Best practices, Standards, and Guidelines to using engineered nanomaterials.

Nanotoolkit

Working Safely with Engineered Nanomaterials in Academic Research Settings

California Nanosafety Consortium of Higher Education 04/19/2012

Acknowledgement

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Background on California Nanosafety Consortium of Higher Education and Development of the Nanotoolkit

Background

The increasing use of nanomaterials in research and development laboratories along with applications in industry are providing breakthroughs for many technologies and solutions for addressing major problems in our society. However, as with all new technologies, the potential health effects of engineered nanomaterials (ENMs) remain uncertain. The aim of this project is to provide practical guidance as to how ENMs should be handled safely in the research laboratory setting in the face of such uncertainty over possible toxic effects.

Currently many government agencies, academic institutions, and industries have issued detailed guidance documents as to how NMs should be monitored, controlled, and handled in different work settings. Only a portion of these practices have been validated by scientific research or reference to peer reviewed literature. Most guidance documents and exposure studies to date have focused primarily on industrial settings, but academic research settings present their own challenges that also need to be addressed. Much of the initial research and development (R&D) in nanotechnology is still performed in academic research laboratories. In academic laboratories, the quantity of materials used tends to be less than those used in industry, but the variety of nanomaterials used tends to be more diverse. As a result, the potential hazards are also more diverse and exposure monitoring is more challenging. Furthermore, academic practices tend to be less standardized and to vary more from lab to lab and from day to day than typical industrial processes. This means that engineering controls which are commonly used in industry may not be practical to apply in academic laboratory research settings.

The nature of research and training in academic institutions dictates that new students and employees with various backgrounds and levels of training are regularly being introduced into the many diverse laboratory settings. Undergraduate student researchers, graduate students and other laboratory personnel often have minimal formal safety training or are lacking the latest hazard information about such new technological developments. All of these factors make a simple adoption or application of standardized industrial best practices for working with NMs in laboratories difficult.

Goals

The goal of this project is to provide an easy to use tool kit for academic researchers to quickly identify safe handling practices based on whether the work they propose is in a low, moderate, or high potential exposure category. The exposure categories and controls were determined from a review and analysis of many related nanomaterial health and safety guidance documents.

Methods

The analysis of the proposed recommendations included summarizing all the relevant recommendations from the various guidance documents into one matrix, conducting a literature search to see if the recommended practices were appropriately validated, and having a group of experienced environmental health and safety professionals from various California universities use their professional judgment and the research literature provided to rank the applicability of each recommendation as well as rate each recommendation in terms of the need for further research.

The working group summarized <u>documents</u> from 19 academic institutions, 14 government agencies and four industrial sources. This project was a collaborative effort by the California Nanosafety Consortium of Higher Education. The group included representatives from:

Government Agencies

National Institute of Occupational Safety and Health (NIOSH) Department of Toxic Substances Control (DTSC)

University Environmental Health and Safety Professionals (EH&S)

University of California Los Angeles (UCLA) University of California Irvine (UCI) University of California Riverside (UCR) University of California (UC) Office of the President University of Southern California (USC) Stanford University California Institute of Technology Claremont University Consortium

In addition, the project involved professor(s) and graduate students from the University of California Los Angeles (UCLA) and University of California Santa Barbara (UCSB).

Through this process we identified existing safety concerns of health and safety professionals and uncovered shortcomings in the current guidance documents, while recommending guidance that is most appropriate and validated by peer reviewed research for application to the research laboratory setting. A practical and easy to use tool kit was developed to help academic researchers to quickly identify proposed laboratory research work with nanomaterials as a low, medium, or high-risk activity and then identify appropriate control measures. Also included are sections with general information about engineered nanomaterials, spill cleanup and waste management.

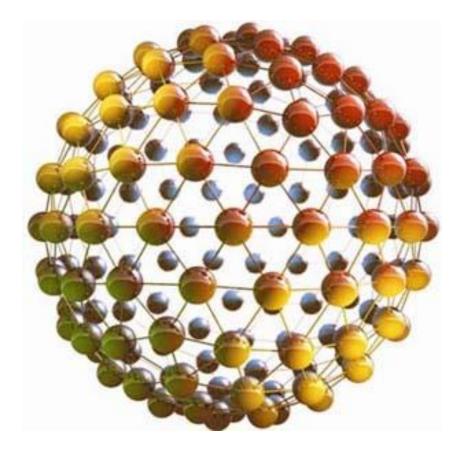
The user of this tool kit is advised that this document provides a best practice guideline to approaching and understanding how to work safely with engineered nanomaterials in the laboratory. Ultimately, it is the responsibility of the faculty member, the principal investigator, or the laboratory supervisor who is directing such work in the laboratory to provide for the safe conduct of all individuals conducting research in their laboratories. If applied diligently and appropriately, these guidelines will help provide for the safety and health of laboratory personnel conducting research using engineered nanomaterials.

What is the Nanotoolkit?

The Nanotoolkit is an easy to use guide for academic researchers to quickly identify safe handling practices when working with Engineered Nanomaterials (ENMs) based on a low, moderate, or high potential exposure category as described in this document.

How to Use:

- 1. Read the *Overview of Nanomaterials* section to obtain general information on ENMs.
- 2. Review the *Planning Your Research* and *Conducting Your Research* sections to obtain information on how to plan and conduct your experiment/operation involving ENMs.
- 3. Use the *Quick Guide: Risk Levels and Control Measures for Nanomaterials* to prepare a Standard Operating Procedure (SOP) for your experiment/operation employing the template provided.



Definitions

Nanomaterial: Material or particle with any external dimension in the nanoscale (range 1 nm to 100 nm) or having internal structure or surface structure in the nanoscale (Source: ISO/TS 80004-1:2010, ISO/TS 27687:2008)^{1,2}

Naturally Occurring Nanomaterial: Particles on the nanoscale occur naturally in the environment. They can also be manufactured and have a variety of commercial applications. More information on naturally occurring nanomaterials can be found in Appendix C.

Engineered Nanomaterials (ENMs): An Engineered Nanomaterial is any intentionally produced material with any external dimension in the nanoscale. It is noted that neither 1 nm nor 100 nm is a "bright line" and some materials are considered engineered nanomaterials that fall outside this range. For example, Buckyballs are also included even though they have a size <1 nm. Excluded are materials that are on the nanoscale, but do not have properties that differ from their bulk counterpart and micelles and single polymers.³

Types of Nanomaterials

	Туре	Examples
h	Carbon Based	Buckyballs or Fullerenes, Carbon Nanotubes*, Dendrimers Often includes functional groups like* PEG (polyethylene glycol), Pyrrolidine, N, N- dimethylethylenediamine, imidazole
Рина Э.	Metals and Metal Oxides	Titanium Dioxide (Titania)**, Zinc Oxide, Cerium Oxide (Ceria), Aluminum oxide, Iron Oxide, Silver, Gold, and Zero Valent Iron (ZVI) nanoparticles
<u>21 m</u>	Quantum Dots	ZnSe, ZnS, ZnTe, CdS, CdTe, CdSe, GaAs, AlGaAs, PbSe, PbS, InP Includes crystalline nanoparticle that exhibits size-dependent properties due to quantum confinement effects on the electronic states (ISO/TS 27687:2008).

* Carbon Nanotubes are subject to a proposed Recommended Exposure Limit¹⁰ of TWA 7 µg/m³ due to the risk of developing respiratory health effects.

**Nano-Titanium Dioxide is subject to a proposed Permissible Exposure Limit¹¹ of TWA 0.3 mg/m³ due to the risk of developing lung cancer. There are mixed studies regarding TiO2 skin penetration. Some studies indicate TiO2 and ZnO does not pass through the stratum corneum^{6,7}, while others indicate significant penetration through the skin⁸.

OCCUPATIONAL HEALTH AND SAFETY CONCERNS

1. ROUTES OF EXPOSURE

Exposure to engineered nanomaterials may occur via inhalation and dermal contact depending on use and handling; ingestion is unlikely but possible.

2. LACK OF INFORMATION ON FULL HEALTH EFFECTS

With a lack of chronic exposure data and reproductive and developmental toxicity data, a precautionary approach when working with engineered nanomaterials is warranted.

3. **Toxicity**

Some potential toxic outcomes can be predicted from what we know about ultrafine particles⁴ and based on known chemical and structural properties⁵. Nanomaterials have the potential to:

- 1. Deposit in the respiratory tract. Small airborne particles penetrate deep into the lungs.
- 2. Cross cell membranes. Some nanomaterials have the ability to cross cell membranes.
- 3. *Penetrate healthy intact skin/translocation to other organ systems*. Reports on this topic are mixed; caution is urged until more is known.

4. OTHER

- a. **Catalytic effects**. In general, nanomaterials are not known to have catalytic effects, however, some nanomaterials are specifically engineered to have catalytic properties.
- b. Fire or explosion. Nanomaterials are generally not explosive or flammable in small is inherently reactive, however some of the synthesis methods may use techniques where fire and explosion are potential hazards.



Exposure Limits



Nanomaterials fall under OSHA General Industry Standards⁹. Established exposure limits for naturally occurring nanomaterials, and detailed information about current state and federal regulations can be found in Appendix C. Although there are currently no established (legal) exposure limits (US or International) for Engineered Nanomaterials, NIOSH has developed Recommended Exposure Limits (RELs) for carbon nanotubes (TWA 7 μ g/m³) and nano-titanium dioxide (TWA 0.3 mg/m³).

Planning your research

1. Gather Information

Select less-hazardous forms. Whenever possible, select engineered nanomaterials bound in a substrate or matrix or in water-based liquid suspensions or gels.

Review Material Safety Data Sheet (MSDS), if available.

NOTE: Information contained in some MSDSs may not be fully accurate and/or may be more relevant to the properties of the bulk material rather than the nano-size particles. The toxicity of the nanomaterials may be greater than the parent compound.

Review your institution's Chemical Hygiene Plan for general laboratory safety guidance.

2. Determine Potential Risks

Common laboratory operations involving ENMs may be categorized as posing a low, moderate, or high potential exposure risk to researchers depending on the state of the material and the conditions of use. Refer to the *Quick Guide: Risk Levels and Control Measures for Nanomaterials.* Follow the instructions in this matrix to identify the potential risk of exposure and recommended control measures. Special consideration should be given to the high reactivity of some nanopowders with regard to potential fire and explosion, particularly if scaling up the process. Consider the hazards of the precursor materials in evaluating the process.

3. Develop a Standard Operating Procedure (SOP)

A standard operating procedure (SOP) is a set of written instructions that describes in detail how to perform a laboratory process or experiment safely and effectively. Employing the hierarchy of controls described in *Quick Guide: Risk Levels and Control Measures for Nanomaterials*, establish an SOP for operations involving nanomaterials. For an example, refer to Appendix B.

4. Obtain Training

and Consultation / Approval

Training. Principal Investigators or laboratory supervisors must ensure that researchers have both general laboratory safety training pursuant to Cal/OSHA's Occupational Exposure to Hazardous Chemicals in Laboratories (8 CCR 5191) and labspecific training relevant to the nanomaterials and associated hazardous chemicals used in the process/experiment. Laboratory-specific training can include a review of this Nanotoolkit, the relevant Material Safety Data Sheets (if available), and the lab's Standard Operating Procedure (SOP) for the experiment.

Consultation / Approval. Consult with and seek prior approval of the Principal Investigator or laboratory supervisor prior to procuring or working with nanomaterials, and/or if working alone in the laboratory is anticipated. [Follow institution's rules on working alone.]

Notification. If dosing animals with the nanomaterial, follow institution's hazard communication processes for advanced notification of animal facility and cage labeling/management requirements.

Conducting your research

Controlling potential exposures to nanomaterials involves elimination of highly hazardous materials through substitution, engineering controls, administrative or work practices, and personal protective equipment. The hierarchy of controls are shown in Figure 1. If the nanomaterial cannot be substituted with a less hazardous substance, then engineering controls must be installed to control exposure.

1. Minimize Exposures

Engineering Controls

CONTROL EXPOSURE WITH EQUIPMENT

Minimize airborne release of ENMs by utilizing one of the following devices:

Work in a laboratory fume hood or

biosafety cabinet. Conduct work inside a fume hood or low flow enclosures to prevent exposure. Biosafety cabinets must be ducted if used in conjunction with volatile compounds.

Use a glove box or fully-enclosed system. Where it is not possible to prevent airborne release, such as in grinding operations or in gas phase, use equipment that fully encloses the process. This includes a glove box.

Use local capture exhaust hoods. Do not exhaust aerosols containing engineered nanoparticles into the interior of buildings. Use High-Efficiency Particulate Air (HEPA) filtered local exhaust ventilation (LEV). HEPA-filtered LEV should be located as close to the possible source of nanoparticles as possible, and the installation must be properly engineered to maintain adequate ventilation capture. Use HEPA-filtered local capture exhaust hoods to capture any nanoparticles from tube furnaces, or chemical reaction vessels or during filter replacements.

ENSURE PERFORMANCE AND MAINTENANCE

Laboratory equipment and exhaust systems used with nanoscale materials should be wet wiped and HEPA vacuumed prior to repair, disposal, or reuse. Make sure fume hoods and any LEV achieves and maintains adequate control of exposure at all times. These systems require regular maintenance and periodic monitoring to ensure controls are working and thorough examination and testing at least once a year.

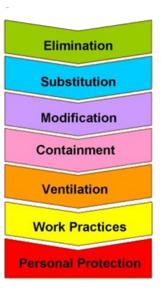


Figure 1 Hierarchy of Controls

Administrative Controls

USE SOLUTIONS OR SUBSTRATES

To minimize airborne release of engineered nanomaterials to the environment, nanomaterials are to be handled in solutions, or attached to substrates so that dry material is not released.

LOCATE SAFETY EQUIPMENT

Know the location and proper use of emergency equipment, such as emergency eyewash/safety showers, fire extinguishers, fire alarms, and spill clean-up kits¹².

USE SIGNS AND LABELS

Restrict access and post signs in area indicating ENM work. When leaving operations unattended, use cautious judgment: 1) Post signs to communicate appropriate warnings and precautions, 2) Anticipate potential equipment and facility failures, and 3) Provide appropriate

containment for accidental release of hazardous chemicals.

CLEAN AND MAINTAIN

Line work area with absorbent pad. When working with powders, use antistatic paper and floor sticky mats. Wet wipe and/or HEPA-vacuum work surfaces potentially contaminated with nanoparticles (*e.g.*, benches, glassware, apparatus) at the end of each operation. Consult with your institution regarding the maintenance of HEPA vacuums and replacement of HEPA filters.

MAINTAIN PERSONAL HYGIENE

To avoid potential nanoparticle or chemical exposure via ingestion in area where ENMs are used or stored, do not: consume or store food and beverages, apply cosmetics, or use mouth suction for pipetting or siphoning. Remove gloves when leaving the laboratory in order to prevent contamination of doorknobs or other common use objects such as phones, multiuser computers, etc. Wash hands frequently to minimize potential chemical or nanoparticle exposure through ingestion and dermal contact.

STORE AND LABEL PROPERLY

Store nanomaterials in a well-sealed container. Label all chemical containers with the identity of the contents (do not use abbreviations/ acronyms); include term "nano" in descriptor (*e.g.*, "nano-zinc oxide particles" rather than just "zinc oxide." Include hazard warning and chemical concentration information, if known.

TRANSPORT IN SECONDARY CONTAINMENT

Use sealed container with secondary containment when transporting nanomaterials between laboratories or buildings.

Table 1. Glove Choices for Nanomaterials

Select glove based on compatibility with material and solvents to be used and, if possible, permeability studies for that category of ENM. Recommend wearing gauntlet-type/wrist-length gloves with extended sleeves. The table below contains information on select ENMs and the associated reference.

Nanomaterial / State	Glove Type		
	(Recommendation)		
Carbon Nanotubes (CNTs)	Nitrile over Latex ^{*, **}		
TiO ₂ and PT	Latex**, Nitrile, Neoprene***		
Graphite	Latex**, Nitrile, Neoprene, Vinyl***		
* Consider potential latex allergies in DRE selection			

The use of PPE is

considered to be the

least desirable option to

control employee

exposure.

Consider potential latex allergies in PPE selection.

Reference: Methner, et. al (NIOSH) * Reference: Golanski, et. al (2010)

Personal Protective Equipment (PPE)

KNOW THE APPLICATIONS AND LIMITS

The use of PPE is generally considered to be the least desirable option to control employee exposure to occupational safety and health hazards. However, in an academic laboratory, there are often scenarios under which PPE can minimize potential employee exposure to occupational safety and health hazards either as a stand-alone control mechanism, or, as a supplement to either administrative or engineering control approaches.

Many occupational safety and health issues associated with ENM's are not fully understood (*i.e.*, ENM toxicity, exposure metrics, fate and transport, etc.). The same

uncertainty exists with how to select the myriad of available types of PPE and effectively use them to minimize the potential hazards associated with employee exposure to ENM hazards.

There is a growing body of evidence resulting from on-going research which indicates that commonly available PPE does have efficacy against specific sizes and types of ENMs. The PPE described

within the Nanotool Ouick Guide was selected as a result of a comprehensive review of available guidance and published research available at the time the Guide was developed.

USE THE QUICK GUIDE

The user of this Nanotool is directed to the Ouick Guide for a description of the recommended PPE. Note that the referenced PPE increases for each Category consistent with the increasing exposure potential. The basic PPE ensemble described under **Category 1** is to be augmented by the specific PPE in Category 2 and **Category 3.** The user is reminded of the following important issues associated with the safe and effective use of PPE:

- Protection. Respiratory Mandatory use of respirators will require full adherence to the requirements of your institution's respiratory protection program. It is imperative that you consult with your institution's EH&S representative prior to utilizing respiratory protection, even if that use is voluntary.
- *Gloves and Clothing.* Glove material, fabrication process and thickness are significant issues which impact the permeation of ENM's. Consequently, consideration should be given to utilizing two layers of gloves. For more information, refer to Table 1.

The selection of dermal PPE for protection against ENM's must also take into account other chemicals

which may be part of the ENM matrix or use conditions (i.e., solvents, surfactants, carrier gases, etc.). Dermal PPE manufacturers provide permeation/penetration tables which allow the end user to select dermal PPE based upon performance criteria to specific For examples, chemical threats. **Controlled** refer to the Environments guide by Du Pont®, or the Chemical Resistance Guide by Ansell © 2003. The technique used to remove gloves (and all

PPE) is very important so that any material contaminating the outer surfaces of the PPE does not impact the wearer. Consult with your EH&S representative to learn the appropriate technique(s) to remove chemical protective clothing.

REDUCE PPE HAZARDS

Under specific use conditions, utilizing PPE may put the user at risk of occupational injury. PPE may impair vision and dexterity and increase the likelihood of trip, slip, or fall hazards in addition to increasing the potential to develop heat-related illnesses. Consult with your EH&S professional for questions pertaining to the appropriate selection and use conditions for PPE.

2. Respond to Exposures and Spills

Actions to be taken in the event of a personnel exposure or a spill exposure are listed as part of the Appendix A "Standard Operating Procedure (SOP)" template.

3. Dispose Properly

Manage waste streams containing ENMs according to the hazardous waste program requirements at your institution. Until more information is available, assume ENM containing wastes to be hazardous waste unless they are known to be non-hazardous (for more information, refer to the *Defining Hazardous Waste* guidance published by the Department of Toxic Substances Control). Recommended management methods for typical research waste streams containing nanomaterials are described in Table 2.

Table 2. Recommended Nanomaterial wastemanagement methods by stream.

Waste Stream	Management Method
Solid • Dry ENM product • Filter media containing ENMs • Debris / dust from ENMs bound in matrix	 Follow General Nanomaterial Waste Management Practices Collect waste in rigid container with tight fitting lid.
Liquid • Suspensions containing ENMs	 Follow General Nanomaterial Waste Management Practices. Indicate both the chemical constituents of the solution and their hazard characteristics, and the identity and approximate percentage of ENMs on container labels. Use leak proof containers that are compatible with all contents. Place liquid waste containers in secondary containment and segregate from incompatible chemicals during storage.
Laboratory trash	1. Follow General Nanomaterial Waste Management Practices.
with trace nanomaterials • PPE • Tacki mats • Spill clean-up materials	 Dispose of in double clear plastic bags, folded over and taped at the neck. Avoid rupturing the bags during storage and transport.
Solid Matrix embedded with nanomaterials (intact and in good condition)	 Consult with your EH&S department, as these materials may be non-hazardous.

General Nanomaterial Waste Management Practices

1. Manage according to

hazardous waste program

requirements at your institution.

2. Label nanomaterial waste

containers at all times. Specify the nanomaterial and its hazard characteristic (or the hazard characteristic of the parent material) on container labels; label information to contain the word "nano" as a descriptor.

- 3. Keep containers closed at all times when not in use.
- Maintain containers in good condition and free of exterior contamination.

Quick Guide

Risk Levels and Control Measures for Nanomaterials

Purpose

This Quick Guide categorizes common laboratory operations involving engineered nanomaterials according to their potential risk of exposure to personnel, which is based on the state of the material and the conditions of use. Controls are provided in the table to minimize exposures. This guide is intended to be used in conjunction with the academic institutions' laboratory safety practices or other established guidelines (e.g., <u>Prudent Practices</u> by The National Research Council).

Instructions

Follow these steps to create a Standard Operating Procedure:

Step 1. Determine your risk levelStep 2. Identify the controls neededStep 3. Develop a Standard Operating Procedure

Below are tables to assist you in completing each step. If your research falls in between two risk categories, consider employing the higher level control.

Risk Level	Material State or Type of Use	Examples	
Category 1 Lower Exposure Potential	Material State or Type of Use Material State No potential for airborne release (when handling) • Solid: Bound in a substrate or matrix • Liquid: Water-based liquid suspensions or gels • Gas: No potential for release into air (when handling) Type of Use • No thermal or mechanical stress	 Non- destructive handling of solid engineered nanoparticle composites or nanoparticles permanently bonded to a substrate 	
Category 2 Moderate Exposure Potential	Material State Moderate potential for airborne release (when handling) • Solid: Powders or Pellets • Liquid: Solvent-based liquid suspensions or gels • Air: Potential for release into air (when handling) Type of Use • Thermal or mechanical stress induced	 Pouring, heating ,or mixing liquid suspensions (<i>e.g.</i>, stirring or pipetting), or operations with high degree of agitation involved (<i>e.g.</i>, sonication) Weighing or transferring powders or pellets Changing bedding out of laboratory animal cages 	
Category 3 Higher Exposure Potential	 Material State High potential for airborne release (when handling) Solid: Powders or Pellets with extreme potential for release into air Gas: Suspended in gas 	 Generating or manipulating nanomaterials in gas phase or in aerosol form Furnace operations Cleaning reactors Changing filter elements Cleaning dust collection systems used to capture nanomaterials High speed abrading / grinding nanocomposite materials 	

Step 1. Determine your risk level

Step 2. Identify the controls needed

Use the table below to identify the controls needed to work with the risk level of your nanomaterial (Category 1, 2, or 3).

Risk level	el Controls		
	Engineering	 Fume Hood or Biosafety Cabinet. Perform work with open containers of nanomaterials in liquid suspension or gels in a laboratory-type fume hood or biosafety cabinet, as practical. 	
Category 1 Low Exposure Potential	Work Practices	 Storage and labeling. Store in sealed container and secondary containment with other compatible chemicals. Label chemical container with identity of content (include the term "nano" in descriptor). Preparation. Line workspace with absorbent materials. Transfer in secondary containment. Transfer between laboratories or buildings in sealed containers with secondary containment. Housekeeping. Clean all surfaces potentially contaminated with nanoparticles (i.e., benches, glassware, apparatus) at the end of each operation using a HEPA vacuum and/or wet wiping methods. DO NOT dry sweep or use compressed air. Hygiene. Wash hands frequently. Upon leaving the work area, remove any PPE and wash hands, forearms, face, and neck. Notification. Follow institution's hazard communication processes for advanced notification of animal facility and cage labeling/management requirements if dosing animals with the nanomaterial 	
	PPE	 Eye protection. Wear proper safety glasses with side shields (for powders or liquids with low probability for dispersion into the air) Face protection. Use face shield where splash potential exists. Gloves. Wear disposable gloves to match the hazard, including consideration of other chemicals used in conjunction with nanomaterials (refer to Table 1. Glove Choices for Nanomaterials) Body protection. Wear laboratory coat and long pants (no cuffs). Closed toe shoes. 	
	Engineering	• Fume Hood, Biosafety Cabinet, or Enclosed System. Perform work in a laboratory-type fume hood, biosafety cabinet* (must be ducted if used in conjunction with volatile compounds), powder handling enclosure, or enclosed system (i.e., glove box, glove bag, or sealed chamber).	
	Work Practices	 Category 1 Work Practices. Follow all work practices listed for Category 1. Access. Restrict access. Signage. Post signs in area. Materials. Use antistatic paper and/or sticky mats with powders. 	
Category 2 Moderate Exposure Potential	PPE	 Category 1 PPE. Wear all PPE listed for Category 1. Eye protection. Wear proper chemical splash goggles (for liquids with powders with moderate to high probability for dispersion into the air). Gloves. Wear two layers of disposable, chemical-protective gloves. Body protection. Wear laboratory coat made of non-woven fabrics with elastic at the wrists (disposable Tyvek®-type coveralls preferred). Closed toe shoes. Wear disposable over-the-shoe booties to prevent tracking nanomaterials from the laboratory when working with powders and pellets. Respiratory Protection. If working with engineering controls is not feasible, respiratory protection may be required. Consult an EH&S professional for more information (i.e., N95 respirator, or one fitted with a P-100 cartridge). 	
	Engineering	• Enclosed System. Perform work in an enclosed system (i.e., glove box, glove bag, or sealed chamber).	
Category 3 High Exposure Potential	Work Practices	 Category 2 Work Practices. Follow all work practices listed for Category 2. Category 2 PPE. Wear all PPE listed for Category 2. Body protection. Wear disposable Tyvek®-type coveralls with head coverage. Respiratory Protection. If working with engineering controls is not feasible, respiratory protection may be required. Consult an EH&S professional for more information (i.e., N95 respirator, or one fitted with a P-100 cartridge). 	

Step 3. Develop a Standard Operating Procedure

Complete Appendix A "Standard Operating Procedures (SOP) for the Laboratory Use of Engineered Nanomaterials". For examples, refer to Appendix B.

Appendix A Standard Operating Procedures (SOP)

For the Laboratory Use of Engineered Nanomaterials

Instructions: Review the *Quick Guide: Risk Levels and Control Measures for Nanomaterials*. Use this template to develop a Standard Operating Procedure for your experiment / process.

	PROCEDURE TITLE:					
	DATE OF CREATION / REVISION:	F CREATION / REVISION:				
	LOCATION: (Building, Room #)					
	PRINCIPAL INVESTIGATOR (PI) OR LABORATORY	SUPERVISOR NAME:	PHONE:	Email	EMAIL:	
OVERVIEW	DESCRIPTION. PROVIDE A 1-2 SENTENCE BRIEF DESCRIPTION OF THE PROVIDE A 1-2 SENTENCE BRIEF DESCRIPTA 1-2 SENTENCE BRIEF DESCRIPTA 1-2 SENTENCE BRIEF DESCRIPTA 1-2 SENTENCE B		CESS. INDICATE IF AEROSOL	S ARE LIKELY TO	BE CREATED.	
	MATERIAL STATE AND CONDITIONS OF USE Nanomaterials are handled in/as: DRY PARTICLES (POWDERS / PELLETS) SUSPENSION / GELS	FREQUENCY (check o	ne):	DURATION PER	EXPERIMENT:	— HOURS
	GASEOUS PHASE	□ OTHER:				
	CATEGORY 3: H POTENTIAL HAZARDS. IDENTIFY POTENTIAL CHI NANOMATERIAL OR PARENT COMPOUND. THE TO	IODERATE POTEN IGH POTENTIAL F EMICAL AND SAFETY HA IXICITY OF THE NANOMA	TIAL FOR EXPOSURE FOR EXPOSURE ZARDS USING THE MATERIA TERIALS MAY BE GREATER T	l Safety Data S fhan the parent	Γ COMPOUND. SPECIA	
	CONSIDERATION SHOULD BE GIVEN TO THE HIGH I PARTICULARLY IF SCALING UP THE PROCESS. CON INFORMATION, REFER TO THE SECTION ON "PLAN	SIDER THE HAZARDS OF	ANY PRECURSOR MATERIAL			MORE
HAZARDS						

INSTRUCTIONS: INDICATE THE ENGINEERING, WORK PRACTICE, AND PERSONAL PROTECTIVE EQUIPMENT (PPE) CONTROLS YOU WILL BE IMPLEMENTING TO REDUCE THE HAZARDOUS EFFECTS OF WORKING WITH YOUR NANOMATERIALS. BASE YOUR SELECTION ACCORDING TO THE "QUICK GUIDE" SECTION.

ENGINEERING CONTROLS. INDICATE ENGINEERING DEVICE(S) TO BE UTILIZED. NOTE: IF WORK CANNOT BE CONDUCTED WITH APPROPRIATE ENGINEERING CONTROLS, CONSULT WITH AN EH&S PROFESSIONAL. **FUME HOOD** (laboratory-type) BIOSAFETY CABINET (must be ducted if used in conjunction with volatile compounds) **ENCLOSED SYSTEM** (i.e., glove box, glove bag, or sealed chamber) □ POWDER HANDLING ENCLOSURE □ OTHER: WORK PRACTICE CONTROLS. THE FOLLOWING CONTROLS WILL BE IMPLEMENTED (check all that apply): **Category 3 work practices Category 1 work practices Category 2 work practices** FOLLOW all work practices listed for FOLLOW all work practices listed for STORE in sealed container with secondary containment with other Category 1. Category 2. compatible chemicals **RESTRICT ACCESS.** LABEL chemical container with the POST signs in area identity of contents and include term USE antistatic paper and/or sticky mats "nano" as descriptor with powders. TRANSFER in sealed container with secondary containment PREPARE work space by lining with absorbent materials CLEAN all surfaces potentially contaminated with nanoparticles (e.g., benches, glassware, apparatus) at the end of each operation using a HEPA vacuum and/or wet wiping methods. WASH hands frequently. Upon leaving the nanomaterial work area, remove any PPE worn and wash hands, forearms, face, and neck. CONTROLS NOTIFY in advance of animal facility and cage labeling / management requirements if dosing animals with nanomaterial Approvals Required. Identify tasks that require prior approval by the Principal Investigator / Laboratory SUPERVISOR BEFORE PERFORMING: **Other**. Describe any additional work practices specific to the experiment / process: **PERSONAL PROTECTIVE EQUIPMENT (PPE)**. INDICATE THE PPE TO BE UTILIZED (check all that apply): **Body Protection:** Long pants (no cuffs) Laboratory coat *made of standard materials* Laboratory coat made of non-woven fabrics with elastics at wrists (i.e., Tyvek®) \Box Coveralls (disposable) with head coverage (*i.e.*, *Tyvek*®) **Eve / Face Protection:** □ Safety glasses with side shields □ Chemical splash goggles □ Face shield **Hand Protection:** □ Latex □ Nitrile □ Neoprene □ Vinvl □ Other: **Foot Protection:** Closed toe shoes Over-the-shoe booties **Other:** □ Respiratory Protection* □ Other:

* Consult with your institution on respiratory program requirements

LOCATION OF NEAREST EMERGENCY EQUIPMENT:

- 1. Flush contamination from eyes/skin using the nearest emergency eyewash /shower for a minimum of 15 minutes. Remove any contaminated clothing.
- 2. Take copy of MSDS(s) of chemical(s) when seeking medical treatment.
- 3. Report potential exposures to your Principal Investigator/Laboratory Supervisor.
- 4. File an incident report with your institution.

Spill Response procedures

- 1. Notify. Alert workers near spill to avoid entering the area. Post signs in area or on door of lab. Eliminate sources of ignition. Report spill to your Principal Investigator/Lab Supervisor.
- 2. Assess. Are you able to cleanup spill yourself?
 - □ YES
 - Proceed with Spill Cleanup if it is a small spill (i.e., 30 mL), you are knowledgeable about the hazards of the spill, it can be cleaned up within 15 minutes, and an appropriate spill kit is available.
 - □ NO

Obtain spill assistance. Contact your institution's hazardous materials unit.

3. Cleanup Spill. Wear existing PPE (NOTE: Respiratory protection may be required if spill / release is outside the engineering control device).

For powders:

- Use a dedicated, approved HEPA vacuum whose filtration effectiveness has been verified.
- Do not sweep dry nanoparticles or use compressed air.
- Consider possible pyrophoric hazards associated with vacuuming up nanoparticles.
- Wet wipe using damp cloths with soaps or cleaning oils, or commercially available wet or electrostatic microfiber cleaning cloths. Consider possible reactivity of nanoparticles with the wipe solvent ..
- For liquid dispersions:
- Apply absorbent material (appropriate for the solvent in the dispersion) to liquid spill.
- 4. Dispose. Dispose of used cleaning materials and wastes as hazardous waste.
- 5. Report. File incident report with your institution.

GENERAL SAFETY TRAINING. DESCRIBE YOUR INSTITUTION'S GENERAL LABORATORY SAFETY TRAINING.

TRAINING

LABORATORY-SPECIFIC TRAINING. (CHECK ALL THE APPLY)

- **REVIEW** THIS NANOTOOL
- **REVIEW** THE MSDS FOR THE NANOMATERIAL(S), *if available*
- **Review** the MSDS for other chemicals involved in the experiment / process

REVIEW THIS SOP

□ OTHER:

	Waste Stream	Management Method
	 Solid Dry ENM product Filter media containing ENMs Debris / dust from ENMs bound in matrix 	 Manage according to hazardous waste program requirements at your institution. Label nanomaterial waste containers at all times. Specify the nanomaterial and its hazard characteristic (or the hazard characteristic of the parent material) on container labels; label information to contain the word "nano" as a descriptor. Keep containers closed at all times when not in use. Maintain containers in good condition and free of exterior contamination. Collect waste in rigid container with tight fitting lid.
	Liquid Suspensions containing ENMs 	 Conect Waste in rigid container with tight fitting iid. Manage according to hazardous waste program requirements at your institution. Label nanomaterial waste containers at all times. Specify the nanomaterial and its hazard characteristic (or the hazard characteristic of the parent material) on container labels; label information to contain the word "nano" as a descriptor. Keep containers closed at all times when not in use. Maintain containers in good condition and free of exterior contamination. Indicate both the chemical constituents of the solution and their hazard characteristics, and the identity and approximate percentage of ENMs on container labels. Use leak proof containers that are compatible with all contents. Place liquid waste containers in secondary containment and segregate from incompatible chemicals during storage.
	Laboratory trash with trace nanomaterials • PPE • Sticky mats • Spill clean-up materials	 Manage according to hazardous waste program requirements at your institution. Label nanomaterial waste containers at all times. Specify the nanomaterial and its hazard characteristic (or the hazard characteristi of the parent material) on container labels; label information to contain the word "nano" as a descriptor. Keep containers closed at all times when not in use. Maintain containers in good condition and free of exterior contamination. Dispose of in double clear plastic bags, folded over and taped at the neck. Avoid rupturing the bags during storage and transport.
	Solid Matrix embedded with nanomaterials (intact and in good condition)	 Consult with your EH&S department, as these materials may be non- hazardous.
DESCRI	BE INSTITUTION'S WASTE MANAGEMENT PROCE	DURES HERE (IF APPLICABLE):

Acknowledgement. *By signing this form the individual certifies that the information provided is true and correct to the best of their knowledge.*

PRINT NAME / SIGNATURE

DATE:

Appendix B Standard Operating Procedures (SOP) sample

For the Laboratory Use of Engineered Nanomaterials

Instructions: Review the *Quick Guide: Risk Levels and Control Measures for Nanomaterials*. Use this template to develop a Standard Operating Procedure for your experiment / process.

	PROCEDURE TITLE:				
Use of fluorescent nanocrystals as biological markers					
DATE OF CREATION/ REVISION:					
	09/24/2011				
	LOCATION:				
	(Building, Room #) Sproul Hall 4127				
	PRINCIPAL INVESTIGATOR (PI) OR LABORATORY	SUPERVISOR NAME: PHONE:		EMAIL:	
	Jane Doe	(951) 827-	6303	jane.doe@university	.edu
		` 1		<i>v v</i>	
	DESCRIPTION. PROVIDE A 1-2 SENTENCE BRIEF D	ESCRIPTION OF THE PROCESS. INDICATE	E IF AEROSOLS ARE LI	KELY TO BE CREATED.	
	To achieve high optical density, mainte	iin thinness, and prevent photo	odegredation, flu	orescent nanocrystals	will be
	used (over organic dyes) as biological	narkers. This study will also in	vestigate fabrica	tion of nanocomposite	<i>25</i>
	(polymer spheres) to avoid slow recogn			•	
	(polymer spheres) to arou stor recogn	see and angle how sp	confice bontaining.		
	MATERIAL STATE AND CONDITIONS OF USE	FREQUENCY (check one):	DURAT	TION PER EXPERIMENT:	
		□ ONE TIME			
	Nanomaterials are handled in/as:				
	DRY PARTICLES (POWDERS / PELLETS)	WEEKLY		30	
	SUSPENSION / GELS			MINUTES; OR	HOURS
	☑ SUSPENSION / GELS □ GASEOUS PHASE	□ MONTHLY □ OTHER:		MINUTES; OR	HOURS
				MINUTES; OR	HOURS
	GASEOUS PHASE RISK LEVEL:		 RE	MINUTES; OR	HOURS
	GASEOUS PHASE RISK LEVEL: CATEGORY 1: LO	DOTHER:		MINUTES; OR	HOURS
	GASEOUS PHASE RISK LEVEL: CATEGORY 1: LO CATEGORY 2: M	OTHER:	XPOSURE	MINUTES; OR	HOURS
	GASEOUS PHASE RISK LEVEL: CATEGORY 1: LO CATEGORY 2: M	DOTHER:	XPOSURE	MINUTES; OR	HOURS
	□ GASEOUS PHASE RISK LEVEL: □ CATEGORY 1: Lo ☑ CATEGORY 2: M □ CATEGORY 3: H	DOTHER: DW POTENTIAL FOR EXPOSU ODERATE POTENTIAL FOR E IGH POTENTIAL FOR EXPOSU	XPOSURE JRE		
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INSTRUCTIONS: INDICATE THE ENGINEERING, WORK PRACTICE, AND PERSONAL PROTECTIVE EQUIPMENT (PPE) CONTROLS YOU WILL BE IMPLEMENTING TO REDUCE THE HAZARDOUS EFFECTS OF WORKING WITH YOUR NANOMATERIALS. BASE YOUR SELECTION ACCORDING TO THE "QUICK GUIDE" SECTION.

ENGINEERING CONTROLS INTERNET	
ENGINEERING CONTROLS. INDICATE ENGINEERING CONTROLS, CONSULT WITH AN EH	GINEERING DEVICE(S) TO BE UTILIZED. NOTE: IF WORK CANNOT BE CONDUCTED WITH APPROPRIATE I&S PROFESSIONAL.
□ FUME HOOD (laboratory-type) ☑ BIOSAFETY CABINET (must be ducted □ ENCLOSED SYSTEM (i.e., glove box, g □ POWDER HANDLING ENCLOSURE □ OTHER:	love bag, or sealed chamber)
WORK PRACTICE CONTROLS. THE FOLD	LOWING CONTROLS WILL BE IMPLEMENTED (check all that apply):
Category 1 work practices	Category 2 work practices
 STORE in sealed container with secondary containment with other compatible chemicals LABEL chemical container with the 	Category 1. Category 2. Category 2.
 identity of contents and include term "nano" as descriptor TRANSFER in sealed container with 	• USE antistatic paper and/or sucky mais with powders.
• PREPARE work space by lining with	
 absorbent materials CLEAN all surfaces potentially contaminated with nanoparticles (e.g., benches, glassware, apparatus) at the end of each operation using a HEPA vacuum and/or wet wiping methods. WASH hands frequently. Upon leaving the nanomaterial work area, 	
remove any PPE worn and wash hands, forearms, face, and neck.	
 NOTIFY in advance of animal facility and cage labeling / management requirements if dosing animals with nanomaterial Approvals Required. IDENTIFY 	
SUPERVISOR BEFORE PERFORMING:	TASKS THAT REQUIRE PRIOR APPROVAL BY THE PRINCIPAL INVESTIGATOR / LABORATORY <i>prior to <u>procuring</u> (purchasing) nanomaterials.</i>
Other . Describe any additional w	ORK PRACTICES SPECIFIC TO THE EXPERIMENT / PROCESS:
	(PPE). INDICATE THE PPE TO BE UTILIZED (check all that apply):
Body Protection:	 Long pants (no cuffs) Laboratory coat made of standard materials Laboratory coat made of non-woven fabrics with elastics at wrists (i.e., Tyvek®) Coveralls (disposable) with head coverage (i.e., Tyvek®)
Eye / Face Protection:	 □ Safety glasses with side shields ☑ Chemical splash goggles □ Face shield
Hand Protection:	□ Latex ☑ Nitrile (2 layers) □ Neoprene □ Vinyl □ Other:
Foot Protection:	✓ Closed toe shoes □ Over-the-shoe booties
Other:	 Respiratory Protection* Other:

* Consult with your institution on respiratory program requirements

LOCATION OF NEAREST EMERGENCY EQUIPMENT:

Item:	Location
Eyewash / Safety Shower	Outside main door of in Sproul Hall 4127
First Aid Kit	Under sink in Sproul Hall 4127
Chemical Spill Kit	Under sink in Sproul Hall 4127
Fire Extinguisher	On the fourth floor of Sproul Hall, near restrooms
Telephone	On desk in corner of Sproul Hall 4127
Fire Alarm Manual Pull Station	On the fourth floor of Sproul Hall, near restrooms

DESCRIBE INSTITUTION'S EMERGENCY PROCEDURES: Follow "In Case of an Accident" poster affixed to laboratory door

Personnel Exposure procedures

- Flush contamination from eyes/skin using the nearest emergency eyewash /shower for a minimum of 15 minutes. Remove any contaminated clothing.
- 2. Take copy of MSDS(s) of chemical(s) when seeking medical treatment.
- 3. Report potential exposures to your Principal Investigator/Laboratory Supervisor.
- 4. File an incident report with your institution.

Spill Response procedures

- Notify. Alert workers near spill to avoid entering the area. Post signs in area or on door of lab. Eliminate sources of ignition. Report spill to your Principal Investigator/Lab Supervisor.
- 2. Assess. Are you able to cleanup spill yourself? IF YES

Proceed with **Spill Cleanup** if it is a small spill (i.e., 30 mL), you are knowledgeable about the hazards of the spill, it can be cleaned up within 15 minutes, and an appropriate spill kit is available.

IF NO

- Obtain spill assistance. Contact your institution's hazardous materials unit.
- Cleanup Spill. Wear existing PPE (NOTE: Respiratory protection may be required if spill / release is outside the engineering control device).
 - For powders:
 - Use a dedicated, approved HEPA vacuum whose filtration effectiveness has been verified.
 - Do not sweep dry nanoparticles or use compressed air.
 - Consider possible pyrophoric hazards associated with vacuuming up nanoparticles.
 - Wet wipe using damp cloths with soaps or cleaning oils, or commercially available wet or electrostatic microfiber cleaning cloths. Consider possible reactivity of nanoparticles with the wipe solvent..
 - For liquid dispersions:
 - Apply absorbent material (appropriate for the solvent in the dispersion) to liquid spill.
- 4. Dispose. Dispose of used cleaning materials and wastes as hazardous waste.
- 5. Report. File incident report with your institution.

GENERAL SAFETY TRAINING. DESCRIBE YOUR INSTITUTION'S GENERAL LABORATORY SAFETY TRAINING.

Laboratory Safety Orientation, Hazardous Waste Management, and Chemical Hygiene are required of all users prior to working in the laboratory. All courses are available online at <u>http://www.university.edu</u>

LABORATORY-SPECIFIC TRAINING. (CHECK ALL THE APPLY)

- **REVIEW** THIS NANOTOOL
- **REVIEW** THE MSDS FOR THE NANOMATERIAL(S), *if available*
- ☑ REVIEW THE MSDS FOR OTHER CHEMICALS INVOLVED IN THE EXPERIMENT / PROCESS
- **REVIEW** THIS SOP
- □ OTHER:

	Waste Stream	Management Method
	Solid	 Manage according to hazardous waste program requirements at your
	Dry ENM product	institution.
	Filter media containing ENMs	2. Label nanomaterial waste containers at all times. Specify the
	Debris / dust from ENMs bound in matrix	nanomaterial and its hazard characteristic (or the hazard characteristi
		of the parent material) on container labels; label information to
		contain the word "nano" as a descriptor.
		3. Keep containers closed at all times when not in use.
		4. Maintain containers in good condition and free of exterior
		contamination.
\checkmark	Liquid	 Collect waste in rigid container with tight fitting lid. Manage according to hazardous waste program requirements at your
	• Suspensions containing ENMs	institution.
		 Label nanomaterial waste containers at all times. Specify the
		nanomaterial and its hazard characteristic (or the hazard characteristi
		of the parent material) on container labels; label information to
		contain the word "nano" as a descriptor.
		3. Keep containers closed at all times when not in use.
		4. Maintain containers in good condition and free of exterior
		contamination.
		5. Indicate both the chemical constituents of the solution and their
		hazard characteristics, and the identity and approximate percentage
		of ENMs on container labels.
		6. Use leak proof containers that are compatible with all contents.
		 Place liquid waste containers in secondary containment and segregate from incompatible chamical during storage
	Laboratory to a but t	from incompatible chemicals during storage.
	Laboratory trash with trace	 Manage according to hazardous waste program requirements at your institution.
	nanomaterials	 Label nanomaterial waste containers at all times. Specify the
	PPE Sticky mats	nanomaterial and its hazard characteristic (or the hazard characteristi
	Spill clean-up materials	of the parent material) on container labels; label information to
		contain the word "nano" as a descriptor.
		3. Keep containers closed at all times when not in use.
		4. Maintain containers in good condition and free of exterior
		contamination.
		5. Dispose of in double clear plastic bags, folded over and taped at the
		neck.
		6. Avoid rupturing the bags during storage and transport.
	Solid Matrix	1. Consult with your EH&S department, as these materials may be non-
	embedded with nanomaterials	hazardous.
	(intact and in good condition)	
DESCRI	BE INSTITUTION'S WASTE MANAGEMENT PROCE	DURES HERE (IF APPLICABLE):
0111		
	e University Online Tag Program (OTI	P) to schedule pickup of hazardous waste with EH&S.
	e University Online Tag Program (OTI	P) to schedule pickup of hazardous waste with EH&S.
	e University Online Tag Program (OTI	P) to schedule pickup of hazardous waste with EH&S.
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Use the	ement. By signing this PRINT NAME	
Use the owledge	ement. By signing this PRINT NAME	/ SIGNATURE DATE:
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Appendix C Additional Information

Health Effects

Table 3. Select publications on the health effects of nanomaterials.²²

Effect	Particle	Reference
Deposit in the alveoli	Ultrafine Ti0 ₂ SWCNT	Sager et al. 2008 Shvedova et al. 2005 Mercer et al. 2008
Evade phagocytosis	SWCNT	Mercer et al. 2008
Enter alveolar walls	SWCNT Ti0 ₂	Mercer et al. 2008 Oberdörster et al. 1994
Produce interstitial inflammation	Ultrafine carbon black	Nikula et al. 1995
Produce fibrosis	SWCNT	Shvedova et al. 2005 Mercer et al. 2008
Produce tumors	Ultrafine Ti0 ₂	Heinrich et al. 1995
Form granulomas	SWCNT	Shvedova et al. 2005

Naturally Occurring Nanomaterials

Table 4. Sources, Notes, and Exposure limits for select naturally occurring nanomaterials

Types	Amorphous Silica	Carbon Black
Sources	Crystalline silica is abundant in sand and soils, rocks (sandstone, granite), minerals (quartz). Amorphous silica is far less abundant in nature (diatomaceous earth, silica glass and opal) but is commonly manufactured ^{14, 15}	Carbon black is a powdered form of elemental carbon. Worldwide production of carbon black in 1993 was approximately 6 million tonnes. Typical classes of chemicals adsorbed onto the carbon black surface are polycyclic aromatic hydrocarbons (PAHs) ¹⁶
Notes	Used for industrial applications such as flow agents, anti-caking agents and flavor carriers in food, polishing agents in toothpastes, flattening agents and thickeners in paints, etc. Man-made silica nanoparticles include: Mesoporous, colloidal precipitated, and pyrogenic. A few examples of the applications are: cosemetics, drugs, food additives and drug delivery systems. Contrary to the well- studied crystalline micron-sized silica, relatively little information exists on the toxicity of its	batteries. ¹⁶
Exposure Limits	amorphous and nano-size forms15Cal/OSHA (respirable)PEL: 3 mg/ m3OSHAPEL: 80 mg/ m3NIOSHREL :6 mg/ m3ACGIH (respirable)TLV: 3 mg/ m3	Cal/OSHAPEL: TWA 3.5 mg/m³OSHAPEL: TWA 3.5 mg/m³NIOSHREL: TWA 3.5 mg/m³TWA 0.1 mg/m³ for carbon blacks with > 0.1% PAHACGIHTLV: TWA 3.5 mg/m³

Regulations

Governmental Agencies and Relevant Legislation to Nanomaterials (as of 2011)

- European Union Registration, Evaluation, Authorization, and Restriction of Chemical Substances, 2007 (REACH)
- US Environmental Protection Agency (EPA) Toxic Substances Control Act (1976)
- Cal EPA Department of Toxic Substance Control (DTSC) Assembly Bill 1879 and Senate Bill 509
- Occupational Safety and Health Administration (OSHA) Nanomaterials fall under OSHA General Industry Standards¹⁷

European Union | REACH18

REACH does not specifically refer to nanomaterials, but nanomaterials are included under the definition of a "substance" in this legislation. In general, REACH requires registration of substance manufactured or imported at 1 metric ton or more, but the initial (November 2010) registration deadline only applies to substances that are manufactured or imported in quantities at 1000 metric tons or more per year. This registration will provide information that is essential to understanding and evaluating the risks associated with specific substances, particularly nanomaterials, since value-chain information for most nanomaterials is currently lacking.

In addition, <u>Classification</u>, <u>Labelling and Packaging of</u> <u>Nanomaterials in REACH and CLP</u>, an amendment to REACH, specifies how hazardous substances must be handled within the EU; nanomaterials that fulfill the criteria for hazardous provided under this regulation must be classified, labeled, and packaged as such. Manufacturers and importers in the EU of nanomaterials that meet these criteria were required to notify the ECHA by January 2011.

An expert group that advises the European Commission on how to manage nanomaterials in accordance with REACH and CLP has released several documents, including:

- <u>Nanomaterials in REACH</u>
 Provides an overview of how REACH applies to
 nanomaterials
- <u>Classification</u>, <u>Labelling</u> and <u>Packaging</u> of <u>Nanomaterials in REACH and CLP</u> Describes how to classify nanomaterials in accordance with REACH and the CLP Regulation.

US EPA | Toxic Substances Control Act (1976)19

In the United States, Toxic Substances Control Act of 1976 (TSCA) is the primary federal legislation that regulates toxic substances. TSCA requires manufactures of new chemical substances to provide information to the EPA prior to manufacturing or introducing new substances into commerce. Under TSCA, the EPA has the authority to control substances that pose an "unreasonable risk to human health or the environment". On April 4, 2012, the US EPA issued a Significant New Use Rule (SNUR) that states that "infused carbon nanostructures (generic) are subject to premanufacture notice (PMN)." This SNUR require persons who intend to manufacture, import, or process new carbon nanostructures to submit a Significant New Use Notice (SNUN) to EPA at least 90 days before commencing that activity. Additional rules related to other types of nanomaterials are expected to be issued from the EPA in the future and individuals wishing to use nanomaterials commercially are encouraged to check the EPA's website for more current information: http://epa.gov/oppt/nano

For an overview of how the TSCA impacts worker health related to nanomaterials see: Sayre, P., S. Prothero, and J. Alwood, *Nanomaterial Risk Assessment and Management Experiences Related to Worker Health Under the Toxic Substances Control Act.* Journal of Occupational and Environmental Medicine, 2011. **53**(6 Supplement): p. S98-S102.

Cal EPA (DTSC) | Assembly Bill 1879 & Senate Bill 509

Two California Green Chemistry Initiative Statutes, Assembly Bill 1879 and Senate Bill 509 provide the Cal EPA/ DTSC with greater authority to regulate toxic substance in consumer products than the federal statues and to create an online Toxics Information Clearinghouse to provide Californians with information on hazardous chemicals. Although these statutes apply to chemical substance more broadly, DTSC has used this authority to create a chemical call-in program for some specific nanomaterials. Thus far, carbon nanotubes, nano cerium oxide, nano silver, nano titanium dioxide, nano zero valent iron, nano zinc oxide, and quantum dots have been included in the call in. The call in requires manufacturers and importers of these materials in the state of California to provide information on their products, including, but not limited to, known toxicological data and supply chain information.^{20, 21}

Other Regulatory Drivers

OECD

Defines terms, and standardize protocols for safety testing. <u>OECD Nanomaterials Website</u>

Appendix D Reference

- ¹ Lövestam, G., Rauscher, H., et al. (2010). Considerations on a Definition of Nanomaterial for Regulatory Purpose. *Joint Research Centre (JRC) Reference Reports*. Luxembourg, European Union [ISO TS 80004-1]
- ² Council for Science and Technology Nanosciences and Nanotechnologies. (2007). A Review of Government's Progress on Its Policy Commitments. *Nano Review* (11). London.
- 3 Good Nano Guide. (2007, March 13). What are nanomaterials? 2011 Retrieved June 16, from http://goodnanoguide.org/tikiindex.php?page=What+are+nanomaterials; and American Chemistry Council, Nanotechnology Panel. (2007, March 13). Consideration for a Definition for Engineered Nanomaterials. Retrieved June 2011 from 16, http://www.americanchemistry.com
- ⁴ Peters, A., Ruckerl, R., et al. (2011). Lessons From Air Pollution Epidemiology for Studies of Engineered Nanomaterials. *Journal of Occupational and Environmental Medicine* 53 (6 Supplement): S8-S13.
- ⁵ Castranova, V. (2011). Overview of Current Toxicological Knowledge of Engineered Nanoparticles. *Journal of Occupational and Environmental Medicine* 53 (6 Supplement): S14-S17.
- ⁶ Nohynek, G. J., EDufour, E.K., et al. (2008). Nanotechnology, Cosmetics and the Skin: Is There a Health Risk? *Skin Pharmacology and Physiology* 21(3): 136-149.
- ⁷ Sadrieh, N., Wokovich, A.M., et al. (2010). Lack of Significant Dermal Penetration of Titanium Dioxide from Sunscreen Formulations Containing Nano- and Submicron-Size TiO2 Particles. *Toxicological Sciences* 115 (1): 156-166.
- ⁸ Wu, J., Liu, W., et al. (2009). Toxicity and penetration of TiO2 nanoparticles in hairless mice and porcine skin after subchronic dermal exposure. *Toxicology Letters* 191 (1): 1-8.
- ⁹ OSHA. Nanotechnology Standards. Retrieved June 24, 2011 from

http://www.osha.gov/dsg/nanotechnology/nanotech stand ards.html

- 10 NIOSH. (2010). Occupational Exposure to Carbon Nanotubes and Nanofiber [DRAFT]. Current Intelligence Bulletin. Rationale: "In this risk analysis, NIOSH has determined that workers may be at risk of developing adverse respiratory health effects if exposed for a working lifetime at the upper limit of quantitation (LOQ) of NIOSH Method 5040, currently the recommended analytical method for measuring airborne CNT. The LOQ for NIOSH Method 5040 is 7 µg/m3. Specifically, the animal data-based risk estimates indicate that workers may have >10% excess risk of developing early stage pulmonary fibrosis if exposed over a full working lifetime at the upper LOQ for NIOSH Method 5040. Until improved sampling and analytical methods can be developed, and until data become available to determine if an alternative exposure metric to mass may be more biologically relevant, NIOSH is recommending a REL of 7 µg/m3 elemental carbon (EC) as an 8-hr TWA respirable mass airborne concentration."
- ¹¹ NISOH. (2011). Occupational Exposure to Titanium Dioxide. *Current* Intelligence Bulletin 63. Rationale: "NIOSH recommends airborne exposure limits of 2.4 mg/m3 for fine TiO2 and 0.3 mg/m3 for ultrafine (including engineered nanoscale) TiO2, as time-weighted

average (TWA) concentrations for up to 10 hr/day during a 40-hour work week. These recommendations represent levels that over a working lifetime are estimated to reduce risks of lung cancer to below 1 in 1,000. The recommendations are based on using chronic inhalation studies in rats to predict lung tumor risks in humans."

- Recommended Spill Kit Contents:
 - Latex or Nitrile gloves
 - Disposable laboratory coat w/elastic wrists or Tyvek suit
 - Absorbent material
 - Pre-moistened wipes
 - Sealable plastic bags and tape
 - Hazardous waste containers with leak proof caps
 - Walk off mats (e.g., Tacki-Mat)
 - Dedicated HEPA vacuum, labeled 'For Nanomaterials Only'
 - Hazardous waste labels
 - 'Do not enter Nanomaterial Spill Clean-up in Progress' sign
- ¹³ Ibid.

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- ¹⁴ Nenogenotox (2010). Definitions Glossary. Retrieved June 15, 2011 from <u>http://www.nanogenotox.eu/index.php?option=com glossar</u> y&id=57&Itemid=100
- ¹⁵ Napierska, D., Thomassen, L. CJ, Lison, D., Martens, J.A., & Hoet, P.H. (2010). The nanosilica hazard: another variable entity. *Particle and Fibre Toxicology*, 7:39. Retrieved March 26, 2012 from <u>http://www.particleandfibretoxicology.com/content/7/1/3</u> 9
- ¹⁶ International Agency for Research on Cancer. (1996). *Carbon Black*, p. 149. Retrieved March 26, 2012 from <u>http://www.inchem.org/documents/iarc/vol65/carbon.html</u>
- ¹⁷ *Ibid.* (See Reference 9)
- ¹⁸ European Commission. (2011). Chemicals: REACH and nanomaterials. Retrieved June 24, 2011 from <u>http://ec.europa.eu/enterprise/sectors/chemicals/reach/na</u> <u>nomaterials/index_en.htm</u>
- ¹⁹ Environmental Protection Agency. (2011). Control of nanoscale materials under the Toxic Substances Control Act. Retrieved June 24, 2011 from http://www.epa.gov/opptintr/nano
- ²⁰ Department of Toxic Substances Control. (2011). DTSC and Nanotechnology. Retrieved June 24, 2011 from <u>http://www.dtsc.ca.gov/TechnologyDevelopment/Nanotechnology/nanoport.cfm</u>
- ²¹ Department of Toxic Substances Control. (2011). Green Chemistry. Retrieved June 24, 2011 from http://www.dtsc.ca.gov/PollutionPrevention/GreenChemistr vInitiative/index.cfm
- ²² Courtesy of Dr. Paul Schulte, NIOSH