaluating hazards associated with their use will probably follow a bell-curve, increasing before decreasing. Thus the information presented above must be considered subject to change.

XII. Spill Cleanup

Anyone attempting to manage any spill involving hazardous agents must be wearing the appropriate personal protective equipment. OSHA advises typically standard approaches to cleaning nanomaterial 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 or liquid traps. (CDC/NIOSH, 2009) Energetic cleaning methods such as dry sweeping or the use of compressed air should be avoided or only be used with precautions that assure that particles suspended by the cleaning action are trapped by HEPA filters. If vacuum cleaning is employed, care should be taken that HEPA filters are installed properly, and bags and filters changed according to manufacturer's recommendations. At a minimum, the following procedures must be followed when managing an accidental spill of nanomaterials (CDC/NIOSH, 2009):

- Small spills (typically involving less than 5 mg of material) of nanomaterials containing powder should be wet-wiped with cloth/gauze that is dampened with soapy water. Affected surfaces should be thoroughly wet-wiped three times over with appropriate cleaning agent and with a clean, damp cloth used for each wipe down. Following completion, all cloth and other spill clean-up materials with a potential for nanomaterial contamination must be disposed of as hazardous waste.
- Small spills (typically involving less 5 ml of material) of nanomaterial-containing solutions should be covered and absorbed with absorbent material. Areas affected by liquid spills should be triple cleaned with soap and water following removal of absorbent paper.

- For larger spills of nanomaterials, contact the Office of Environmental Health and Safety at 713-500-5832.

As with any spill or clean-up of contaminated surfaces, handling and disposal of the waste material should follow existing Federal, State, or local regulations.

XIII. Waste Disposal

Nanomaterials are potentially hazardous materials. Surplus stocks and other waste materials containing greater than trace contamination must be disposed of through the UTHealth Environmental Protection Program. Due to the fact that certain nanomaterials may be unaltered during metabolism, all potentially contaminated animal carcasses, bedding, and other materials must be disposed through incineration. In addition, all contaminated sharps waste materials must be placed in proper sharps container and disposed as biohazardous waste.

XIV. Instrumentation, Research, and Collaboration

UTHealth's Environmental Health and Safety Department maintains several instruments used to analyze nano- and ultrafine- particle size distribution, mass distribution, and concentration. Collaboration on research projects, evaluation of current projects, and design setup consultations for nanoparticle measurements are available through the Chemical Safety Division at 713-500-5832 (www.uth.edu/safety/chemical-safety/). The following is a list of available nanoparticle measuring equipment:

1) TSI Optical Particle Sizer 3330 – provides particle concentration up to 3,000 particles per cubic centimeter and mass concentration from 0.001 to 275,000 micrograms per cubic meter.

2) TSI NanoScan Scanning Mobility Particle Sizer 3910 – provides size distribution of nanoparticles from 10 to 420 nanometers in size and concentration up to 1,000,000 particles per cubic centimeter.

3) TSI PTrak Ultrafine Particle Counter – provides cumulative concentration of ultrafine particles in the range of 20 to 1000 nanometers.

4) TSI Aerotrak 9000 Nanoparticle Aerosol Monitor – provides particle size range from 10 to 1000 nanometers and aerosol concentration ranges for tracheobronchial deposition (1 to 2,500 square micrometers per cubic centimeter) and alveolar deposition (1 to 10,000 square micrometers per cubic centimeter).

XV. Glossary

Agglomerate – A group of particles held together by relatively weak forces, including van der Waals forces, electrostatic forces and surface tension.
Aggregate – A heterogeneous particle in which the various components are held together by relatively strong forces, and thus not easily broken apart.
Buckyballs - Spherical fullerenes composed entirely of carbon (C60).
Fullerenes - Molecules composed entirely of carbon, usually in the form of a hollow sphere, ellipsoid, or tube.
Graphene - A one-atom thick sheet of graphite.
Nanoscience – The study of phenomena and manipulation of materials at atomic, molecular and micromolecular scales, where properties differ significantly from those at a larger scale.
Nanoaerosol – A collection of nanomaterials suspended in a gas.

Nanocolloid – A nanomaterial suspended in a gel or other semi-solid substance.
Nanocomposite – A solid material composed of two or more nanomaterials having different physical characteristics.
Nanoparticle – A substance with dimensions less than 100 nanometers in size.
Nanohydrosol – A nanomaterial suspended in a solution.
Nanotechnology – The understanding and control of matter at dimensions of roughly 1 to 100 nanometers, where unique phenomena enable novel applications.
Nanotubes - A sheet of graphene rolled up into a seamless cylinder with diameter on the order of a nanometer.
Nanowires - A wire of dimensions on the order of a nanometer.
Nucleation - The first step in the process by which gases are converted to small liquid droplets.
Physiochemical – The underlying molecular organization of life that is manifested as chemical and energy transformations.
Pyrolysis - Chemical change brought about by the action of heat.
Quantum Dots – A nanomaterial that confines the motion of conduction band electrons, valence band holes, or excitons (pairs of conduction band electrons and valence band holes) in all three spatial directions.
Single-Walled Carbon Nanotube – A single sheet graphene wrapped into a tube approximately 1.5 nanometers in diameter.
Thermites – A mixture of aluminum powder and a metal oxide (as iron oxide) that when ignited evolves a great deal of heat and is used in welding and in incendiary bombs.
Translocation – The act, process, or an instance of changing location or position.
Transmission Electron Microscopy (TEM) – A microscopy technique whereby a beam of electrons is transmitted through an ultra-thin specimen, interacting with the specimen as it passes through, and produces an image formed from the interaction of the electrons transmitted through the specimen which is then magnified and focused onto an imaging device.
Ultra-Fine Particles - Airborne particles with an aerodynamic diameter of 0.1 m (100 nm) or less.

XVI. References

Aitken, R.J., Creely, K.S., Tran, C.L. *Nanoparticles: An Occupational Hygiene Review*. Research Report 274. Prepared by the Institute of Occupational Medicine for the Health and Safety Executive, North Riccarton, Edinburgh, England. 2004.

Approaches to Safe Nanotechnology. Department of Health and Human Services, Center for Disease Control, National Institute for Occupational Safety and Health. 2009.

Nanotechnology and Nanoparticles – Safe Working Practices Information. Virginia Commonwealth University. Office of Environmental Health and Safety. 2007

Occupational Safety and Health Act of 1970 (29 U.S.C. 654). Section 5(a) (1).