UAH NANOMATERIALS SAFETY MANUAL

Nanotechnology is the field of science dealing with material specifically engineered to sizes of 100 nanometers (ηm – 10^{-9} m) or less. Information presented in this document provides guidance to maintain health and safety while working with nanomaterials.

Reviewed and revised 2022

Table of Contents

Introduction

Nanotechnology is the field of science dealing with material specifically engineered to sizes of 100 nanometers (ηm – 10^{-9} m) or less. Nanotechnology is "the understanding and control of matter at the nanoscale, at dimensions between approximately 1 and 100 nanometers (nm)". A nanometer is one billionth of a meter, which is near-atomic scale. Engineered nanomaterials are assembled from nanoscale structures such as carbon nanotubes and filaments or from nanoparticles of materials such as titanium dioxide or cadmium selenide.

Classification of Nanomaterials

Nanomaterial (NM): nano-sized material having at least one external dimension in the size range of 1-100 nanometers. NMs include nanoparticles (NPs), nanostructured materials and ultrafine particles, and their agglomerates and aggregates.

Nanoparticle (NP): NM having all three external dimensions in the size range of 1-100 nanometers and its physicochemical properties are distinctly different than its bulk material of the same composition.

Nanostructured material: NM having distinct structural elements with dimensions in the size range of 1 to 100 nm. Nanostructured materials include nano-sized clusters, nano-crystallites or molecular composites.

Ultrafine particles: aerosolized NMs including incidental NPs derived from aerosols and their agglomerates are defined as ultrafine particles.

Agglomerates: group of NPs held together by weak interactions, such as Van der Waals forces, electrostatic forces and surface tension such that NPs are separated relatively easily with mild perturbation.

Aggregates: heterogeneous NPs in which various components are not easily separated as they are held together by relatively strong forces.

Different Type of Nanomaterials

Nanoparticles fall into three major groups: natural, incidental, and engineered.

Naturally Occurring

- Forest Fires
- Sea spray
- Mineral composites
- Volcanic ash
- Viruses

Human Origin (Incidental)

Incidental nanoparticles are often by-products produced as a result of industrial processes.

- Cooking smoke
- Diesel exhaust

- Welding fumes
- Industrial effluents
- Sandblasting

Engineered Nanomaterials (ENMs)

These are materials that have been specifically designed for function, such as fullerene C_{60}, which is used for fuel cell applications. Other types of ENMs include:

- Carbon Based Materials, such as carbon nanotubes
- Metal Based Materials, such as nanogold, nanosilver and metal oxides
- Dendrimers, which are nanosized polymers built from branched units
- Composites, which combine various nanoparticles together or with larger, bulk-type materials

This safety manual primarily addresses the safe use of Engineered Nanomaterials in the workplace.

OSHA-Identified Nanomaterial Standards

- 1904, Recording and reporting occupational injuries and illness
- 1910.132, Personal protective equipment, general requirement
- 1910.133, Eye and face protection
- 1910.134, Respiratory protection
- 1910.138, Hand protection
- 1910.141, Sanitation
- 1910.1200, Hazard communication
- 1910.1450, Occupational exposure to hazardous chemicals in laboratories
- Certain substance-specific standards (e.g., 1910.1027, Cadmium)

Potential Hazards

Information from research and animal studies on nanomaterials has identified some potential safety hazards and health effects. Because nanotechnology is a rapidly emerging field, more information will likely become available about potential health and safety hazards associated with some nanomaterials. The health hazard potential depends on the particular nanomaterial and a person's exposure level. Current research also indicates that the toxicity of engineered nanoparticles will depend on the physical and chemical properties of the particle. And, ENMs may have unique chemical and physical properties that differ substantially from those of the same material in bulk or in macro-scale form.

NIOSH (National Institute for Occupational Safety and Health) has determined the following potential exposure and health concerns:

- Nanomaterials have the greatest potential to enter the body through the respiratory system if they are airborne and in the form of respirable-sized particles (nanoparticles). They may also come into contact with the skin or be ingested.
- Based on results from human and animal studies, airborne nanoparticles can be inhaled and deposited in the respiratory tract; and based on animal studies, nanoparticles can enter the blood stream, and translocate to other organs.

- Experimental studies in rats have shown that equivalent mass doses of insoluble incidental nanoparticles are more potent than large particles of similar composition in causing pulmonary inflammation and lung tumors. Results from in vitro cell culture studies with similar materials are generally supportive of the biological responses observed in animals.
- Studies in workers exposed to aerosols of some manufactured or incidental microscopic (fine) and nanoscale (ultrafine) particles have reported adverse lung effects including lung function decrements and obstructive and fibrotic lung diseases. The implications of these studies to engineered nanoparticles, which may have different particle properties, are uncertain.

The consensus among public health organizations, domestic and international (such as NIOSH and the World Health Organization), is that the health effects associated with nanomaterials are not yet clearly understood. Therefore, it is important for staff to take precautions to reduce exposures and manage risks appropriately.

Routes of Occupational Exposure:

Inhalation

Inhalation has been a major focus of the nanotoxicology research community. Nanoparticle (NP) penetration into the lung depends on its aggregation state. Airborne NPs can be inhaled and deposited in the respiratory tract. Inhaled NPs may enter the blood stream and translocate to other organs. Certain nanomaterials can:

- Induce cancers, including mesothelioma
- Cause rapid and persistent pulmonary fibrosis
- Cause cardiovascular dysfunction
- Migrate along the olfactory nerve into the brain

Nanoparticles should be handled in solution or as part of a substrate whenever possible to minimize risk of inhalation. All work with nanoparticles should be handled within a containment device such as a fabricated bench-top enclosure, chemical fume hood or fully exhausted biosafety cabinet, such as a Class II, Type B2 or a Class II, Type A2 that is exhausted to the outside through a canopy thimble connection. Laboratory personnel should wear the appropriate respiratory protection (P-100 HEPA filtration) when working with nanoparticles outside of primary containment devices. Individuals wearing P-100 respiratory protection mustbe enrolled in the University Respiratory Protection Program.

Dermal

Available data are limited and often conflict. Skin cannot be ruled out as a potential route of exposure.

- Several studies show little to no penetration of nanoscale oxides beyond surface skin layers
- Polysaccharide and metal nanoparticles have been shown to penetrate flexed, damaged or diseased skin
- Quantum dots were found to penetrate intact pig skin within 8-24 hours at occupationally relevant doses

Various nanoparticles have been shown to
- Inhibit cell proliferation (iron oxide, nanotubes, TiO_2, silver)
- Affect cell morphology (silver, nanotubes)
- Initiate irritation response (quantum dots, nanotubes)
- Damage cell membrane (fullerenes)
- Induce DNA damage (cobalt chrome alloy)

Researchers are required to wear gloves (nitrile or other chemically impervious gloves) during all handling of nanoparticles and nanomaterials. Researchers are required to wear disposable Tyvek laboratory coats or cloth laboratory coats with disposable Tyvek or vinyl sleeves during all handling of nanoparticles and nanomaterials. Laboratory Attire Guidelines specified in the University Laboratory Safety Manual must also be followed. Consult OEHS for Guidelines.

Ingestion

Ingestion is a viable route of exposure because nanoparticles can translocate throughout the body via the digestive system.
- Ingestion may occur after inhalation exposure when mucus is brought up the respiratory tract and swallowed
- Poor work practice can result in hand-to-mouth transfer
- Ingested nanoparticles do translocate to other organ systems. Single walled carbon nanotubes (SWCNT) delivered into gut for treating Alzheimer's disease was found in liver, brain and heart. Ingestion of colloidal silver can result in permanent discolorationof skin, nails and eyes

Various nanoparticles have been shown to:
- Slightly damage liver (silver)
- Trigger immune response in intestinal dendritic cells (TiO_2 and SiO_2)
- Be cytotoxic to human intestinal cells (TiO_2, SiO_2 and ZnO)
- Damage DNA of human intestinal cells (ZnO)
- Be genotoxic to liver and lungs after oral administration (C_{60} and single-walled nanotubes (SWNT))

Eating, drinking, applying cosmetics, handling contact lenses is not permitted in the laboratory per University Guidelines. Laboratory personnel should remove PPE when work with nanoparticles is completed and wash their hands.

Injection

Nanoparticles can be introduced to the body via a needlestick. Standard precautions should be followed when utilizing sharps with nanoparticles or nanomaterials.

Current Occupational Exposure Limits for Nanomaterials

Few occupational exposure limits exist specifically for nanomaterials. Certain nanoparticles may be more hazardous than larger particles of the same substance. Therefore, existing occupational exposure limits for a substance may not provide adequate protection from nanoparticles of that substance. However, some specific exposure limits already exist. For example:

- OSHA recommends that worker exposure to respirable carbon nanotubes (CNT) and carbon nanofibers not exceed 1.0 micrograms per cubic meter (µg/m3) in an 8-hour time-weighted average, based on the National Institute for Occupational Safety and Health (NIOSH) proposed Recommended Exposure Limit (REL).
- OSHA recommends that worker exposure to nanoscale particles of TiO2 not exceed NIOSH's 0.3 milligrams per cubic meter (mg/m3) REL. By contrast, NIOSH's REL for fine-sized TiO2 (particle size greater than 100 nm) is 2.4 mg/m3.
- NIOSH's REL for carbon black is 3.5 mg/m^3, and OSHA's permissible exposure limit for respirable synthetic graphite is 5 mg/m^3.

Because exposure limits for other nanomaterials do not exist yet, UAH researchers and staff should minimize worker exposure by using the hazard control measures and best practices identified in this manual.

Assessing Worker Exposures to Nanomaterials

As necessary, the UAH OEHS will assess worker exposure to nanomaterials to identify the control measuresneeded and determine if the controls used are effective in minimizing and preferably eliminating exposures. This assessment will include:

- Identifying and describing processes and job tasks where workers may be exposed to nanomaterials;
- Determining the physical state of the nanomaterials such as dust, powder, spray, or droplets;
- Determining routes of exposure (e.g., inhalation, skin contact or ingestion) of particulates, slurries, suspensions or solutions of nanomaterials;
- Identifying the most appropriate method to evaluate exposures; and
- Determining what additional controls may be needed based on the exposure assessment results and evaluating the effectiveness of controls already in place. OEHS will adopt the most effective control measures available to protect staff.

Lab Safety Plan Requirements

Because the research and use of nanomaterials continues to expand and information aboutpotential health effects and exposure limits for these nanomaterials is still being developed, one of the main ways to ensure employee safety in the research environment is through the development of a Safety Plan. The Principal Investigator (PI) must create a Safety Plan that outlines safe work practices for research involving nanomaterials. After review and approval by OEHS, the Safety Plan will be communicated to all affected research personnel working on the project or within the same laboratory area. The control measures described below should be incorporated into the Safety Plan.

PIs and other staff are expected to use a combination of the following measures and best practices to control potential exposures:

Engineering Controls

- Work with nanomaterials in ventilated enclosures (e.g., glove box, laboratory hood, process chamber, biological safety cabinets, etc.) equipped with high-efficiency particulate air (HEPA) filters. If biological safety cabinets are being used, the preferred type is one that is fully exhausted through the facility exhaust system to the outside, such as the Class II, Type B2 cabinet. A Class II, Type A2 cabinet can be used if it is exhausted to the outside through a canopy thimble connection. Because air is recirculated *within* the Class II, Type A1, A2 and B1 cabinets, tasks involving volatile materials should be evaluated to determine if this type of cabinet is appropriate for the task.
- Where operations cannot be enclosed, use local exhaust ventilation (e.g., capture hood, enclosing hood) equipped with HEPA filters and designed to capture the contaminant at the point of generation or release.
- Ensure that the ventilated enclosure (e.g., laboratory hood, biological safety cabinet, or other local exhaust ventilation system) is evaluated periodically to verify that it is functioning properly.

Administrative Controls

- Provide handwashing facilities and information that encourages the use of good hygiene practices.
- Establish procedures to address cleanup of nanomaterial spills and decontamination of surfaces to minimize worker exposure. For example, prohibit dry sweeping or use of compressed air for cleanup of dusts containing nanomaterials, use wet wiping, sticky mats and vacuum cleaners equipped with HEPA filters.

Personal Protective Equipment (PPE)

- Provide workers with appropriate personal protective equipment such as respirators,gloves and protective clothing.

Medical Screening and Surveillance

- Medical screening and surveillance is available for workers exposed to nanomaterials if appropriate.
- Staff who use respirators for protection against nanoparticles will receive medical evaluations, training and fit testing as specified in the University's Respiratory Protection Program.
- Contact OEHS at 824-2171 for more information about the medical screening and surveillance program.

General Guidelines for Handling Nanoparticles in University Laboratories

In addition to the PI's Safety Plan which is communicated with their staff, the following general guidelines should be followed for all research involving nanomaterials.

1. PI is responsible for maintaining SDSs (Safety Data Sheets) for all nanomaterials to be available and kept upto date within the laboratory in which nanomaterials are stored and used.
2. All manipulations of nanoparticles should occur in a dedicated chemical fume hood (annual certification of fume hood is required), hard ducted biological safety cabinet, glove bag, glove box or enclosed HEPA filtered glove box. Horizontal laminar flow hoods (with air flow directed toward worker) are NOT permitted to be used withnanomaterials.
3. Work with nanoparticles outside of an exhausted enclosure require researchers to wear a NIOSH-approved P-100 particulate respirator (annual OEHS approved fit-test is required).
4. Nanoparticles should be handled while in solution or part of a substrate to minimize airborne release.
5. All containers (primary, secondary, and tertiary if applicable) should be labeled with the full name of the nanomaterials (avoid abbreviations and acronyms). "Nano" should be used in the chemical name.
6. Sealed, secondary containers should be utilized to transport nanomaterials between laboratories and buildings.
7. Every effort should be made to prevent the release of nanoparticles into the environment. OEHS recommends the use of a sticky mat at the exit of lab spaces where nanoparticles are handled.
8. For laboratory fume hood use, ensure that the sash is set at the certification mark for proper hood face velocity. Ensure that the sash is lowered and between the worker and the nanomaterial operations.
9. Avoid opening and closing the sash quickly and minimize rapid arm movements to reduce material leakage.
10. Follow other fume hood best practices such as placing materials and equipment as far back in the hood as possible, avoiding overcrowding in the hood and blocking the exhaust slots, and working with the nanomaterials at the center of the hood for best containment efficiency.
11. Clean work areas at the end of each work shift (at a minimum) using a HEPA-filtered vacuum cleaner or wet wiping methods. Dry sweeping or air hoses should not be used to clean work areas.
12. Do not store or consume food or beverages in workplaces where nanomaterials are handled.
13. Prevent the inadvertent contamination of non-work areas (including take-home contamination) by showering and changing into clean clothes at the end of each workday.

General Handling Requirements Based on Nanomaterial Risk Level (NRL)

The following table provides safe work recommendations based on the risks associated when working with different types and forms of nanomaterials. The risk levels range from 1 to 4 (with 4 being the highest risk level) and take into account the health hazard potential and the probability of occurrence. Working with dry powder nanomaterials represents the highest potential for risk of exposure and, therefore, would require the highest safety standards in regards to work practices, engineering controls, and personal protective equipment.

NRL	Type of nanomaterial	Practices	Engineering Controls	PPEs
1	Polymer matrix	Standard Laboratory Practicesincluding: 1.Lab Safety Plan should beupdated with NRL defined 2.Labeling of storage containersof nanomaterials with both thechemical contents and the nanostructure form	Fume hood **or** biological safety cabinet (Class II Type A1, A2 vented via a thimble connection, B1 or B2)	Standard PPE (lab coat, gloves, safety glasses with side shields)
2	Liquid dispersion	1. NRL-1 practice plus: 2. Use secondary containment for containers that store nano-materials 3. Wipe contaminated areas with wet disposable wipes 4. Dispose of contaminated cleaning materials as segregated nanomaterial waste	Fume hood **or** biological safety cabinet (Class II Type A1, A2 vented via a thimble connection, B1 or B2) **or** approved vented enclosure (e.g., Flow Sciences vented balance safety enclosure [VBSE])	NRL-1 practice plus: Nitrile gloves, safety goggles
3	Dry powders or aerosols	1. NRL-2 practice plus: 2. Vacuum with HEPA-equippedhand vacuum cleaner 3. Label work areas with "Caution Hazardous Nanoscale Materials inUse"	1. Fume hood **or** biological safety cabinet (Class II Type A1, A2 vented via a thimble connection, B1 or B2) **or** approved vented enclosure (e.g., Flow Sciences vented balance safety enclosure [VBSE]). 2. HEPA filtered exhaust preferred for fume hoods containing particularly"dusty" operations.	1. NRL-2 practice plus: 2. P100 respirators are requiredif work operation must be done outside of containment
4	Dry Powders or aerosols of parent materials with known toxicity or hazards	1. NRL-3 practice plus: 2. Baseline medical evaluation or employees including physical exam, pulmonary function test(PFT) and routine blood work. 3. Access to the facility should bepermitted only to persons who areknowledgeable about the hazards of the material and the specificcontrol measures implemented to avoid exposures and/or environmental releases. Thesecontrol measures should includework practices (SOPs),engineering controls, spill andemergency procedures, personal protective equipment, disposal procedures, and decontamination / clean up procedures. Departmentprocedures should address the designation and posting of the laboratory, how access will be controlled, and any required entryand exit protocols.	1. Fume hood **or** biological safety cabinet (Class II Type B1 or B2) **or** glove box **or** approved vented enclosure (e.g., Flow Sciences vented balance safety enclosure [VBSE]). HEPA filtered exhaust with Bag-In/Bag-Out capability preferred for hoods, BSCs, and glove boxes.	NRL-3 practice plus: Need determined and respirator selected with reference to the engineering controls in use and potential for aerosol generation

Design and Operational Considerations for Engineering Controls

During routine maintenance of the facility exhaust system, UAH Facilities staff may have exposures to nanoparticles and other health hazards. Specifically, these exposures may occur during the periodic filter change-outs. Where feasible, these systems should be equipped with Bag In/Bag Out filter change-out systems to reduce the risk of exposure to facilities staff.

General Guidelines for Disposal of Nanoparticles and Associated Hazard Waste Solutions

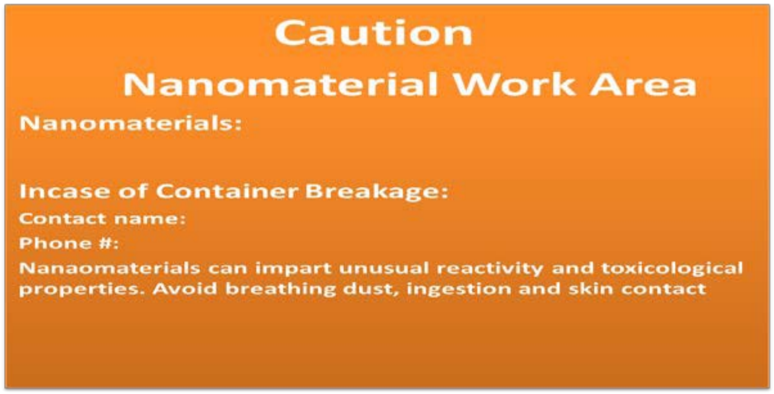
1. Since the toxicology and environmental fate of nanoparticles is still largely unknown, nanoparticle waste (solid material and liquids) should be managed through the University's Hazardous Waste program. Do not dispose of nanoparticle waste in regular trash or down the drain.
2. Waste container must be labeled at all times, no abbreviations on labels and must havethe start date of waste collection.
3. Collect nanoparticle waste in a sealable container that remains closed except when addingthe waste.
4. NM-containing wastes including NM dispersions must be disposed of through OEHS.
5. Sharps and needles should be disposed of as bio-hazardous waste in approved sharps containers.
6. Unused NM solids and NM dispersed solutions must be identified on the waste label.
7. If the nanoparticles are in solution, the solution should be managed accordingly (e.g., flammable solvents are handled as flammable waste materials).
8. Contact OEHS at 824- 2171 for further information about how to handle specific wastes.

General Guidelines for Nanomaterial Spill Clean-up

1. Secure area where spill occurred, restrict access to the area and notify others in the laboratory of the spill.
2. Dry nanomaterials should NOT be brushed or swept.
3. Spill cleanup should be done using a wet wipe method and/or HEPA-filtered vacuum.
4. Appropriate PPE (gloves, lab coat, and P-100 respirator) should be donned.
5. Spills of nanomaterials should be covered with a wet paper towel or bench paper.
6. Clean-up should begin from the outside of the spill and work inward.
7. All spill cleanup material should be collected in a leak proof plastic bag and should be disposed through OEHS.
8. Chemical Waste label should be placed on the plastic bag and "Nanomaterial SpillCleanup Material" should be written on the label (along with specific chemical name).
9. In the event of a large spill, the spill area should be secured and OEHS should be contacted (824-2171).

Work Area Designation

1. NMs work should be performed within a designated area as outlined in the PI Safety Plan.
2. Work area must have warning signage as shown below.



Container labeling

1. Primary containers should be labeled for laboratory-generated NMs. Primary container information should include “Nano Chemical Name”, solvent name (for dispersed solutions), concentration or quantity and contact person name.
2. At a minimum, reaction flasks and small storage vials, centrifuge tubes, etc., and secondary containers should include the material identity, researcher name, and date ofpreparation.

Transportation

1. Primary storage containers made of glass are preferred for the storage and transport ofNMs (glass reduces electrostatic charges that can cause dry materials to become easilyairborne when opening the container).
2. Sealed secondary containers should be used to transport NMs/solutions between labs.
3. The use of secondary containers made of shatter proof plastics is recommended to prevent the accidental breakage of primary glass containers during transport betweenlabs.
4. If nanomaterials are required to be shipped off of the University campus via an external shipment company (Ex. UPS or FedEx) then applicable DOT shipping regulations mustbe followed. OEHS should be contacted to assist in the shipment of nanomaterials.
5. If nanomaterials are transported to off campus locations via a personal vehicle, then applicable DOT packaging requirements must be followed.
6. The SDS should be included in packages for NM shipment to outside institutions.

Training

If UAH staff are working with nanomaterials or where they will be potentially exposed to nanomaterials, information and training will be provided so employees can take appropriate precautions to prevent exposures. This information and training will include at least the following:

- Identification of nanomaterials and processes in which they are currently being used;
- Results from any exposure assessments conducted at the work site;
- Identification of engineering and administrative controls and personal protective equipment (PPE) to reduce exposure to nanomaterials;
- The use and limitations of PPE; and
- Emergency measures to take in the event of a nanomaterial spill or release.

Contact OEHS at 824-2171 for further information about training opportunities

Additional Related Resources

1. Current Intelligence Bulletin 70: Health Effects of Occupational Exposure to Silver Nanomaterials | NIOSH | CDC, 2021
2. Controlling Health Hazards When Working with Nanomaterials: Questions to Ask Before You Start | NIOSH | CDC, 2018
3. Workplace Design Solutions: Protecting Workers during the Handling of Nanomaterials | NIOSH | CDC, 2018
4. RESPIRATORY-PROTECTION-FOR-NANOPARTICLES.pdf (navy.mil), 2013
5. OSHA_FS-3634.pdf – OSHA Fact Sheet – Working Safely with Nanomaterials, 2013
6. DHHS (NIOSH) Pub. No. 2012-147, General Safe Practices for Working with Engineered Nanomaterials in Research Laboratories (cdc.gov)
7. NIOSH - Approaches to Safe Nanotechnology
8. Strategic Plan for NIOSH Nanotechnology Research and Guidance
9. IRSST - Best Practices Guide to Synthetic Nanoparticle Risk Management
10. Home | National Nanotechnology Initiative