General Principles and Practices for Working Safely with Engineered Nanomaterials

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Purpose:

This document provides environmental, health and safety guidance to researchers working with engineered nanomaterials in Stanford University laboratories. It is intended to supplement the requirements of Stanford University’s Chemical Hygiene Plan and its companion Laboratory Safety Toolkit which are available at:

- [https://suehsaps5.stanford.edu/lcst/docs/Chemical_Hygiene_Plan.pdf](https://suehsaps5.stanford.edu/lcst/docs/Chemical_Hygiene_Plan.pdf)

As the scientific community continues to gather data to assess the potential health and safety risks associated with engineered nanomaterials, these guidelines may be updated as information becomes available. Until more is known about the possible risks of nanomaterials, it is prudent and appropriate to take a precautionary approach and utilize good laboratory safety practices when working with these materials.

### Action Items for Faculty Working With or Creating Engineered Nanomaterials


2. Instruct all research personnel in your lab to follow the work practices described in this document.

3. Create Standard Operating Procedures (SOPs) for processes and experiments involving nanomaterials using the template contained in this document. Priority for SOP development should be given to those operations where there is higher risk of exposure (e.g., manipulation of nanoparticles in gas stream, work with dry dispersible nanoparticles). A SOP template for work with nanomaterials is available at the end of this document.

### What Are Nanomaterials?

Nanomaterials are defined as materials with at least one external dimension in the size range from approximately 1-100 nanometers. Nanoparticles are objects with all three external dimensions at the nanoscale. Nanoparticles that are naturally occurring (e.g., volcanic ash, soot from forest fires) or are the incidental byproducts of combustion processes (e.g., welding, diesel engines) are usually physically and chemically heterogeneous and often termed ultrafine particles. Engineered nanoparticles are intentionally produced and designed with very specific properties related to shape, size, surface properties and chemistry. These properties are reflected in aerosols, colloids,

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or powders. Often, the behavior of nanomaterials may depend more on surface area than particle composition itself. Relative-surface area is one of the principal factors that enhance its reactivity, strength and electrical properties.

Engineered nanoparticles may be bought from commercial vendors or generated via experimental procedures by researchers in the laboratory (e.g., CNTs can be produced by laser ablation, HiPCO (high-pressure carbon monoxide, arc discharge, and chemical vapor deposition (CVD)). Examples of engineered nanomaterials include: carbon buckeyballs or fullerenes; carbon nanotubes; metal or metal oxide nanoparticles (e.g., gold, titanium dioxide); quantum dots, among many others.

**Current Occupational Health and Safety Concerns**

Exposure to nanomaterials may occur through inhalation, dermal contact, or ingestion depending on how personnel use and handle them. The full health effects of exposures to nanomaterials are not fully understood at this time. For example, a peer-reviewed toxicity study on carbon nanotubes (CNTs) indicated that the toxicity of nanoparticles depends on specific physiochemical and environmental factors and thus the toxic potential of each nanoparticle needs to be evaluated separately [Helland et al., 2007]. Results of existing studies in animals or humans provide some basis for preliminary estimates of areas of concern. According to the National Institute for Occupational Safety and Health (NIOSH)², studies to date have indicated:

- Increased toxicity of ultrafine particles or nanoparticles as compared to larger particles of similar composition. Chemical composition and other particle properties can also influence toxicity. [Oberdörester et al., 1992, 1994a,b, 2005a; Lison et al., 1997; Tran et al., 1999, 2000; Brown et al., 2001; Duffin et al., 2002; Barlow et al. 2005; Maynard and Kuempel 2005; Donaldson et al. 2006].

- A greater proportion of inhaled nanoparticles will deposit in the respiratory tract as compared to larger particles. [ICRP 1994; Jaques and Kim 2000; Daigle et al. 2003; Kim and Jaques 2004.]

- Nanoparticles can cross cell membranes and interact with sub cellular structures where they have been shown to cause oxidative damage and impair function of cells in culture. [Möller et al. 2002, 2005; Li et al. 2003; Geiser et al. 2005].

- Nanoparticles may be capable of penetrating healthy intact skin and translocating to other organ systems following penetration. [Tankenaka et at. 2001; Kreyline et al 2002; Oberdörester et al. 2002, 2004; Semmler et al. 2004; Geiser et al. 2005.]

• Catalytic effects and fire or explosion are other hazards to consider. [Pritchard 2004].

Lab Safety Guidelines for Handling Nanomaterials

Exposure standards have not been established for engineered nanoparticles in the United States or internationally [Safe Nanotechnology 2008.] Until more definitive findings are made regarding the potential health risks of handling nanomaterials, researchers planning to work with nanomaterials must implement a combination of engineering controls, work practices, and personal protective equipment to minimize potential exposures to themselves and others. For a quick guide to the exposure risks and prudent control measures to be used for common laboratory operations involving nanomaterials, refer to the table at the end of this section. It is important to consider if the nanoparticles are in an agglomerated or aggregated form, functionalized, suspended in liquid, or bound, as these conditions may affect the exposure potential.

1. Engineering Controls:
   • Use glove bags, glove boxes, fume hoods, or other containment or exhausted enclosures when there is a potential for aerosolization, such as: handling powders; creating nanoparticles in gas phase; pouring or mixing liquid media which involves a high degree of agitation. (DO NOT use horizontal laminar flow hoods (clean benches), as these devices direct the air flow towards the worker.) Consult with EH&S if engineering controls are not feasible.
   • Use fume hoods or other local exhaust devices to exhaust tube furnaces and or chemical reaction vessels.
   • Perform any maintenance activities, such as repair to equipment used to create nanomaterials or cleaning/replacement of dust collection systems, in fume hoods or under appropriate local exhaust.

2. Work Practices:
   • Selection of Nanomaterials:
     o Whenever possible, handle nanomaterials in solutions or attached to substrates to minimize airborne release.
     o Consult the Material Safety Data Sheet (MSDS), if available, or other appropriate references prior to using a chemical or nanomaterial with which you are unfamiliar. 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.
   • Safety Equipment:
     o Know the location and proper use of emergency equipment, such as safety showers, fire extinguishers, and fire alarms.
• **Hygiene:**
  o Do not consume or store food and beverages, or apply cosmetics where chemicals or nanomaterials are used or stored since this practice increases the likelihood of exposure by ingestion.
  o Do not use mouth suction for pipetting or siphoning.
  o Wash hands frequently to minimize potential chemical or nanoparticle exposure through ingestion and dermal contact.
  o Remove gloves when leaving the laboratory, so as not to contaminate doorknobs, or when handling common use objects such as phones, multiuser computers, etc.

• **Labeling and Signage:**
  o Store in a well-sealed container, preferable one that can be opened with minimal agitation of the contents.
  o Label all chemical containers with the identity of the contents (avoid abbreviations/ acronyms); include term “nano” in descriptor (e.g., “nano-zinc oxide particles” rather than just “zinc oxide.” Hazard warning and chemical concentration information should also be included, if known.
  o Use cautious judgment when leaving operations unattended: i) Post signs to communicate appropriate warnings and precautions, ii) Anticipate potential equipment and facility failures, and iii) Provide appropriate containment for accidental release of hazardous chemicals.

• **Cleaning:**
  o Wet wipe and or HEPA-vacuum work surfaces regularly.

• **Transporting:**
  o Use sealed, double-contained container when transporting nanomaterials inside or outside of the building.

• **Buddy System:**
  o Communicate with others in the building when working alone in the laboratory; let them know when you arrive and leave. Avoid working alone in the laboratory when performing high-risk operations.

3. **Personal Protective Equipment:**
   • Wear gloves, lab coats, safety goggles, long pants, closed-toe shoes, and face shields, as appropriate dependent on the nature of the materials and procedure.
   • If work cannot be conducted inside a fume hood or other ventilated enclosure, consult with EH&S’s Occupational Health and Safety Program (723-0448) regarding the need for respiratory protection or other alternative controls.

4. **Training:**
   • Ensure that researchers have both general safety training and lab-specific training relevant to the nanomaterials and associated hazardous chemicals used in the process/experiment. See SU’s Laboratory Chemical Safety
Toolkit (SU Toolkit) for guidance on training (http://chemtoolkit.stanford.edu/ChemSafetyTraining)

- Lab-specific training can include a review of this safety fact sheet, the relevant Material Safety Data Sheets (if available), and the lab’s Standard Operating Procedure for the experiment.

5. **Standard Operating Procedures:**

- Prepare a Standard Operating Procedure (SOP) for operations involving nanomaterials. A general use Standard Operating Procedure for working with nanomaterials is available at the end of this document. The SOP should be tailored to be specific to the proposed experimental procedure.
- Consider the hazards of the precursor materials in evaluating the process.
- Special consideration should be given to the high reactivity of some nanopowders with regard to potential fire and explosion. [Pritchard 2004].

6. **Consultation:**

Consult with your Principal Investigator prior to procuring or working with nanomaterials. See SU’s Toolkit for information regarding consultation and prior approvals (http://chemtoolkit.stanford.edu/PriorApprovals). For additional assistance, contact EH&S’s Occupational Health & Safety Program at 723-0448.
**Quick Guide: Exposure Risks and Control Measures for Common Laboratory Operations Involving Nanomaterials**

<table>
<thead>
<tr>
<th>Activity types, by Risk of Exposure</th>
<th>Primary Control Measures</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Low Probability:</strong></td>
<td></td>
</tr>
<tr>
<td>- Non-destructive handling of solid nanoparticle composites or nanoparticles permanently bonded to a substrate</td>
<td>- Disposable nitrile or PVC gloves. Do not reuse gloves.</td>
</tr>
<tr>
<td></td>
<td>- Wet cleaning procedures and/or HEPA vacuum for surfaces/equipment.</td>
</tr>
<tr>
<td><strong>Medium / High Probability:</strong></td>
<td></td>
</tr>
<tr>
<td>- Working w/ nanomaterials in liquid media during pouring or mixing, or where a high degree of agitation is involved (e.g., sonication)</td>
<td>- Conduct task within a fully enclosed system (e.g., glovebox), or fume hood</td>
</tr>
<tr>
<td>- Handling nanostructured powders*</td>
<td>- Disposable gloves appropriate for the solvent in which the particles are suspended. Do not reuse gloves.</td>
</tr>
<tr>
<td>- High speed abrading/grinding nano-composite materials</td>
<td>- Safety eyewear (+ face shield if splash potential exists)</td>
</tr>
<tr>
<td>- Maintenance on equipment used to produce nanomaterials</td>
<td>- Wet cleaning procedures for surfaces/equipment</td>
</tr>
<tr>
<td>- Cleaning of dust collection systems used to capture nanoparticles</td>
<td></td>
</tr>
<tr>
<td><strong>High Probability:</strong></td>
<td></td>
</tr>
<tr>
<td>- Generating nanoparticles in the gas phase or in aerosol (spill or liquid)</td>
<td>- Work in enclosed systems only (e.g., glovebox, glovebag, or sealed chamber).</td>
</tr>
<tr>
<td>- Manipulation of nanoparticles in gas stream</td>
<td></td>
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</tbody>
</table>

* EH&S recognizes that low-density nanomaterials (e.g., carbon-based) become aerosolized by even the slightest air movement and may not be practical when weighed or handled in laboratory fume hoods. Consult with EH&S on alternative sets of controls.
Spill Response

In addition to following EH&S general spill response directions (http://chemtoolkit.stanford.edu/emergencies), integrate the additional measures for spills involving nanomaterials:

- Use wet clean up methods or vacuum cleaners equipped with HEPA-filters.
- Do not dry sweep or use conventional vacuum cleaners.
- Collect spill cleanup materials in a tightly closed container
- Manage spill cleanup debris as hazardous waste.

Disposal

- As a prudent measure, manage nanoparticle wastes, including contaminated lab debris, as a part of your normal laboratory hazardous waste stream.
- Collect and store waste materials in a tightly closed container. Include information describing the nanoparticulate nature of the materials on the waste tag (e.g., contains nanosilver material).

Additional Information and References

The field of nanotechnology is rapidly evolving. The following entities provide additional information regarding the research efforts underway by governmental agencies and other institutions to fill in knowledge gaps.

- National Institute for Occupational Safety and Health (NIOSH) - Nanotechnology www.cdc.gov/niosh/topics/nanotech
- United States Department of Labor http://www.osha.gov/dsg/nanotechnology/nanotechnology.html
- American Chemical Society: Nanotechnology Safety Resources http://membership.acs.org/C/CCS/nano.htm
- Environmental Protection Agency Perspective on Nanotechnology http://es.epa.gov/ncer/nano/index.html
- National Nanotechnology Initiative http://www.nano.gov
References:


#1 **Contact Information:**

<table>
<thead>
<tr>
<th>Procedure Title</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Procedure Author</td>
<td></td>
</tr>
<tr>
<td>Date of Creation/Revision</td>
<td></td>
</tr>
<tr>
<td><strong>Name of Responsible Person</strong> <em>(The PI, Lab Supervisor, or Autonomous Researcher)</em>:</td>
<td></td>
</tr>
<tr>
<td>Work phone:</td>
<td></td>
</tr>
<tr>
<td>e-mail:</td>
<td></td>
</tr>
<tr>
<td><strong>Location of Work</strong> <em>(building/lab #)</em></td>
<td></td>
</tr>
</tbody>
</table>

#2 **Process or Experiment Overview:** *Description of the process or experiment that the SOP covers. This process may be described in general terms, such as cleaning and purification of single walled carbon nanotubes.*

<table>
<thead>
<tr>
<th>Frequency:</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>□ one time □ daily □ weekly □ monthly</td>
<td></td>
</tr>
<tr>
<td>□ other:__________</td>
<td></td>
</tr>
<tr>
<td><strong>Duration per Expt:</strong></td>
<td></td>
</tr>
<tr>
<td>_______ minutes; or _____ hours</td>
<td></td>
</tr>
</tbody>
</table>

#3 **Risk Assessment:** *Identify potential chemical and safety hazards. Special consideration should be given to the high reactivity of some nanopowders with regard to potential fire and explosion. Consider the hazards of the precursor materials in evaluating the process.*
#4 Controls:  (Check those that apply to the risks and procedures for the work that will be done)

**#4a Engineering/Ventilation Controls:**

<table>
<thead>
<tr>
<th>Engineering Controls</th>
<th>Activity type</th>
</tr>
</thead>
<tbody>
<tr>
<td>□ General laboratory ventilation</td>
<td>• Non-destructive handling of solid nanoparticle composites or nanoparticles permanently bonded to a substrate</td>
</tr>
<tr>
<td>□ Laboratory fume hood; or</td>
<td>• Working w/ nanomaterials in liquid media during pouring or mixing, or where a high degree of agitation is involved (e.g., sonication) • Handling nanostructured powders* • Maintenance on equipment used to produce nanomaterials • Cleaning of dust collection systems used to capture nanoparticles</td>
</tr>
<tr>
<td>□ Exhausted enclosure</td>
<td>□ Glove box; or □ Other sealed enclosure</td>
</tr>
<tr>
<td>□ Laboratory fume hood; or</td>
<td>• Generating nanoparticles in the gas phase or in aerosol • Manipulation of nanoparticles in gas stream</td>
</tr>
<tr>
<td>□ Exhausted enclosure</td>
<td></td>
</tr>
</tbody>
</table>

*If work cannot be conducted with appropriate engineering controls, consult with EH&S, 723-0448.

**#4b Personnel Protective Equipment:**

<table>
<thead>
<tr>
<th>Protection</th>
<th>Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>□ gloves; indicate type:</td>
<td>____________________</td>
</tr>
<tr>
<td>□ safety goggles □ face shield □</td>
<td>____________________</td>
</tr>
<tr>
<td>□ lab coats □ other:</td>
<td>____________________</td>
</tr>
<tr>
<td>□ appropriate street clothing</td>
<td></td>
</tr>
</tbody>
</table>

Respiratory protection is generally not required for lab research, provided the appropriate engineering controls are employed. For additional guidance on respiratory protection, consult with EH&S, 723-0448.
#4c Location of Nearest Emergency Safety Equipment:

<table>
<thead>
<tr>
<th>Item:</th>
<th>Location:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eyewash/Safety Shower</td>
<td></td>
</tr>
<tr>
<td>First Aid Kit</td>
<td></td>
</tr>
<tr>
<td>Chemical Spill Kit</td>
<td></td>
</tr>
<tr>
<td>Fire Extinguisher</td>
<td></td>
</tr>
<tr>
<td>Telephone</td>
<td></td>
</tr>
<tr>
<td>Fire Alarm Manual Pull Station</td>
<td></td>
</tr>
</tbody>
</table>

#5 Step-By-Step Operating Procedure: Provide a sequential description of work, including details such as chemical concentrations and when special safety equipment is to be utilized. Clearly label areas where nanomaterials are used.

#6 Decontamination:

- Upon leaving the nanomaterial work area, remove any personal protective equipment worn and wash hands, forearms, face, and neck.
- After each use (or day), wipe down and or HEPA vacuum the immediate work area and equipment to prevent accumulation of nanoparticles.
Spill and Accident Procedures:

Health Threatening Emergencies (ex. Fire Explosion, Serious Injury, or other Immediate Danger)
1. CALL 9-911 (286 in School of Medicine) for the Fire Department.
2. Alert people in the vicinity, activate local alarm systems.
3. Evacuate the area.
4. REMAIN NEARBY TO ADVISE EMERGENCY RESPONDERS.
5. Once personal safety is established, call EH&S at 725-9999 (or in the School of Medicine, x286) and proceed with local notifications, below.

If Personnel Exposed:
1. Remove exposed/contaminated individual(s) from area, unless unsafe to do so because of (a) medical condition of victim(s), or (b) potential hazard to rescuer(s).
2. If immediate medical attention is required, notify SU Emergency 9-911 (or 286 at the School of Medicine).
3. Notify EH&S to report the potential exposure by calling 5-9999 (or in the School of Medicine, x286).
4. Administer First Aid as appropriate.
5. Flush contamination from eyes/skin using the nearest emergency eyewash /shower for a minimum of 15 minutes. Remove any contaminated clothing.
6. Take copy of MSDS(s) of chemical(s) to hospital with victim.
7. Contact EH&S’s Occupational Health Center at (650) 725-5308 for follow-up.

Non-Health Threatening Emergencies (ex. spills requiring cleanup assistance)
In the event of a spill or release, which may or has impacted the environment (storm drain, soil, air outside the building), or spill or release that cannot be cleaned up by local personnel:
1. Notify Stanford Responders: Call Notify Stanford Responders: Call 725-9999 (286 in the School of Medicine) (24 hours/day, 7 days/week).
2. Provide local notifications to your supervisor.

Small Spills/Local Cleanup:
In the event of a minor spill or release that can be cleaned up by local personnel using readily available equipment (absorbent, available from EH&S in Small Spill Kit):
1. Notify personnel in the area and restrict access. Eliminate all sources of ignition.
2. Review the MSDS for the spilled material, or use your knowledge of the hazards of the material to determine the appropriate level of protection.
3. Wearing appropriate Personal Protective Equipment, clean up spill involving nanomaterials using wet methods and/or HEPA vacuum. DO NOT SWEEP SPILLED OR DRIED NANOMATERIALS. Collect spill cleanup materials in a tightly closed container. Manage spill cleanup debris as Hazardous Waste.
4. If greater than 30 ml, or if it will take longer than 15 minutes for you to clean-up, immediately call EH&S at 725-9999 (or in the School of Medicine, x286) to report the spill, and notify your supervisor.
5. Submit on-line waste pickup request to EH&S.

Waste Disposal:
- Manage nanoparticle wastes, including contaminated lab debris, as a part of your normal laboratory Hazardous Waste stream.
- Collect and store waste materials in a tightly closed container. Include information describing the base nanoparticle materials on the waste tag.
<table>
<thead>
<tr>
<th>#9</th>
<th>Training Requirements:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><strong>General Training (check all that apply):</strong></td>
</tr>
<tr>
<td></td>
<td>□ General Safety &amp; Emergency Preparedness (EHS-4200)</td>
</tr>
<tr>
<td></td>
<td>□ Chemical Safety for Laboratories (EHS-1900)</td>
</tr>
<tr>
<td></td>
<td>□ Other:__________________________</td>
</tr>
</tbody>
</table>

| Location Where Records Maintained: |

| #10 | Approval Required: Identify any tasks that require prior approval by the PI/ Laboratory Supervisor (e.g., use of Restricted Chemical and other higher hazard chemicals, and running of higher hazard operations). Refer to [http://chemtoolkit.stanford.edu/RestrictedChem](http://chemtoolkit.stanford.edu/RestrictedChem) for more information. |