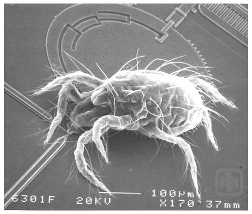
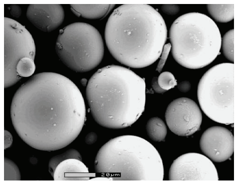
# The Scale of Things – Nanometers and More

## Things Natural



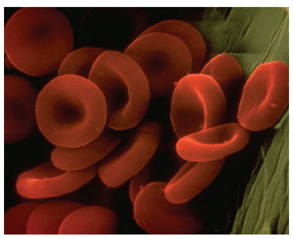

**Dust mite**
200 µm

**Ant**
~ 5 mm

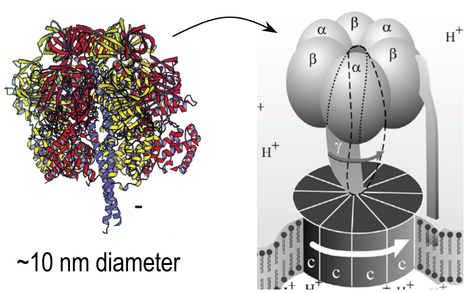


**Fly ash**
~ 10-20 µm

**Human hair**
~ 60-120 µm wide

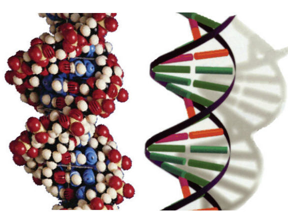


**Red blood cells**
(~7-8 µm)

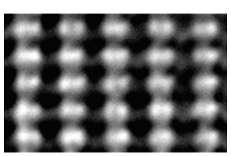



~10 nm diameter

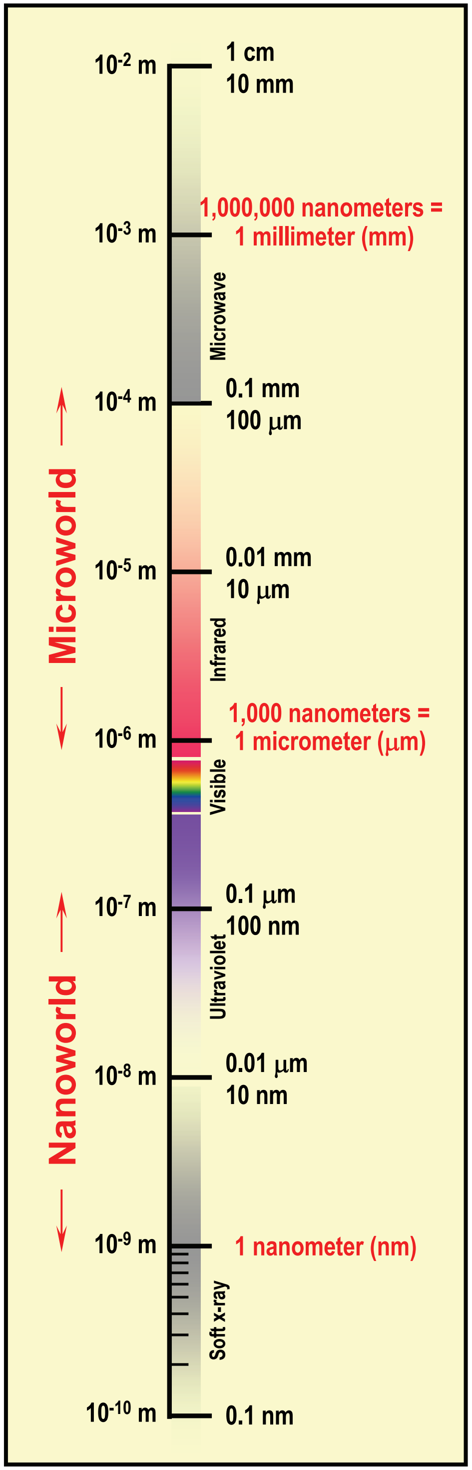
**ATP synthase**



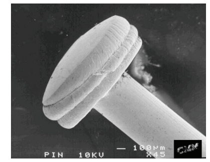
**DNA**
~2-1/2 nm diameter



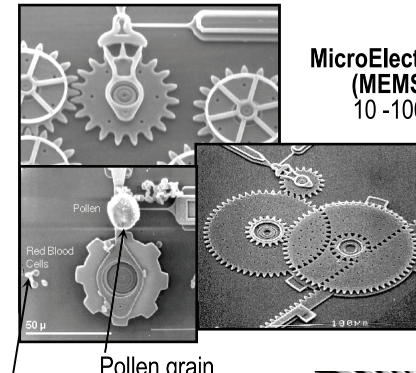
**Atoms of silicon**
spacing 0.078 nm




## Things Manmade

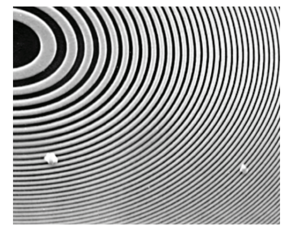


**Head of a pin**
1-2 mm

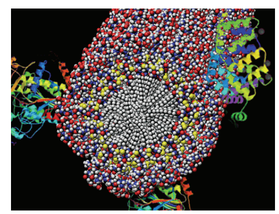



Pollen grain
Red blood cells

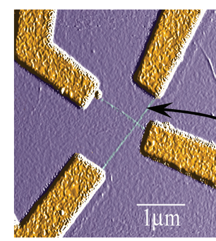
**MicroElectroMechanical (MEMS) devices**
10 -100 µm wide



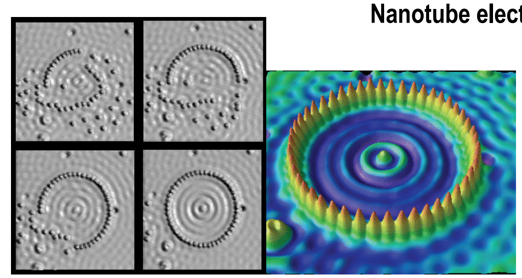
**Zone plate x-ray "lens"**
Outer ring spacing ~35 nm



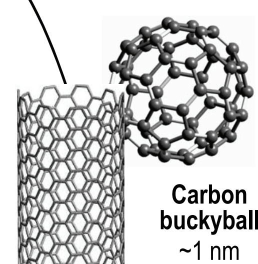
**Self-assembled, Nature-inspired structure**
Many 10s of nm




**Nanotube electrode**



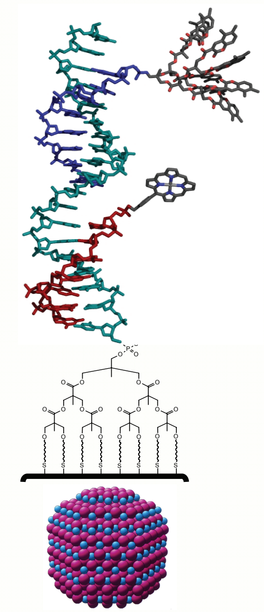
**Quantum corral of 48 iron atoms on copper surface positioned one at a time with an STM tip**
Corral diameter 14 nm



**Carbon nanotube**
~1.3 nm diameter

**Carbon buckyball**
~1 nm diameter

### The Challenge



*Fabricate and combine nanoscale building blocks to make useful devices, e.g., a photosynthetic reaction center with integral semiconductor storage.*

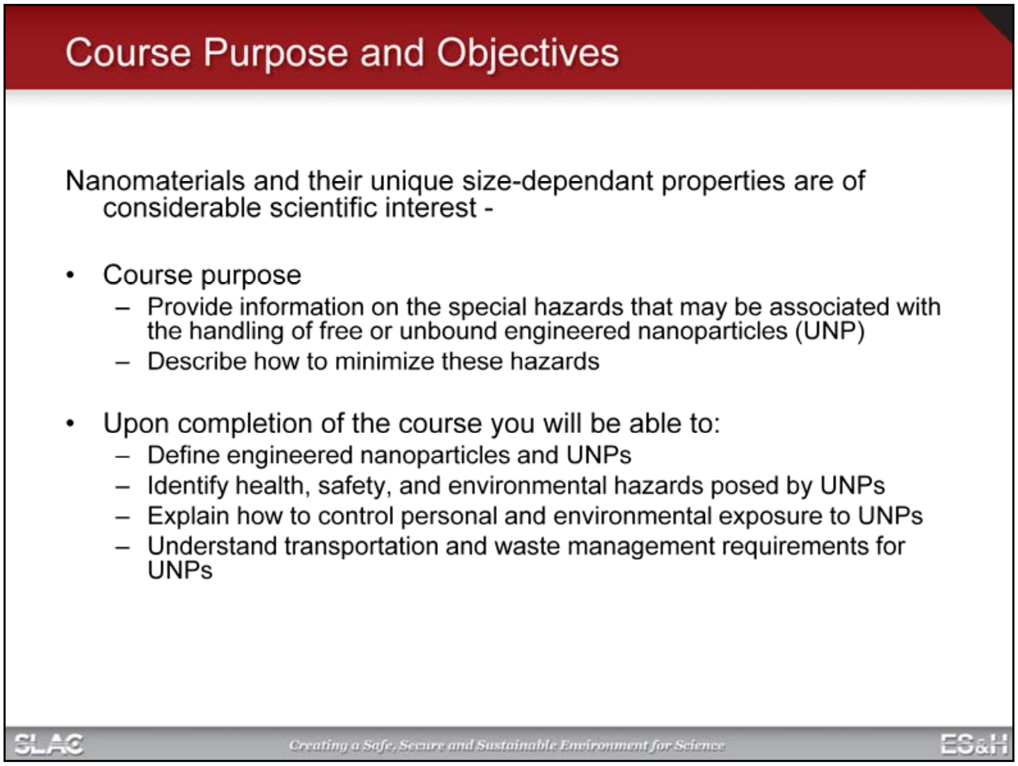

*Office of Basic Energy Sciences*
*Office of Science, U.S. DOE*
*Version 05-26-06, pmd*

SLAC
NATIONAL ACCELERATOR LABORATORY

# Nanomaterial Laboratory Safety

ES&H Course 161

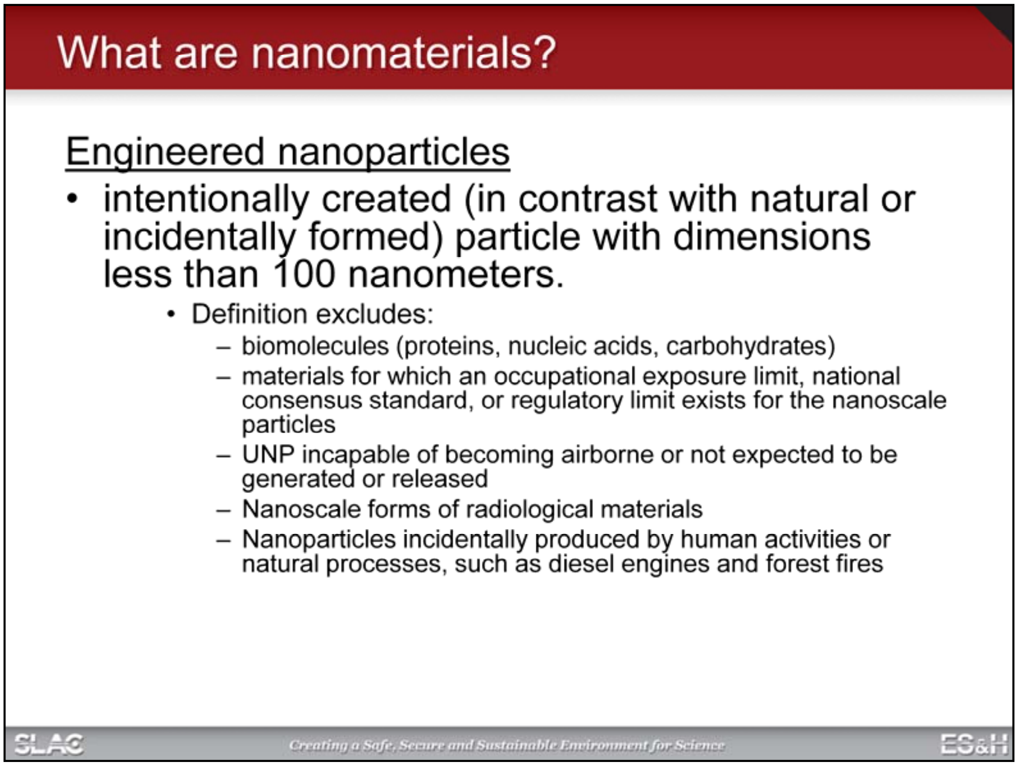
Rev. 12/16/2010




Nanoscale materials are of considerable scientific interest because some material properties can change at this scale. These changes challenge our understanding of hazards, and our ability to anticipate, recognize, evaluate, and control potential health, safety, and environmental risks.

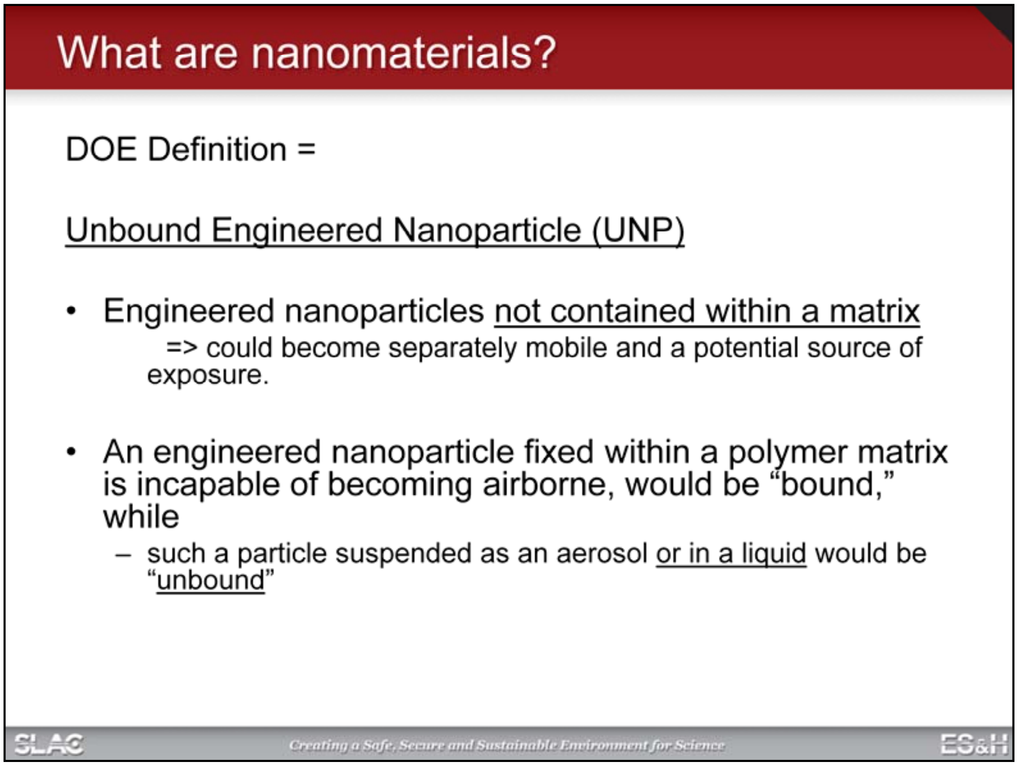
This course will provide information on the special hazards that may be associated with the handling of free or unbound engineered nanoparticles (UNP), and describe SLAC policies and controls for managing environmental, safety, and health concerns associated with laboratory activities involving nanomaterials.

SLAC staff who work with nanomaterial in laboratories (nanoparticle workers and their supervisors) must complete this course upon initial assignment. Visiting scientists, guest researchers, and other lab users who are not SLAC employees or subcontractors must take ES&H Course 161 or demonstrate that they understand applicable chemical hygiene principles. This can be accomplished by providing acceptable proof of nanomaterial laboratory safety training from another institution or passing an exam.

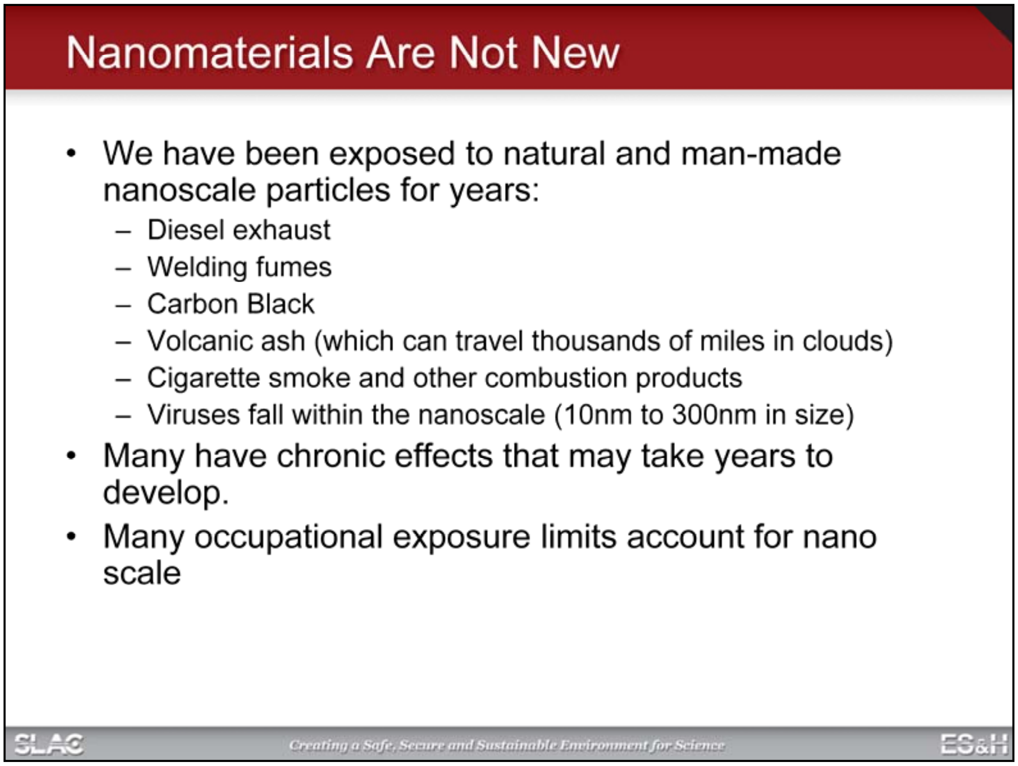



The scope of SLAC's Nanomaterial safety plan is concerned with:

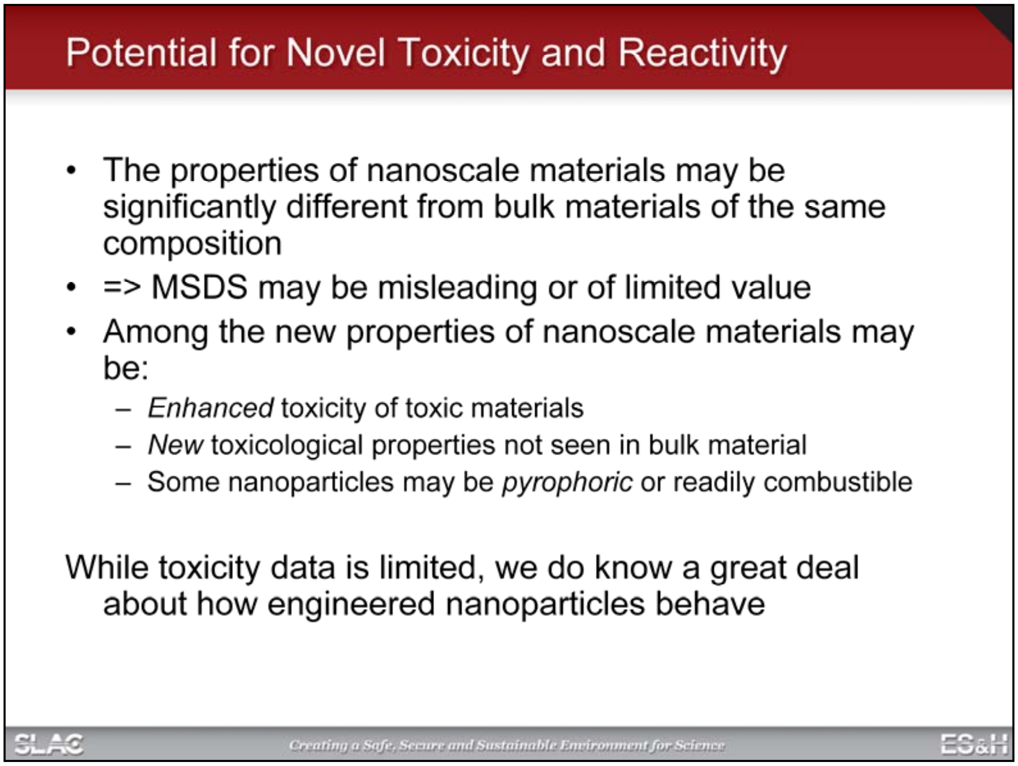
*Engineered* nanoparticles, that is, intentionally created – in contrast with natural or incidentally formed – engineered nanomaterials with dimensions of less than 100 nanometers. This definition excludes biomolecules (proteins, nucleic acids, and carbohydrates) and materials for which an occupational exposure limit (OEL), national consensus, or regulatory standard exists. Nanoscale forms of radiological materials are also excluded from this definition.




***Unbound engineered nanoparticles (UNP)*** are defined by the DOE to mean those engineered nanoparticles that, under reasonably foreseeable conditions encountered in the work, are not contained within a matrix that would be expected to prevent the nanoparticles from being separately mobile and a potential source of exposure. An engineered nanoparticle dispersed and fixed within a polymer matrix, incapable, as a practical matter, of becoming airborne, would be "bound", while such a particle suspended as an aerosol or in a liquid would be "unbound".




Humans have always been exposed to nanoscale particles via dust storms, volcanic eruptions, and other natural processes. Human activity and technological advancement has increased the variety of nanoparticles to which we are exposed. While the body is well adapted to protect itself from exposure to tiny particles, and the vast majority cause little ill effect, some can cause appreciable harm and many have chronic effects that may take years to develop.




The properties of nanoparticels are often strikingly different from the properties of the same material in bulk, which forms the motivation for our scientific interest.

It should be noted that MSDSs may be misleading and should be considered of limited value when based on the bulk properties of the material, which has often proven to be the case.

Among the new properties of nanoscale materials may be:

- *Enhanced* toxicity of toxic materials
- *New* toxicological properties not seen in bulk material
- Some nanoparticles may be *pyrophoric* or readily combustible

Nanotoxicology is an emerging field, and early work was plagued by methodological problems. Our understanding is beginning to coalesce however, and we do know a great deal about how engineered nanoparticles behave. We will review some aspects to motivate our concern regarding the potential occupational hazards of nanoparticles.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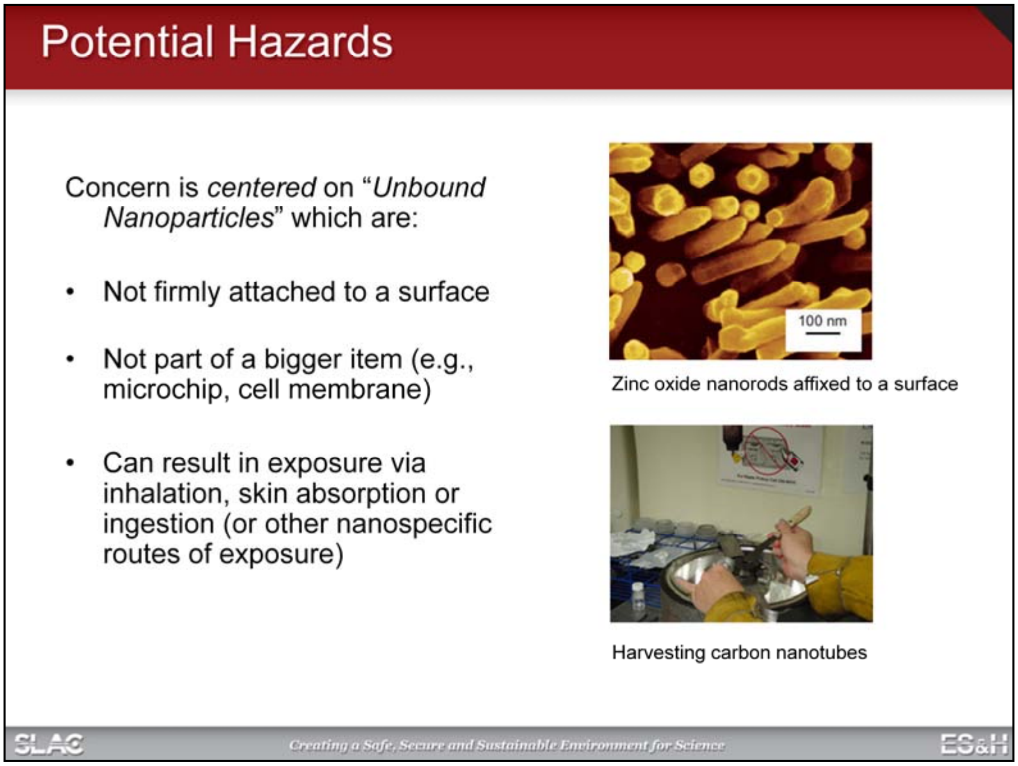
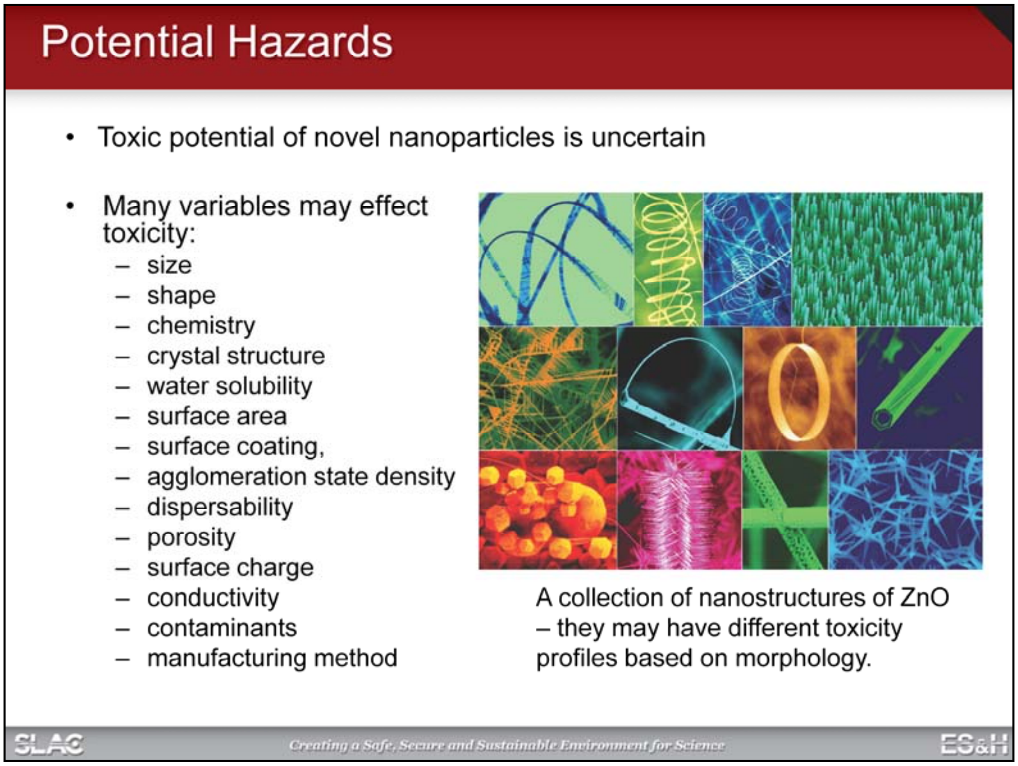
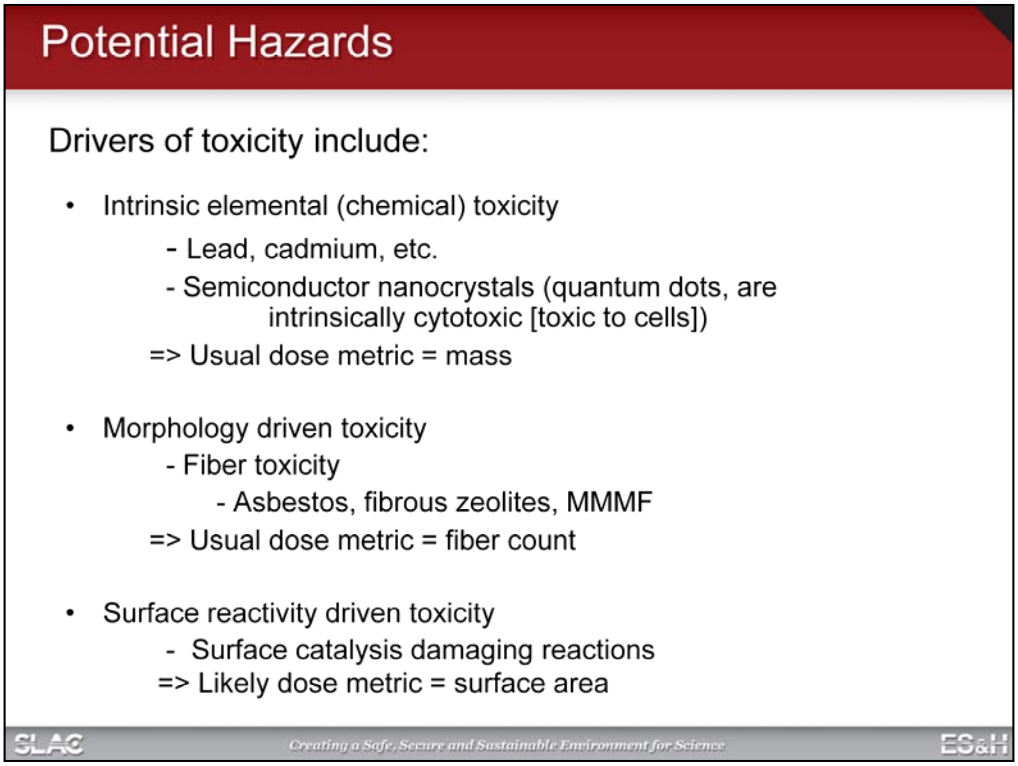



We are most concerned with unbound nanoparticles because they are capable of being dispersed. Routes of occupational exposure to free nanoparticles can occur by inhalation, skin absorption or ingestion, and we are most concerned about inhalation where their small size allows nanoparticles to deposit in the head airways and reach deep into the lungs.

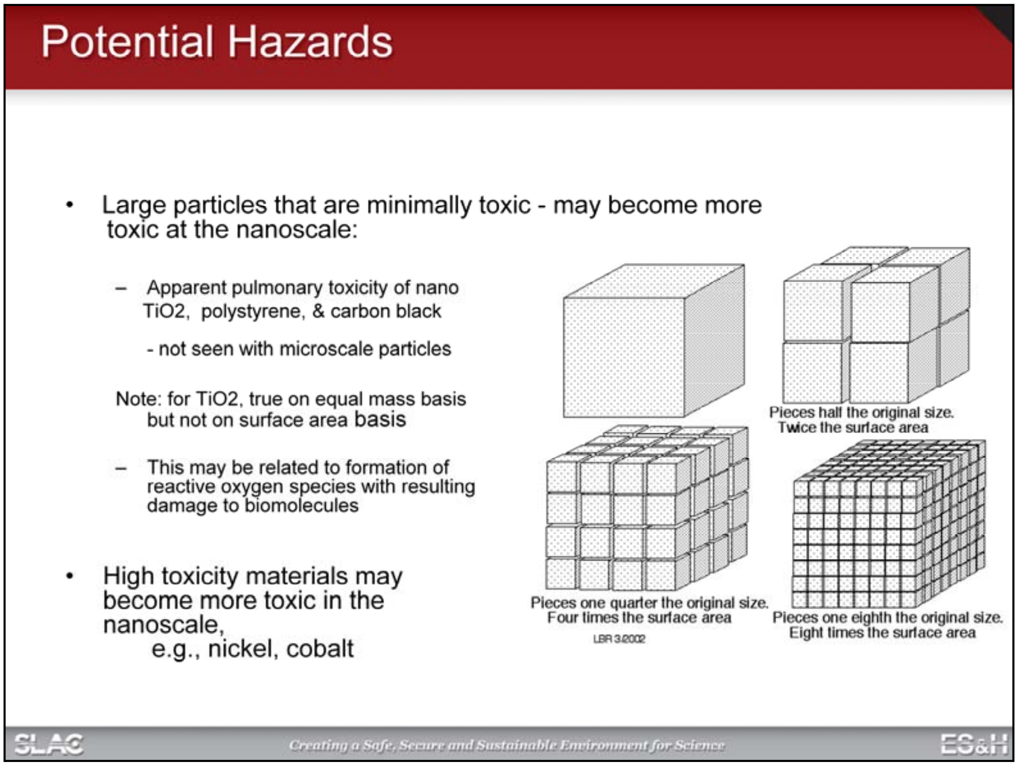



The toxic potential of novel nanoparticles is not easily characterized and it is difficult to generalize.  A wide range of chemistries are used in nanoparticle production, especially for research purposes, and the potential structures are almost unlimited. The photomicrographs above show various morphologies of zinc oxide, each one of which may have a different potential toxicity.



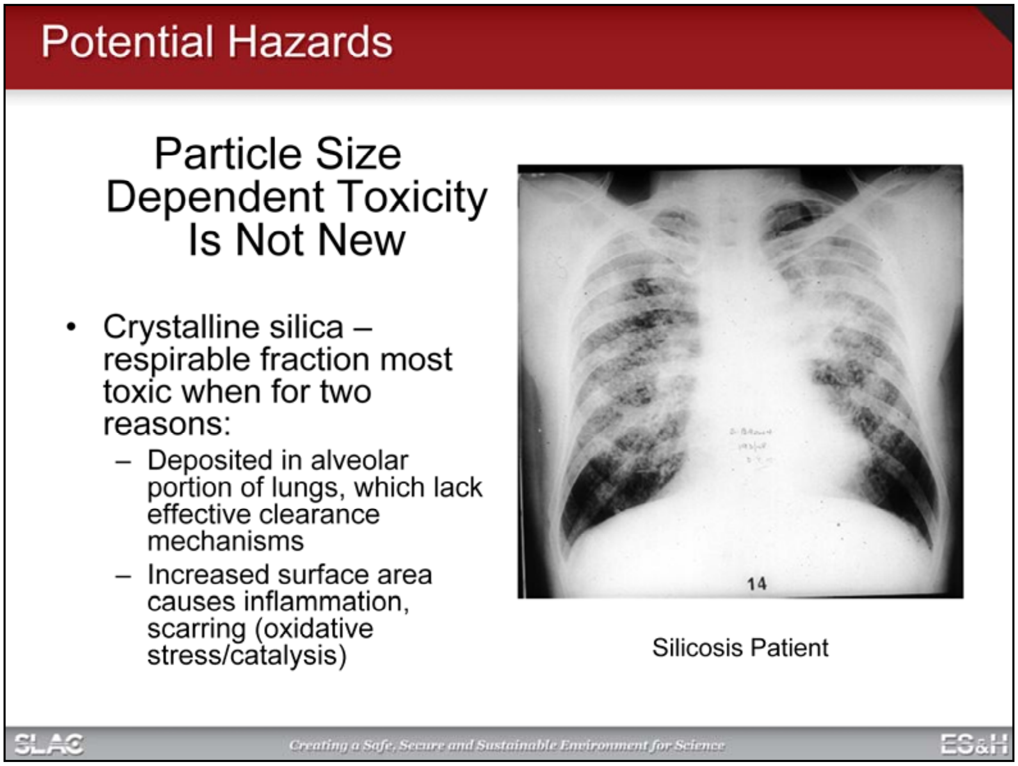

Drivers of nanoparticle toxicity include:

1. **Intrinsic elemental (chemical) toxicity** – For usually soluble materials, individual atoms may or ions may interfere with biological systems. Metals such as lead and cadmium are known to be toxic upon inhalation, ingestion or dermal exposure. Many uncoated quantum dots are intrinsically cytotoxic due to their metal content (e.g., lead, cadmium, selenium, etc.), and it has been suggested that their toxicity exceeds the sum of their components toxicity.
   Toxicological effects normally correlate to the mass of the material absorbed by the individual.
2. **Morphology driven toxicity** – Fiber toxicity is an example; asbestos is a good example of a toxic nanomaterial, causing lung cancer and other diseases. Asbestos exists in several forms, with slight variations in shape and chemistry yet significantly varying toxicity. Fibrous zeolites and man-made mineral fibers are additional examples.
   Toxicological effects normally correlate to the number of fibers absorbed by the individual.
3. **Surface reactivity driven toxicity** – Surface area is the key factor in catalysis and the generation of reactive oxygen species is enhanced by particles of very high surface area. See next slide.



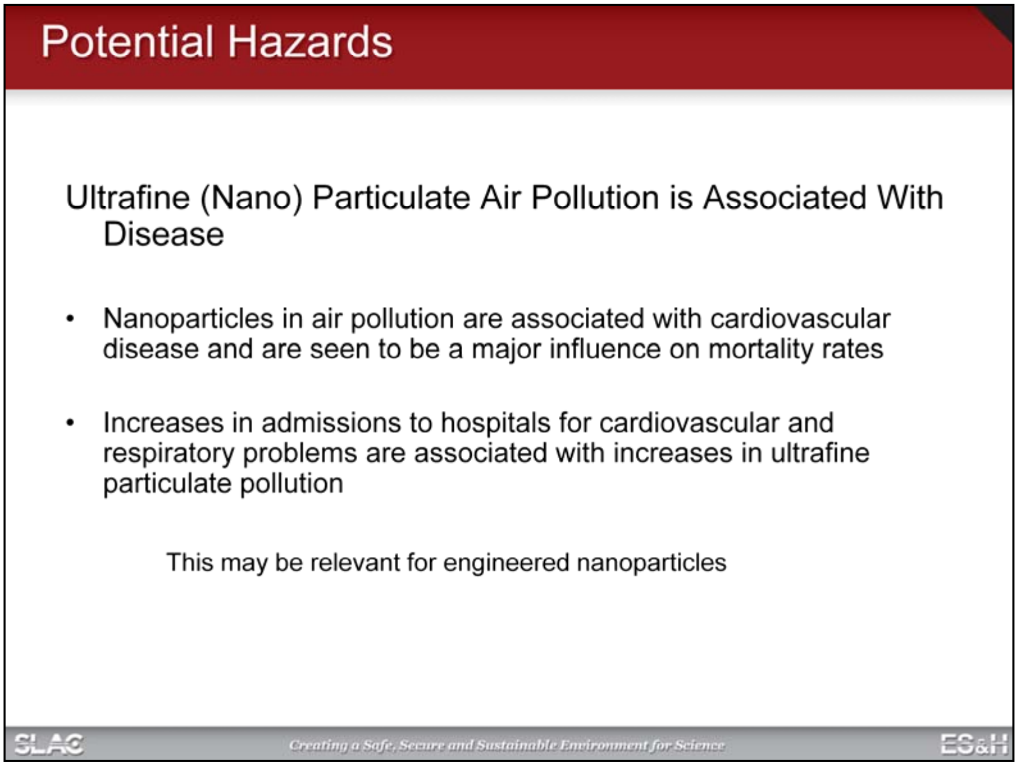

For a given mass of particles, as the diameter of the particles decreases the number of particles increases exponentially and the specific surface area increases linearly. As particle size decreases below 10 nm, the number of molecules on the surface of the particle increases rapidly, at 4 or 5 nm roughly half of the molecules are on the surface. For a single walled carbon nanotube, every atom is on the surface.

There is significant evidence that many nanoparticles are uncharacteristically toxic when compared to their bulk properties due to the accelerated generation of reactive oxygen species that lead to bimolecule damage, inflammation, and even cell death.



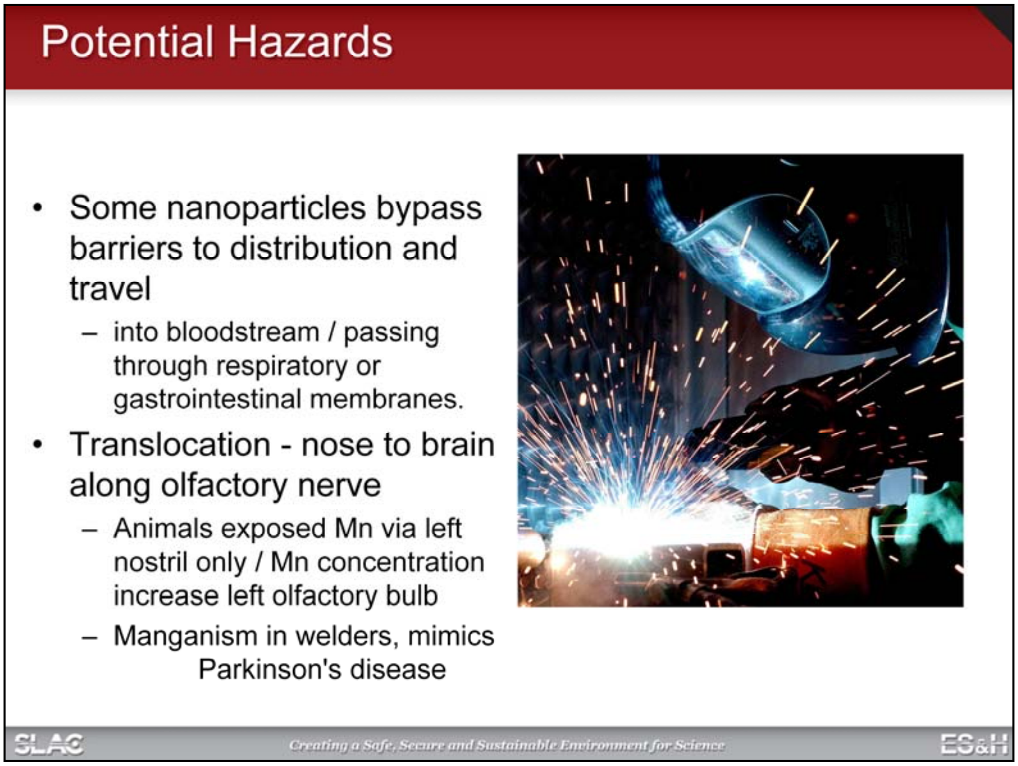

X-ray of a patient suffering from fibrosis due to crystalline silica exposure

Silicosis is a dramatic example of particle size dependant toxicity. Micron sized crystalline silica particles are deposited in the upper respiratory tract with little effect. However smaller particles reach the alveolar spaces in the lungs where a cascade of effects leads to inflammation and lung scaring.



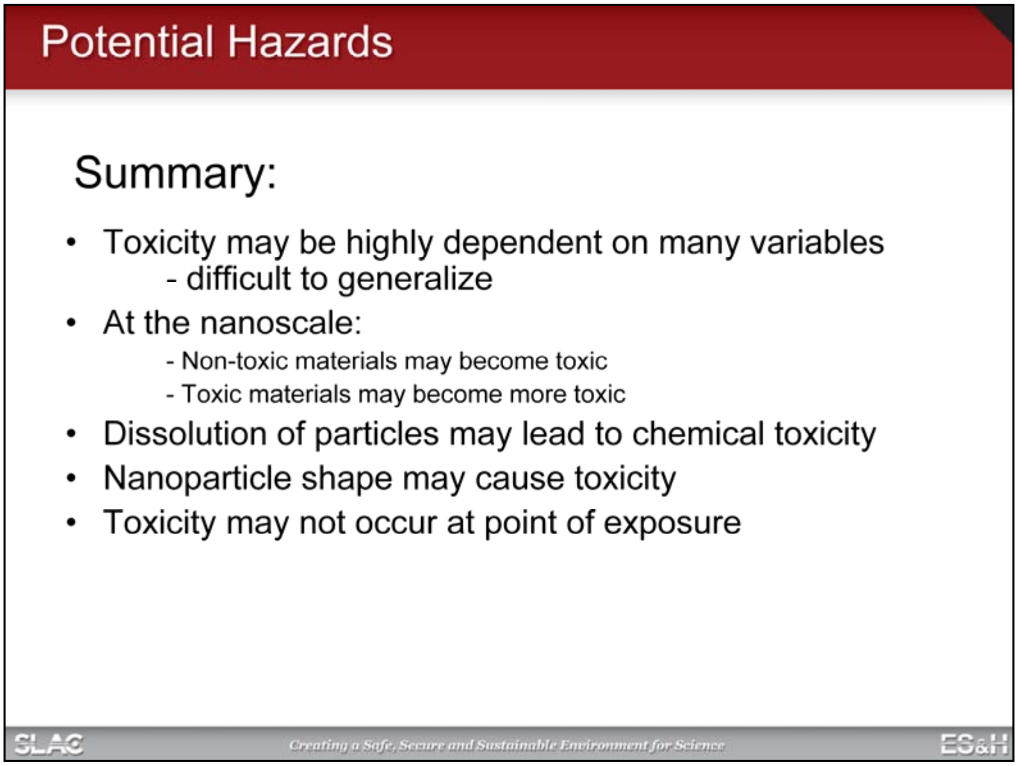

Nanoparticles in air pollution - cardiovascular disease and mortality rates:

- Atmospheric particle pollution from automobile exhaust seems to have a major influence on mortality, with a strong association between increased cardiopulmonary mortality and living near major roads.
- Measurements of nanoparticle concentration near highways shows an exponential decrease over several hundreds meters away from traffic.
- Childhood cancers were also found to be strongly determined by prenatal or early postnatal exposure to oil-based combustion gases, primarily engine exhaust .
- Professional drivers show elevated rates of heart attack.
- The correlation between ambient particles exposure and heart disease has been established for 15 years – e.g., hospital admission for cardiovascular illness were noted to increase on days with high concentrations of particles.




Nanoparticles have been shown to bypass normal body barriers to distribution in at least the following:

- Through intact skin – sometimes
- Static skin application - no penetration; flexed skin - some penetration (follicle penetration); nitrile gloves offer the best protection
- Through the gastrointestinal epithelium – yes
- Through respiratory tract – yes
- Along nerve axons from the nose to the brain - yes




Potential hazards of nanoparticles are summarized above.

It should be noted that there are currently no consensus occupational exposure limits for nanomaterials, although some occupational exposure limits do are affected by the ultrafine scale of the particles. Examples of the latter are: crystalline silica, and carbon black.

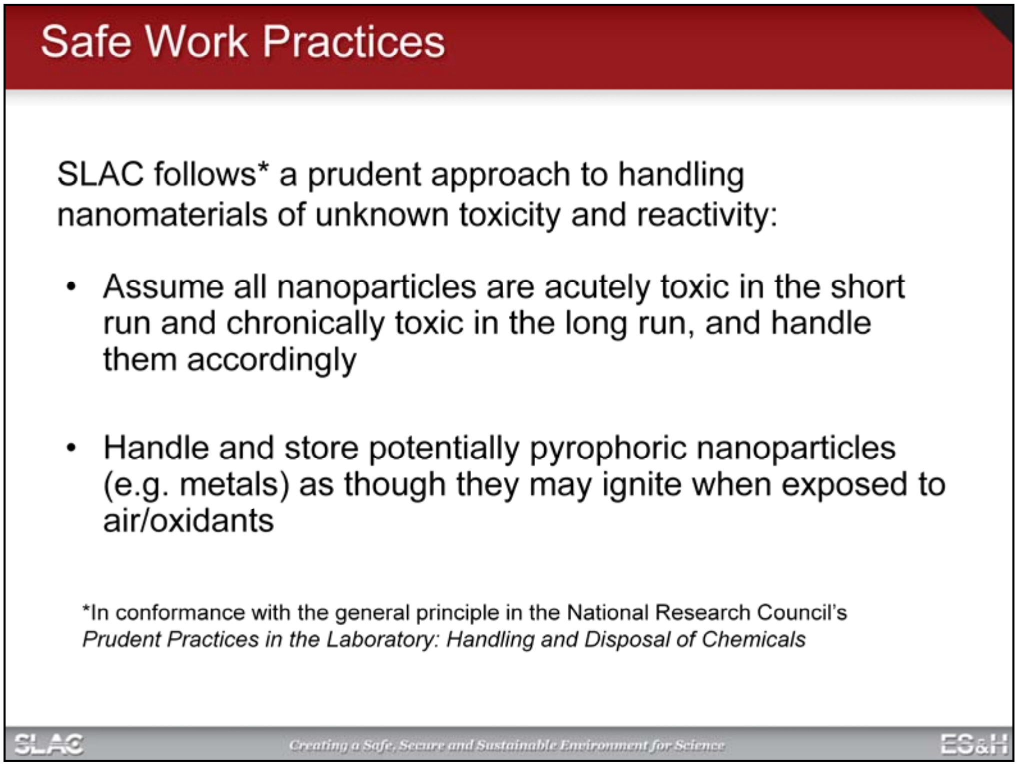
NOTE:

NIOSH has draft recommended exposure limits (RELs) for :

- 1.5 mg/m$^3$ fine $TiO_2$;
- 0.1 mg/m$^3$ ultrafine $TiO_2$
- Reflects greater inflammation & tumor risk of ultrafine on mass basis

For reference, the current American Conference of Industrial Hygienists (ACGIH) exposure limit (TLV, Threshold Limit Value) is 10 mg/m$^3$

# Safe Work Practices

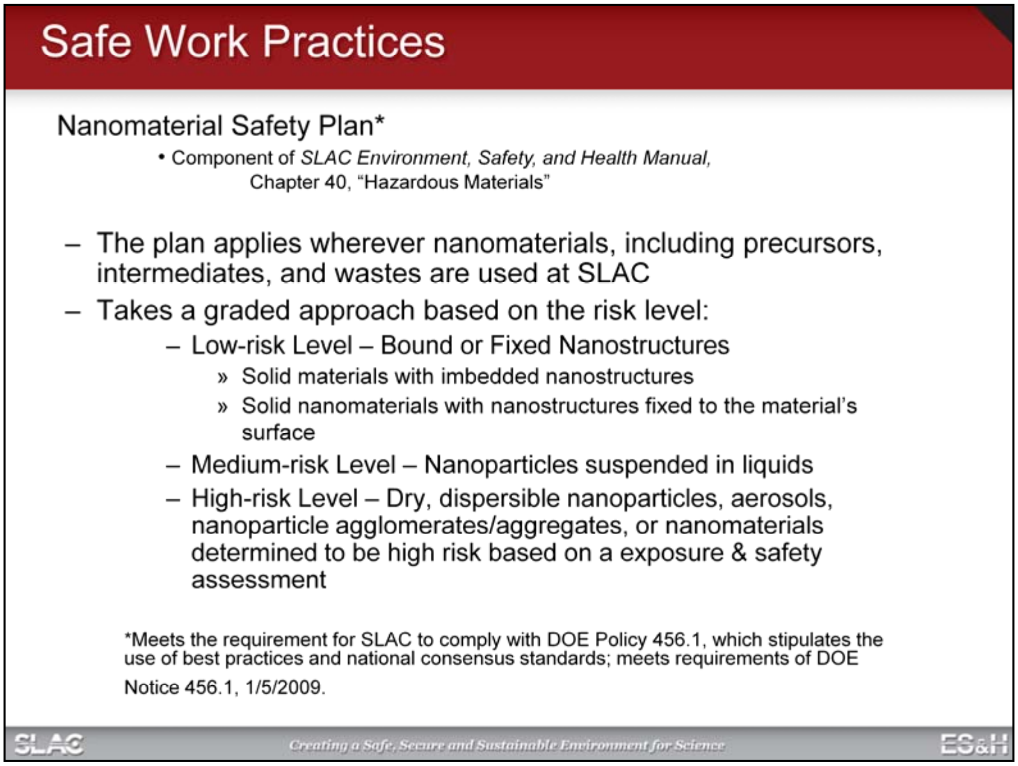



As a prudent measure, the SLAC Nanomaterial Safety Plan adopts the following approach:

- All nanoparticles are assumed to be acutely toxic in the short run and chronically toxic in the long run, and are to be handled accordingly
- Potentially pyrophoric nanoparticles (e.g. metals) are to be handled as though they may ignite when exposed to air or oxidants

Controls:

- Engineered controls work about as expected for nanoparticles
- Mechanical filters (HEPA) work exactly as predicted by classical filtration theory down to about 3 nm and fail progressively below this size
- Protective clothing works just about as expected – less air permeable fabrics do a better job of keeping out nanoparticles
- Effectiveness of gloves is still under investigation. They work pretty well (nitrile among the best), they may fail under some circumstances (can consider wearing two pair).




The Nanomaterial Safety Plan is found in Chapter 40 – Hazardous Materials of the SLAC Environment, Safety, and Health Manual. It can be accessed on line at:

http://www-group.slac.stanford.edu/esh/eshmanual/references/hazmatPlanNano.pdf

The plan takes a graded approach to safety based on the risk posed:

- Low-risk Level – Bound or Fixed Nanostructures
  - Solid materials with imbedded nanostructures
  - Solid nanomaterials with nanostructures fixed to the material's surface
- Medium-risk Level – Nanoparticles suspended in liquids
- High-risk Level – Dry, dispersible nanoparticles, aerosols, nanoparticle agglomerates/aggregates, or nanomaterials determined to be high risk based on a exposure & safety assessment

## Safe Work Practices

Assigned risk-level determines: required review / approval & controls:

| Risk | Proposal Reviewed */ Approved by | Controls and Work Practices |
|---|---|---|
| Low-risk Level | Division Safety Coordinator | NSC Approved SOPs |
| Medium-risk Level | Division Safety Coordinator | NSC Approved SOPs |
| High-risk Level | NSC | Project specific work plan |

NSC = SLAC Nanoscience Safety Committee

* Exposure and Safety Assessment - All nanomaterial work will be reviewed for ES&H concerns

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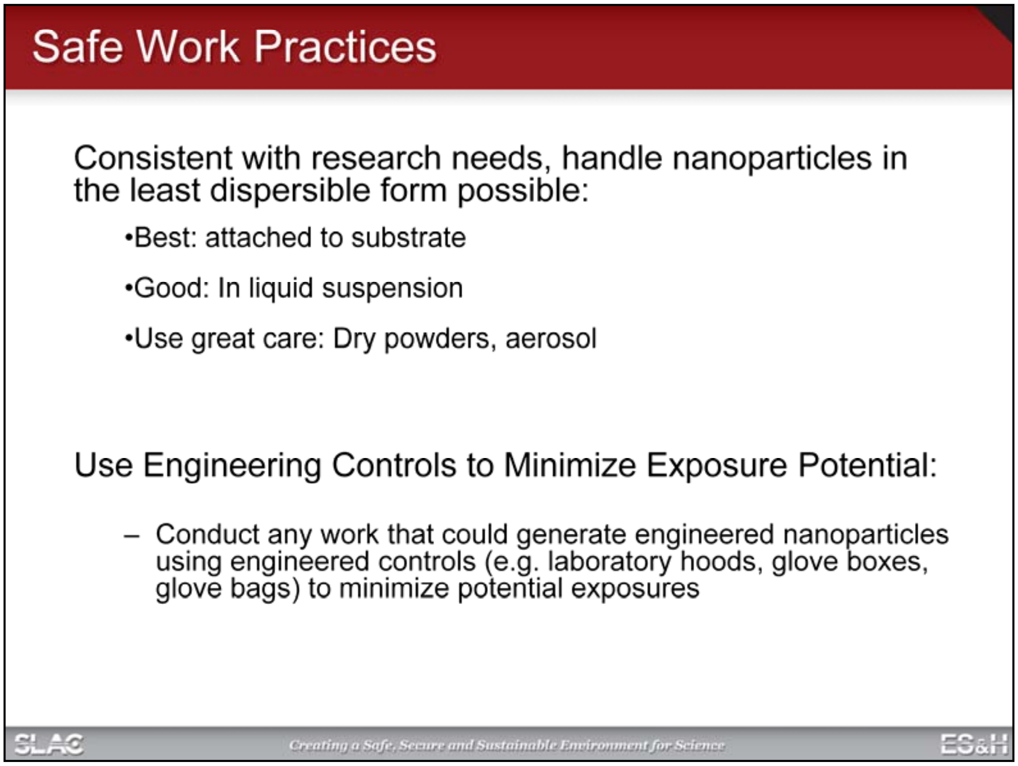
The nanomaterial risk-level determines the appropriate review, approval, and work controls required. The Safety Coordinator of the appropriate Division (e.g., SSRL, LCLS, etc.) must review ***every*** **low-** and **medium-risk** level for ES&H concerns – note that in practice, most such work falls into categories such that most can be approved to follow existing standard operating procedures.

All work with **high-risk** level nanomaterials must be reviewed and approved by the SLAC Nanoscience Safety Committee (NSC). In such cases, researchers must submit a draft work plan to the Division Safety Coordinator, who will present the information to the NSC and communicate any special controls or requirements to the researcher.

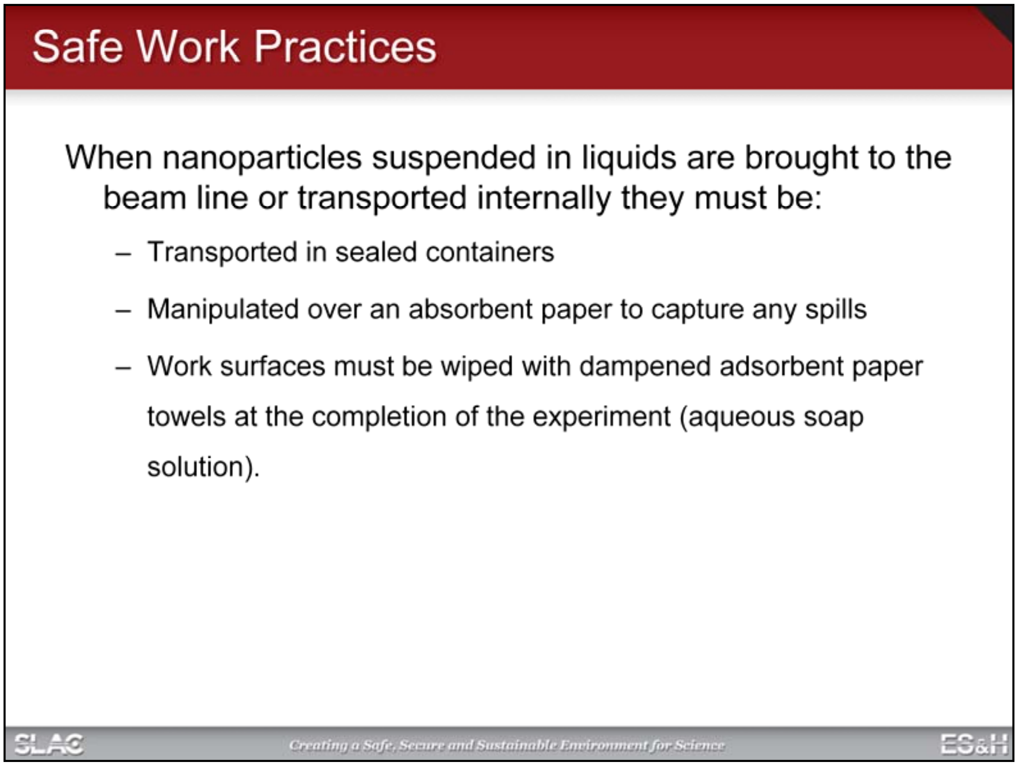
***Note***:

- No nanomaterials may be brought on-site or manufactured until approved by the Division Safety Coordinator.
- All work or research with nanomaterials may only be performed by personnel who are authorized by their division and who have been properly trained.



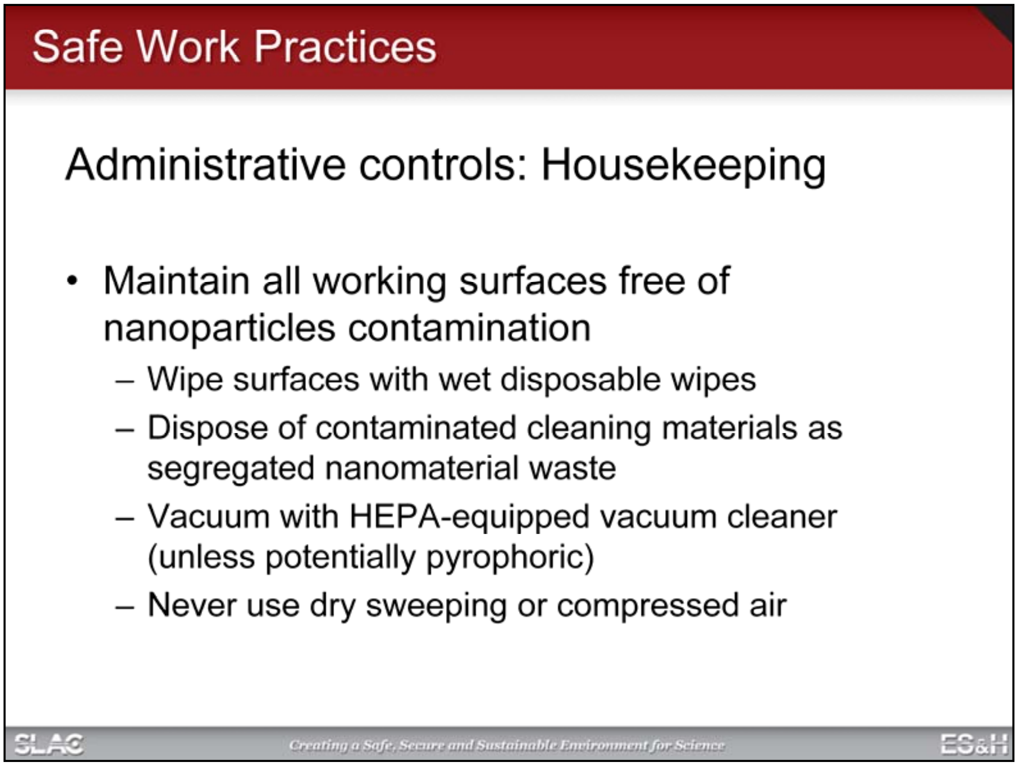

The least dispersible form of nanoparticles possible should be used that is consistent with research goals.

Conduct **any work** that **could generate engineered nanoparticles** using engineered controls (e.g. **laboratory hoods**, **glove boxes**, glove bags) to minimize potential exposures.



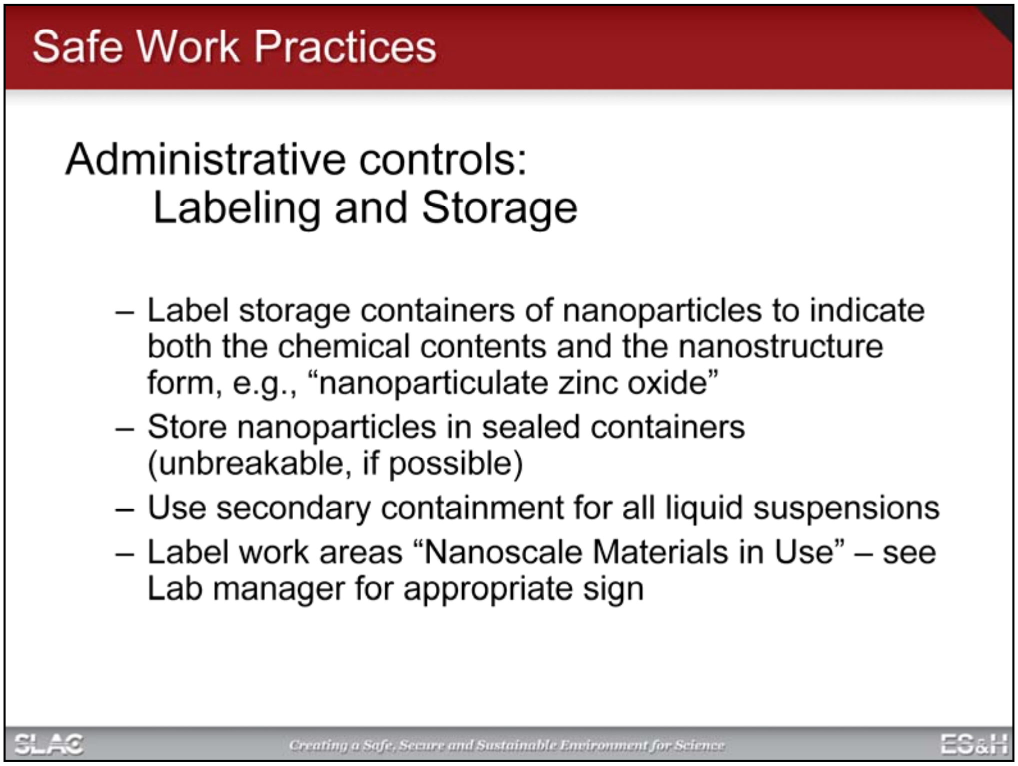

When nanoparticles suspended in liquids are brought to the beam line or transported internally within SLAC (e.g., between labs or from a lab to the beam line at SSRL or LCLS) they must be:

- Transported in sealed containers
- Manipulated over an absorbent paper to capture any spills
- Work surfaces must be wiped with dampened adsorbent paper towels at the completion of the experiment (aqueous soap solution)



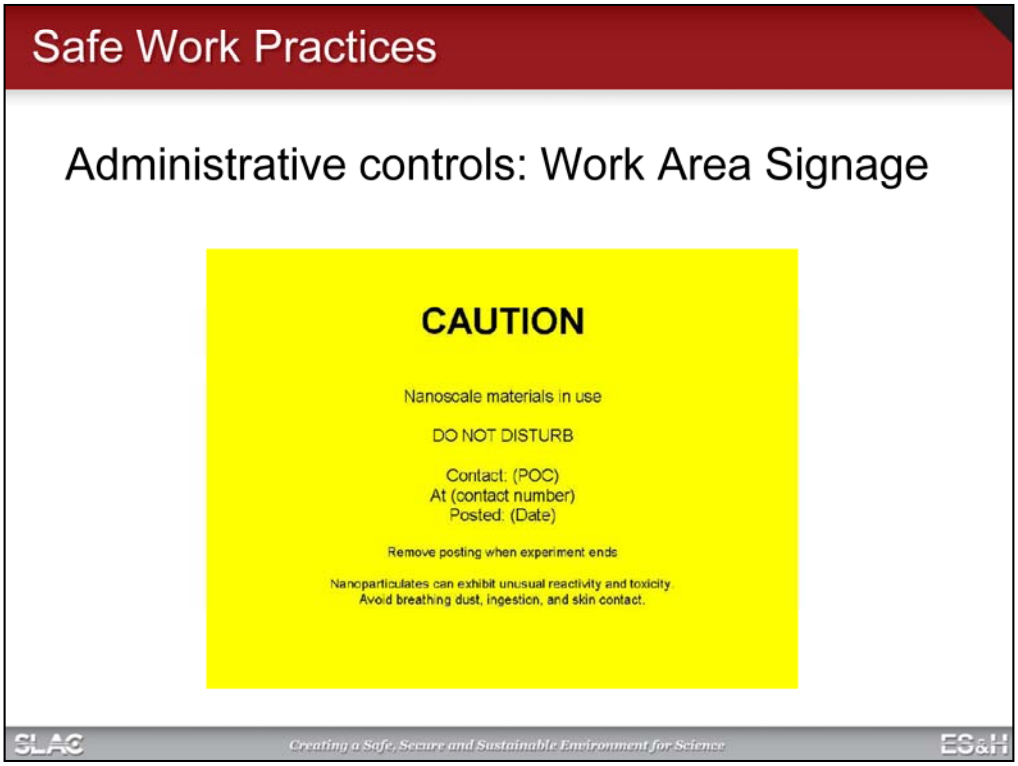

Good chemical hygiene housekeeping practices must be followed when working with nanoparticles:

- Wipe surfaces with wet disposable wipes
- Dispose of contaminated cleaning materials as **segregated nanomaterial waste**
- Vacuum with HEPA-equipped vacuum cleaner (unless potentially pyrophoric)
- Never use dry sweeping or compressed air

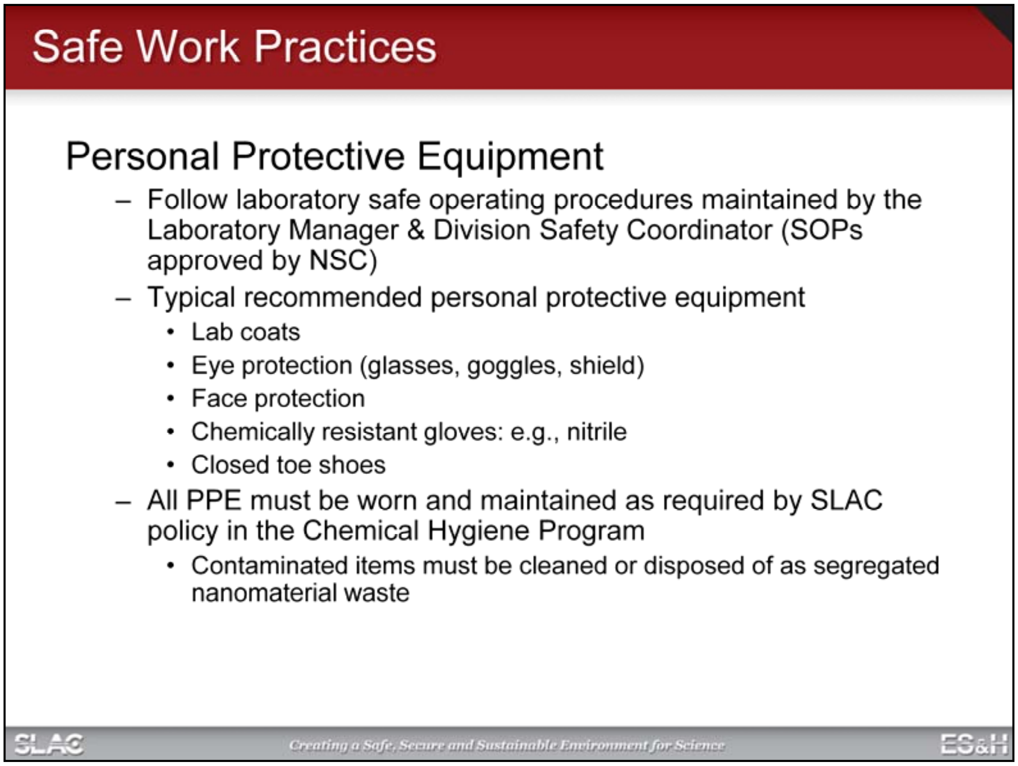



Labeling and Storage

- Label storage containers of nanoparticles to indicate both the chemical contents and the nanostructure form, e.g., “nanoparticulate zinc oxide”
- Store nanoparticles in sealed containers (unbreakable, if possible)
- Use secondary containment for all liquid suspensions
- Label work areas “Nanoscale Materials in Use” – see Lab manager for appropriate sign




Work area signage must be used as shown above. Appropriate signs can be provided by Safety Coordinators, Laboratory Managers, or control Operator at SSRL or LCLS.

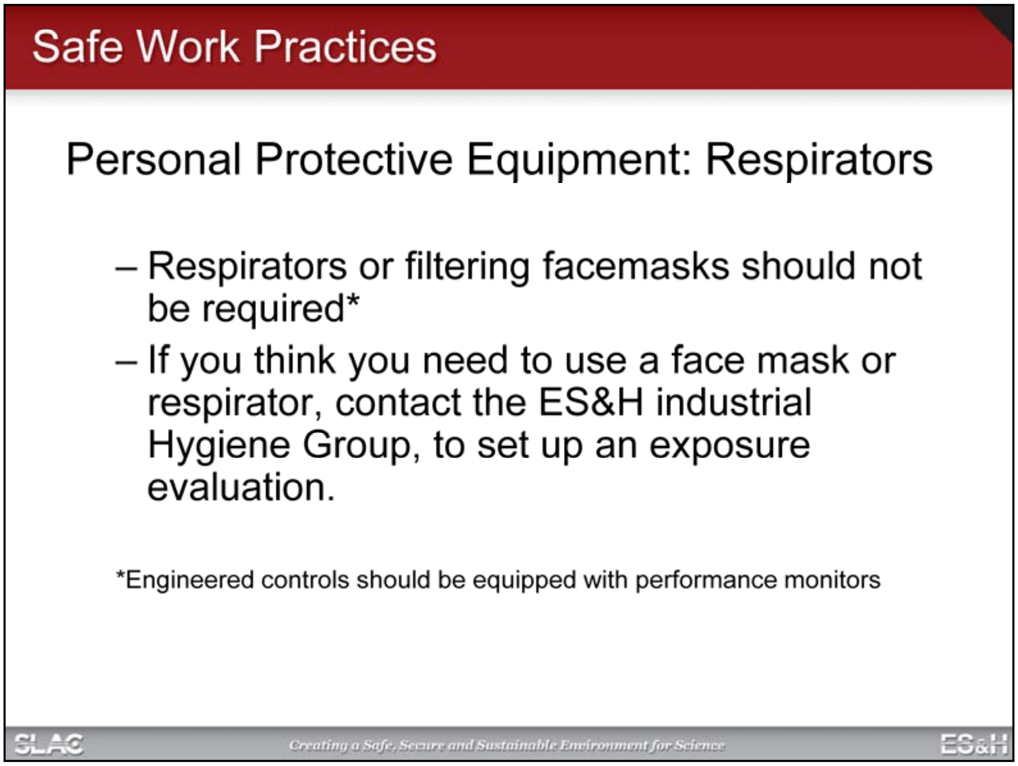



Personal Protective Equipment

- Follow laboratory safe operating procedures maintained by the Laboratory Manager and Division Safety Coordinator (SOPs approved by NSC)

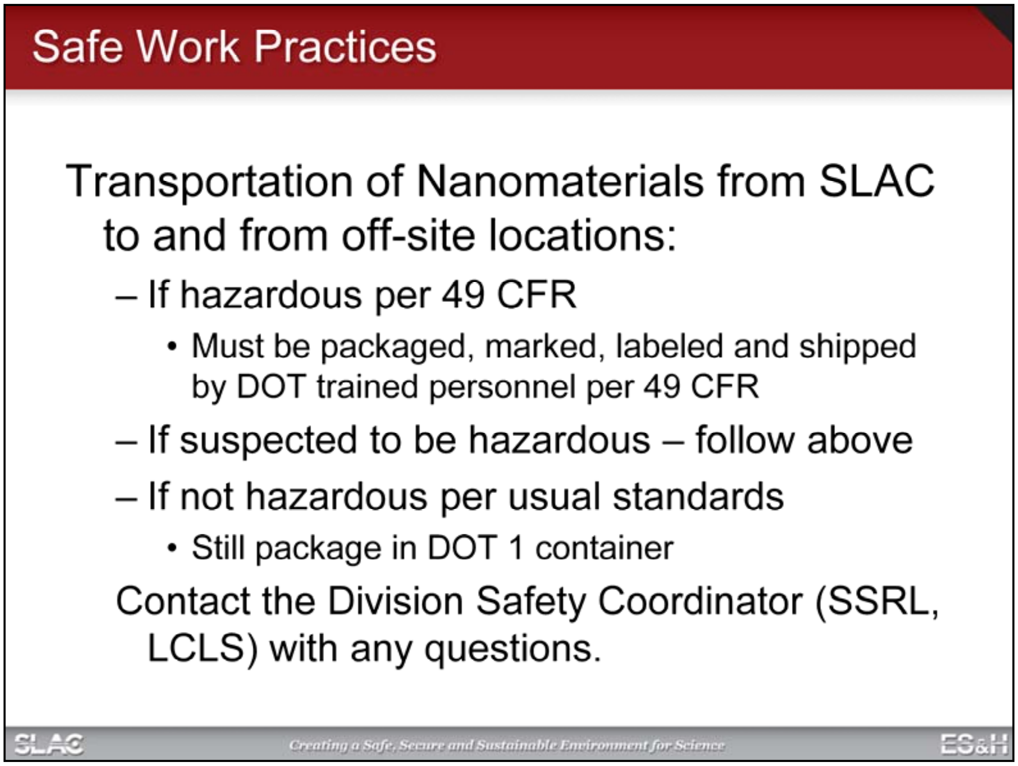
- Typical recommended personal protective equipment follow good chemical hygiene practice
  - Lab coats
  - Eye protection (glasses, goggles, shield)
  - Face protection
  - Chemically resistant gloves: e.g., nitrile
  - Closed toe shoes

- All PPE must be worn and maintained as required by SLAC policy in the Chemical Hygiene Program
  - Contaminated PPE must be cleaned or disposed of as segregated nanomaterial waste




Note - Respirators or filtering facemasks **should not be required**

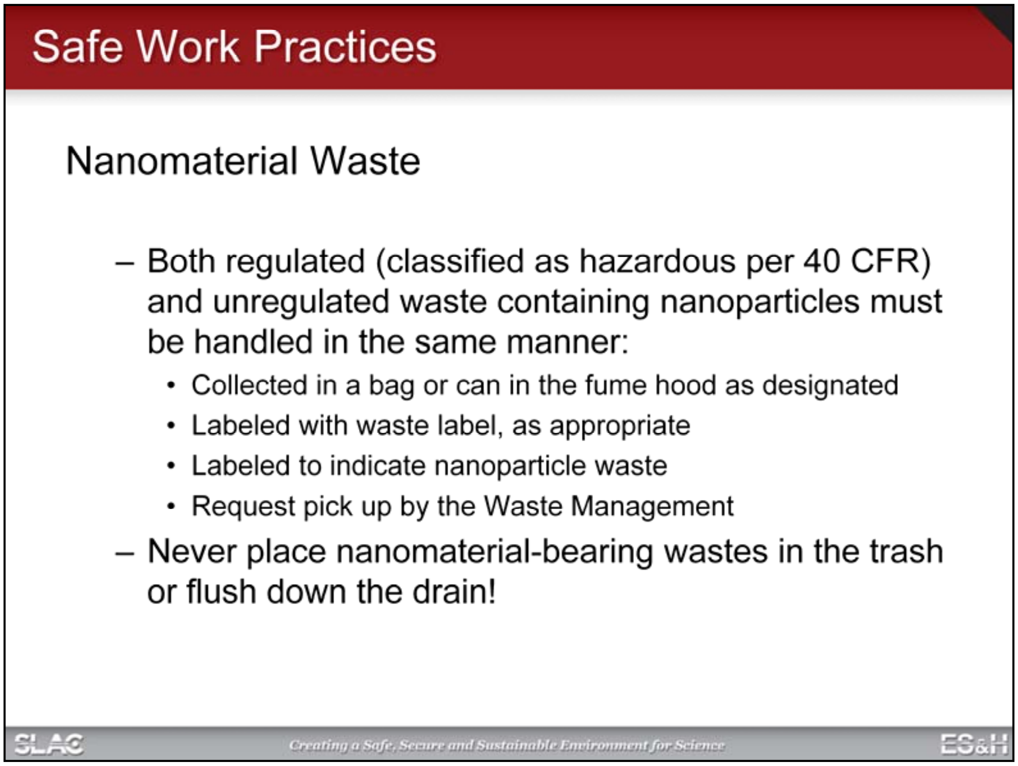
Engineered controls should be more than adequate for safety. However, if you think you need to use a face mask or respirator, **contact the ES&H industrial Hygiene Group**, to set up an exposure evaluation.




Transportation of Nanomaterials from SLAC to and from off-site locations:

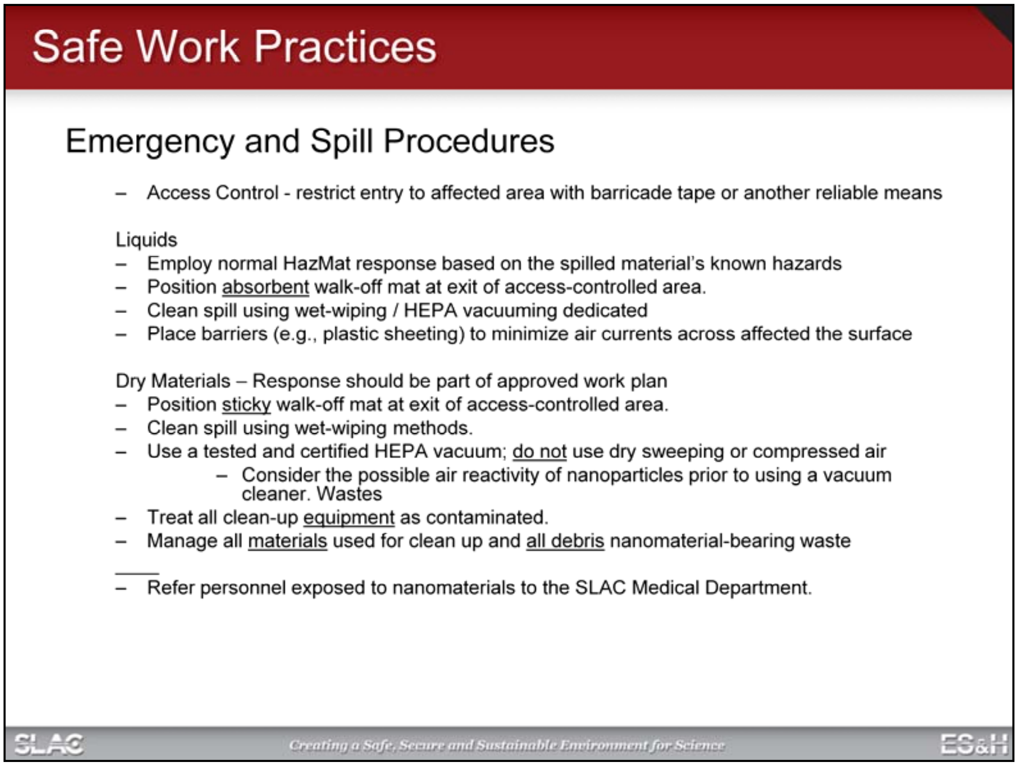
- If hazardous per federal regulations, package, mark, and ship per 49 CFR.

  ***Note*** that the material must be packaged, marked, labeled and shipped by DOT trained personnel per 49 CFR. There are DOT trained staff at SSRL, LCLS, and SLAC Shipping and Receiving – please contact the Safety Coordinator in the appropriate Division (e.g., SSRL, LCLS, etc.)
- If suspected to be hazardous – follow above
- If not hazardous per usual standards, still package in DOT 1 container (sealed container inner, absorbent, exterior container)
- Contact the Division Safety Coordinator (SSRL, LCLS) with any questions.



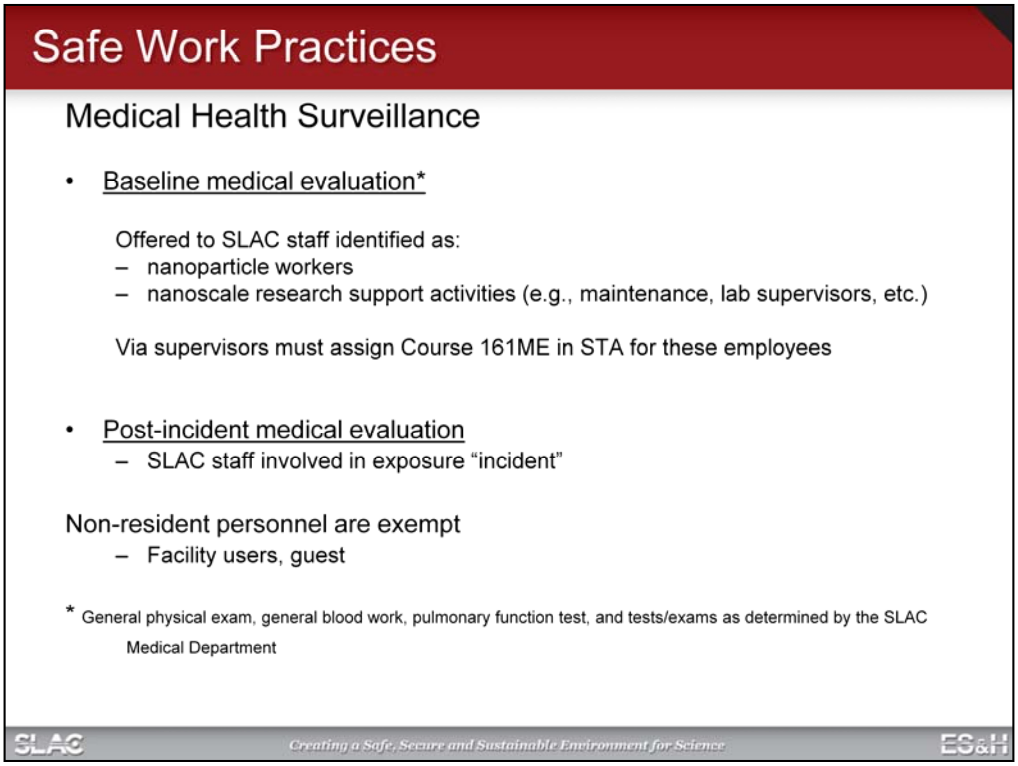

Nanomaterial Waste

- Both regulated (classified as hazardous per 40 CFR) and unregulated waste containing nanoparticles must be handled in the same manner:
    - Collected in a bag or can in the fume hood or work area as designated
    - Labeled with waste label, as appropriate
    - Labeled to indicate nanoparticle waste
    - Request pick up by the Waste Management
- Never place nanomaterial-bearing wastes in the trash or flush down the drain!
- Note: SLAC waste management will provide appropriate, labeled containers. Contact the Division Safety Coordinator (SSRL, LCLS) with any questions.

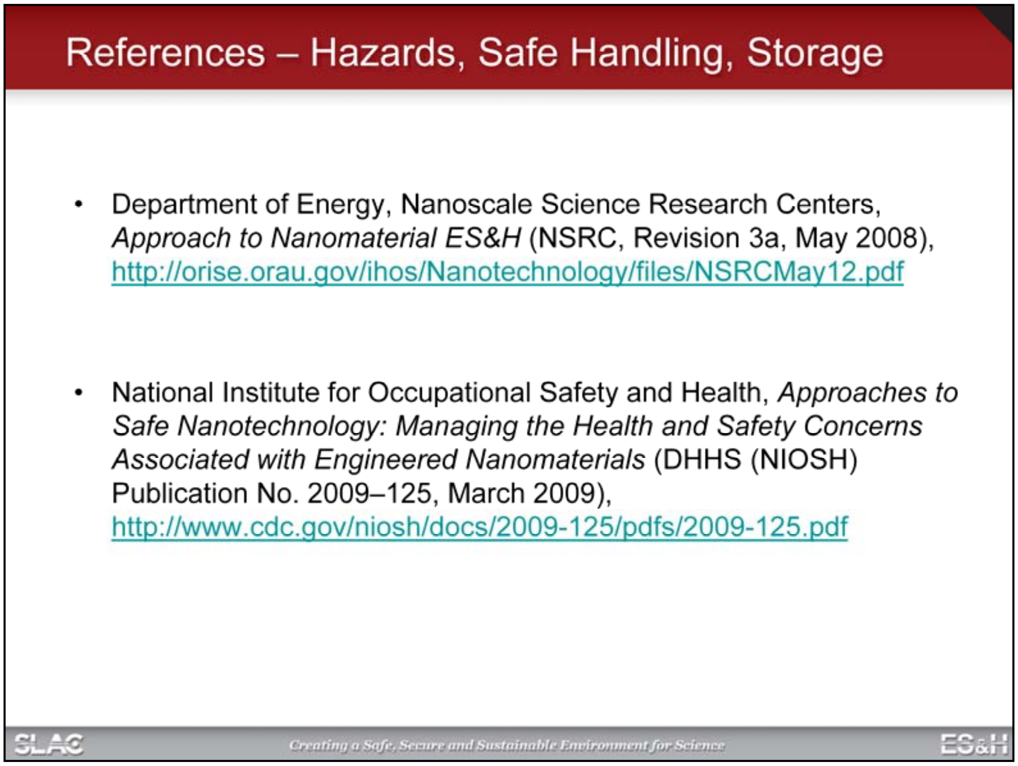



The appropriate emergency and spill procedures for nanoparticles are outlined above.

You are expected to understand the hazards of the material you are working with and to have planned for any potential spill or emergency before initiating the work. For example, work with nanoparticles suspended in liquids should be performed over an absorbent paper and wipes should be readily at hand. Internal transportation (lab to bench, or lab to beam line, etc.) of nanoparticles suspended in liquids should be in sealed containers.



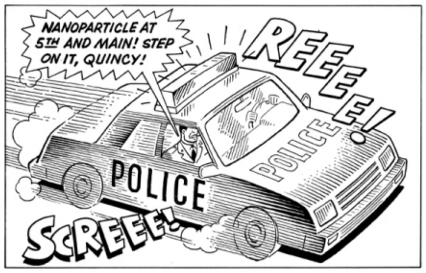

Baseline medical evaluations will be *offered* for SLAC staff designated as nanoparticle workers engaged in nanoscale science research or nanoscale research support activities. The baseline medical evaluation will include a comprehensive physical exam, pulmonary function test, and routine blood work. Other tests or exams will be offered at the discretion of the Medical Department. Non-resident personnel (for example, facility users) will be exempted from medical surveillance.




Useful references for additional information are provided above. The SLAC Nanomaterial Safety Plan can be accessed at:

http://www-group.slac.stanford.edu/esh/eshmanual/references/hazmatPlanNano.pdf

For your future reference, Table 1, “Requirements by Risk / Material Form” from the SLAC Nanomaterial Safety Plan is provided as an attachment. Table 1 summarizes required controls, review, and approval for nanomaterial work.




The New York Times
nytimes.com

January 14, 2007

BERKELEY LEGAL

## Teeny-Weeny Rules for Itty-Bitty Atom Clusters

By BARNABY J. FEDER

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SLAC NATIONAL ACCELERATOR LABORATORY

See attached reference

## Table 1 Requirements by Risk / Material Form

From SLAC Nanomaterial safety Plan

SLAC *Creating a Safe, Secure and Sustainable Environment for Science* ES&H

**Table 1** Requirements by Risk / Material Form

| | Risk / Material Form | | |
|---|---|---|---|
| | Low | Medium | High |
| Requirements | Bound or Fixed Nanostructures | Nanoparticles Suspended in Liquids | Dry Dispersible Nanoparticles and Agglomerates (or otherwise hazardous – see Section 3.1.3) |
| Review / Approval | SSRL Safety Coordinator | SSRL Safety Coordinator | NSC |
| PPE Requirements for Handling | Standard PPE required for the work area. No additional PPE is needed for this nanomaterial work. | Standard PPE required for the work area plus:<br>▪ Gauntlet-type nitrile gloves or wrist length disposable nitrile gloves with extended sleeves<br>▪ Eye protection: safety glasses with side shields for handling powders only. Chemical splash goggle for handling either powders or liquids. | |
| Handling Requirements | For work outside of a HEPA-filtered exhaust hood:<br>▪ No mechanical abrasion<br>▪ No thermal stresses that might crack binder material<br>▪ Cover samples when practical to protect the sample, for example use a slide cover<br>▪ Store in sealed container when not in use | If there is a potential for particle aerosol formation, manipulate within a HEPA-filtered laboratory exhaust hood over adsorbent paper to capture any spills.<br>Solutions brought to the beam line must be:<br>▪ Transported in sealed containers<br>▪ Manipulated over an absorbent paper to capture any spills<br>Work surfaces must be wiped with dampened adsorbent paper towels at the completion of the experiment (aqueous soap solution). | At a minimum:<br>▪ Material must be manipulated within a HEPA-filtered laboratory exhaust hood over water-soaked absorbent paper to capture any spilled materials.<br>▪ Exhaust hood work surfaces must be wiped with dampened adsorbent paper towels at the completion of the experiment (aqueous soap solution).<br>▪ When ejecting samples from a capillary, that sample must be directed to water for capture. Compressed nitrogen (<5 psi) or other inert gas must be used to eject the sample from the capillary tube. A covered beaker is best to contain any splash. This must be completed within a laboratory HEPA exhaust hood.<br>▪ Nanoscale materials brought to the beam line must be sealed within a sample holder, a capillary tube, or with at least two layers of Kapton, Mylar or cellophane tape.<br>▪ Only sealed containers are allowed at the beam lines for storage during an experiment.<br>▪ Experiments that involve gas flow over particles must include a water scrub of the gas exhaust to provide a final barrier to particle loss. |
| Spill Response | NA | Powder spills within an exhaust hood can be cleaned by using paper towels and an aqueous soap solution. Liquid spills within a hood can be cleaned with paper towels and then wiped with an aqueous soap solution. For spills outside of an exhaust hood, control access to the area and immediately notify the laboratory supervisor. | |

<table>
<tr><td rowspan="2"></td><td colspan="3">Risk / Material Form</td></tr>
<tr><td>Low</td><td>Medium</td><td>High</td></tr>
<tr><td>Requirements</td><td>Bound or Fixed Nanostructures</td><td>Nanoparticles Suspended in Liquids</td><td>Dry Dispersible Nanoparticles and Agglomerates (or otherwise hazardous – see Section 3.1.3)</td></tr>
<tr><td>Posting</td><td>No posting requirements</td><td colspan="2">Post required sign at each designated nanomaterial workstation (beam line hutch and laboratory exhaust hood) for the duration of experiment. See Section 3.4.5, “Marking, Labeling, and Signage”.</td></tr>
<tr><td>Labeling of Containers</td><td colspan="3">Follow the labeling requirements list below in Section 5, “Transportation of Nanomaterials”.</td></tr>
<tr><td>Transportation and Labeling</td><td colspan="3">Any nanomaterial that meets the definition of hazardous materials according to 49 CFR 171.8 (http://www.gpoaccess.gov/cfr/) or has known hazardous properties (toxic, flammable, reactive) must be shipped according to the SLAC Shipping Requirements for Hazardous Materials (SLAC Shipper Form, https://www-bis1.slac.stanford.edu/Public/shipper/shipintro.asp)<br>Other nanomaterials may be carried in private vehicles when labeled and packaged as follows:<br>Labeling:<br>1. The inner package must be labeled as follows:<br><br>CAUTION<br>Nanomaterials Sample<br>Consisting of (technical description here)<br>Contact: (POC)<br>At (contact number)<br>in case of container breakage.<br>Nanoparticulates can exhibit unusual reactivity and toxicity.<br>Avoid breathing dust, ingestion, and skin contact.<br>For dry particulates<br><br>CAUTION<br>Nanomaterials Sample<br>Consisting of (technical description here)<br>Contact: (POC)<br>At (contact number)<br>in case of container breakage.<br>For non-particulates<br><br>Packaging:<br>1. Inner containers must be a tightly sealed, rigid, and leak proof. Use tape on the cap to prevent the container from being unintentionally opened.<br>2. Place the inner container in a >=6 mil plastic bag.<br>3. The outer package (sealed cardboard box “or” sealed plastic container) must be filled with absorbent material to protect the inner container and absorb liquids during an inner container failure.</td></tr>
<tr><td>Waste Management</td><td colspan="3">All waste in contact with nanomaterials must be disposed as hazardous waste (eg, swabs, Kim wipes, blotter paper, beakers, flasks, tape, sample holders). Chemicals containing nanomaterials must NOT be released to the sink or disposed in the regular trash.</td></tr>
</table>

| | Risk / Material Form | | |
|---|---|---|---|
| | Low | Medium | High |
| Requirements | Bound or Fixed Nanostructures | Nanoparticles Suspended in Liquids | Dry Dispersible Nanoparticles and Agglomerates (or otherwise hazardous – see Section 3.1.3) |
| | 1. Waste containers:<br>a. Liquids: must be stored in a rigid leak proof container.<br>b. Particulates: must be stored in a rigid leak proof containers OR >=6 mil plastic bags.<br>2. Satellite accumulation areas:<br>a. Liquids: must be stored in a secondary tray on the bench top or in a HEPA exhaust hood.<br>b. Particulates: must be stored in a secondary container inside the designated nanomaterials HEPA-filtered exhaust hood. Waste must be placed into a clean secondary bag, within the HEPA exhaust hood, before transferring to the 90-day area.<br>3. Waste container labeling:<br>a. No formulas, spell out the chemical name.<br>b. The contents line on the label must contain the chemical composition and the word NANOMATERIALS.<br>c. A second label is required on the outside of the bag stating CONTAINS NANOMATERIALS. | | |