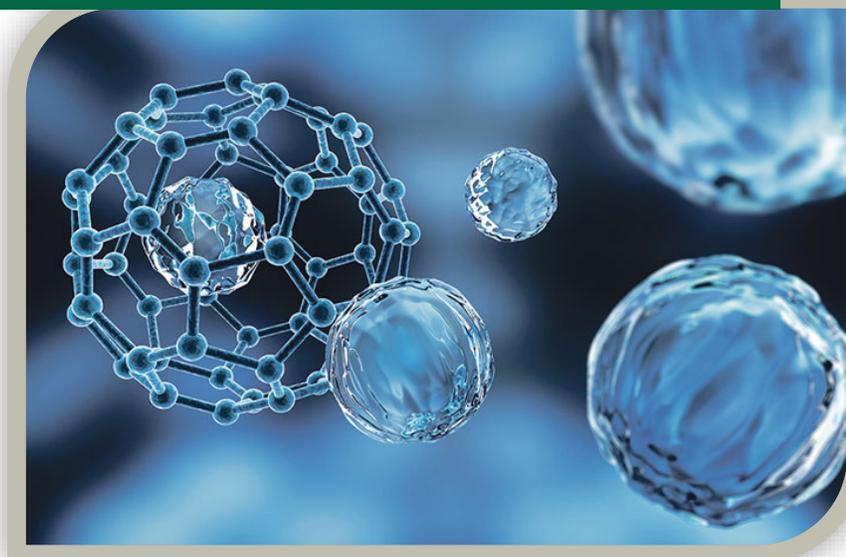


Nanomaterial Safety Guide



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Introduction

Any material measuring less than 100nm in any dimension is a nanomaterial. There are three broad categories of nanomaterials:

1. **Natural Nanomaterials** include proteins and biological molecules and may be produced by natural processes such as erosion or sea spray;
2. **Incidental Nanomaterials** are byproducts of combustion, manufacturing, and other human activities;
3. **Engineered Nanomaterials** are any materials intentionally produced with a size in 1, 2, or 3-dimensions of 1-100nm, including nanoparticles, nanotubes, fullerenes, dendrimers, and quantum dots.

Engineered nanomaterials (NMs) have emerged as a topic of interest in research laboratories across multiple disciplines, including medicine, materials engineering, environmental science, and computer science. However, the same properties that make NMs beneficial also present occupational hazards. For instance, some NMs are small enough to enter deep tissues of the lungs, cross the blood-brain barrier, or enter the bloodstream through skin contact. It is therefore essential to understand the hazards of NMs and implement appropriate safety protocols for their use.

Purpose

The purpose of the Nanomaterial Safety Guide is to provide a summary of the hazards and best practices for working with nanomaterials at the University of South Florida (USF).

Definitions

- **Nanometer (nm)** – One-billionth of a meter.
- **Nanoscale** – a size measurable in nanometers or microns.
- **Nanomaterial** – Any material measuring less than 100nm in any dimension.
- **NM** – Abbreviation for engineered nanomaterial.
- **Nanotechnology** – The manipulation of matter at the nanoscale to produce new structures, materials, and devices exhibiting different properties than their individual components at the macroscale.

Regulations

Due to the rapidly evolving nature of nanotechnology research and the wide variety of types and applications, no regulations germane to NMs apply to the university research environment. The following is a list of the current federal regulations applicable to NMs:

- Some NMs, like Carbon Nanotubes (CNTs), are subject to reporting under Section 5 of the Environmental Protection Agency's (EPA) Toxic Substances Control Act (TSCA) prior to commercial distribution.

- The US Food and Drug Administration (FDA) evaluates products containing NMs, including drug delivery devices, cosmetics, and food ingredients.
- Pesticides containing NMs are subject to the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA).
- NMs may be regulated under programs such as the Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA), Resource Conservation and Recovery Act (RCRA), Clean Water Act (CWA), or Clean Air Act on a site-specific basis depending on their use and byproducts.

The Occupational Safety and Health Administration (OSHA) currently has no regulations or occupational exposure limits (OELs) for NMs. However, existing OSHA regulations may be relevant, including the [Hazard Communication](#), [Respiratory Protection](#), or [Laboratory Standards](#). Several agencies, including the National Institute for Occupational Safety and Health (NIOSH), FDA, and the National Institute of Health (NIH), have produced [guidance documents](#) regarding the safe use of nanotechnology.

At USF, all labs utilizing NMs must follow the policies, procedures, and standards listed in the [Chemical Hygiene Plan](#). Contact USF Environmental Health & Safety (EH&S) with any specific questions.

It should be noted that the full extent of the adverse effects of many NMs are not yet known. As the field of nanotechnology rapidly evolves, so too will the understanding of the risks and appropriate management techniques. Researchers are strongly encouraged to remain aware of these developments.

Forms of Nanomaterials

In regards to safety, the various types of NMs may be discussed in three different forms. These forms, in order of increasing exposure hazard, are as follows:

1. Physically bound or encapsulated in solid materials
2. Liquid Suspension
3. Dry Powders

Dry NM powders possess the highest potential for aerosolization and therefore require the highest level of containment. Aerosolization not only poses a risk of inhalation, but may also lead to dust formation on tools, benches, and equipment, thereby presenting a further hazard of skin absorption or ingestion from later handling. Suspending these powders in liquid reduces the likelihood of aerosolization. Physically embedded NMs are least likely to produce aerosols, and therefore pose the lowest risk of exposure.

Health Hazards

The toxicological effects of NMs are not fully understood. It is known that the toxicity of NMs is dependent on the NM's physical and chemical properties, the route of exposure, and the duration and frequency of exposure.

Nanomaterial Properties

NMs exhibit properties different from the same materials in macroscale. For instance, gold is red in color at the nanoscale level. This means it can be hard to predict the effect an NM will have on the body. Studies in animals and tissue cultures have shown that NMs are more toxic than the same mass of larger particles. Studies have shown that the following properties of NMs have an effect on their toxicity:

Size

Size plays an important role in the cellular uptake and distribution of NMs throughout the body. Due to their small size, NMs have a greater surface area to volume ratio than larger molecules, granting them a greater degree of chemical interaction in comparison to larger structures. NMs can penetrate deeper tissues than larger particles, translocate between organs via the bloodstream or lymphatic system, and are more likely to accumulate in the lungs than larger particles. Studies have demonstrated size-dependent toxicity of NMs in the kidneys and liver. NMs also possess a low weight due to their size, meaning that they can remain suspended in the air for days or weeks.

Shape

Studies have shown that shape can affect an NM's distribution and clearance from the body. For example, long fibrous particles like nanotubes are difficult for the body to clear, and may instead accumulate in organs.

Surface Charge

NMs possessing a surface charge have shown a higher chance of accumulating in organs than uncharged NMs.

Surface Chemistry

Conjugation of polysaccharides has been shown to increase the accumulation of NMs in various organs, inducing toxicity. However, certain coating materials have shown the ability to reduce the toxicity of NMs, including polyethylene glycol (PEG).

Solubility

The solubility of NMs in the body has shown a significant effect on toxicity. It is believed that inorganic NMs like metal oxide nanoparticles dissolve upon exposure to release toxic ions. In

contrast, insoluble nanoparticles of ceria, titania, and zirconia demonstrated no measurable toxicity [in vitro](#).

Degradability

NMs that degrade or are metabolized quickly by the body experience brief interactions with cells. Therefore, degradable NMs have short exposure times and are generally less toxic. Other NMs stay in the body for a prolonged period of time. Little is known regarding the chronic effects of these persistent NMs, and they should therefore be handled with caution.

Exposure Routes

Though some exposures are intentional (i.e. injection of drug delivery devices, application of skin products, etc.), unintentional exposures to NMs can lead to serious adverse health effects. There are four routes by which NMs may enter the body; inhalation, ingestion, absorption, and injection.

Inhalation

Inhalation is the most common route of exposure to NMs. Inhalation of NMs causes inflammation, which may in turn cause asthma, fibrosis, cancer, or necrosis of lung tissues. This inflammation may also allow NMs to reach nearby lymph nodes, where they may accumulate or translocate to other organs. Other studies have shown that NMs may travel to the brain via the nasal passages upon inhalation.

Ingestion

Ingestion may occur in conjunction with inhalation or may occur as a result of hand-to-mouth transfer or contamination of food and drinks. Ensure no food or drinks are present in the laboratory and enforce handwashing to avoid ingestion of NMs. After ingestion, some NMs are absorbed by the digestive system and transported to lymphatic tissues. Others may accumulate in the digestive system, potentially leading to gastrointestinal blockages.

Skin Absorption

The permeability of the skin to many NMs is currently unknown. Dermal exposure to NMs may occur during manufacturing or via application of consumer products like cosmetics and sunscreens. Some NMs may penetrate the skin through sweat glands or hair follicles. Titanium dioxide nanoparticles, for instance, have been shown to cause cell death (apoptosis).

Skin absorption is a major route of exposure to incidental nanomaterials produced by welding, waste incineration, or NM manufacturing. If they penetrate the skin, incidental nanomaterials may cause DNA damage or apoptosis.

Injection

Injections of NMs may be accidental (i.e. needle stick) or intentional (e.g. drug delivery devices). If NMs reach the bloodstream, they may accumulate in various organs, including the liver, spleen, lungs, and kidneys.

Exposure Duration/Frequency

While some NMs may produce an immediate (acute) toxic effect after limited exposure, other toxic effects only present after prolonged or repeated exposure. Acute systemic exposure to NMs may cause oxidative stress, inflammation, and DNA damage. NMs present a unique challenge as some are designed to degrade slowly in the body, and the products of degradation or dissolution may be toxic. However, the full extent of the chronic effects of NMs is currently unknown. Animal studies have demonstrated that chronic exposure to some nanoparticles may cause cancer, developmental toxicity, or DNA damage. Therefore, caution must be taken to prevent repeated exposures to NMs.

Physical Hazards

Nanoscale combustible materials may present a higher risk of flash fires than the same materials at a larger scale. For example, in one [study](#), nanoscale Al/MoO₃ thermites ignited 300 times faster than a larger form of the same material. Aerosolization of finely granulated particles pose a fire risk. However, some NMs are specifically designed to generate heat through a series of nanoscale reactions, presenting a unique hazard. In addition, reducing the size of a material can increase its combustion potential and combustion rate, meaning that materials that are inert in their bulk form may become highly reactive at the nanoscale. Some metals, for instance, show increased explosion risk with decreased particle size. Other NMs have been used as catalysts to increase the rate of reaction or decrease the required temperature for reactions to occur in liquids or gases. It is therefore imperative to implement appropriate fire safety measures when working with NMs.

Hazard Minimization

Though the risk of working with nanomaterials cannot be completely eliminated, there are best practices that can be followed to reduce this risk. In addition to adhering to general laboratory safety guidelines (See [USF Chemical Hygiene Plan](#) Section 6.6), considering the control strategies shown below during experimental design will help protect laboratory workers from the hazards of NMs.

Elimination/Substitution

The most effective strategy for hazard control is to eliminate the hazard. However, this is often not feasible in the laboratory setting. A process may instead be modified to substitute a hazardous step or material. For example, modifying a procedure to allow for the use of a liquid suspension of a NM instead of a dry powder will greatly reduce the risk of aerosolization.

Substituting a solvent used in NM production for a less hazardous alternative may be another option.

Engineering Controls

If a hazardous process or material cannot be eliminated or substituted, then engineering controls should be used to protect laboratory workers. Engineering controls refer to any physical changes or barriers implemented to reduce employee exposure. Chemical fume hoods, glove boxes, biosafety cabinets, and specialized NM handling enclosures are a few examples of engineering control methods. Contact EH&S for assistance implementing engineering controls before starting work with NMs.

Administrative Controls

In addition to engineering controls, administrative controls should be introduced to protect laboratory workers. Below are administrative controls to consider while working with NMs.

Employee Training

All laboratory workers at USF are required to complete [EH&S training](#) as well as lab-specific training by a supervisor. Lab-specific training should include proper handling procedures for the specific equipment, chemicals, and methods to be used by the laboratory worker, including NMs. Safety data sheets (SDS) are a valuable resource for hazard information. In the case of NMs, however, the SDS may contain general information regarding bulk materials. If the hazards of a specific NM are unknown, it must be regarded as hazardous.

Standard operating procedures (SOPs) must be developed stating the hazards of a material or process as well as safety protocols regarding its use (see the [USF Chemical Hygiene Plan](#) Appendix A). The considerations below should be included in SOPs and lab-specific training.

Labeling, Storage, and Signage

All chemical containers in the laboratory must be labeled. Any flammable, corrosive, or toxic NMs or NM-containing mixtures should be stored in the appropriate cabinet. Liquids and dry powders containing NMs should be stored in sealed containers and secondary containment should be used when appropriate. Signage indicating the hazard, PPE requirements, and other pertinent information may be posted in the area to increase awareness.

Scheduling

The amount of exposure experienced by a worker may be limited by reducing the time one employee is handling the NM. This may be accomplished by rotating tasks or personnel.

Housekeeping

Eating, drinking, and smoking are prohibited in USF laboratories. Handwashing stations must be available and should be used after working with NMs or other laboratory materials. All surfaces

and/or equipment potentially contaminated with NMs should be cleaned at the end of each day by wet wiping; do not sweep or use compressed air to clean these surfaces.

Personal Protective Equipment

If the above controls are infeasible or insufficient, personal protective equipment (PPE) must be used. Lab coats, safety glasses/goggles, disposable gloves, shoe covers, and respirators are all examples of PPE. Please see the [PPE Hazard Assessment Guide](#) for further guidance. Please note, that all respirator users must participate in the [USF Respiratory Protection Program](#), including the completion of an EH&S assessment, training, medical evaluation, and fit testing.

Waste Management

At USF, like all chemical waste, all waste containing NMs should be considered hazardous waste and must be disposed through EH&S. See the [USF Hazardous Waste Management Procedure](#) for details. All generators of hazardous waste must complete annual [Hazardous Waste Awareness and Handling training](#).

Emergency Response

Should an accident occur, follow the procedures outlined in Appendix D of the [USF Chemical Hygiene Plan](#) as well as the [USF Reporting Procedures](#). All incidents must be reported to a supervisor. If there is an emergency, call 9-1-1.

Spills

All laboratories must be equipped with an appropriately stocked [spill kit](#). Use your spill kit to clean small spills and contact EH&S for pickup and disposal. If the spill is large, contains highly toxic chemicals, or enters a drain or body of water, contact EH&S.

Exposures

In case of an exposure, consult applicable SDS's and SOPs for first aid information. Beware that some SDS contain general information regarding bulk materials. If the hazards of a specific NM are unknown, it must be regarded as hazardous. Report instances of exposure to EH&S after medical attention has been received.

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