Working with Nanomaterials - Guideline

1. SCOPE

Nanotechnology is an emerging field, as such, the hazardous effects are not completely understood with many nanoparticles. Since these materials are relatively new, they are to be considered toxic and handled cautiously until adequate amount of data on the hazards of these nanomaterials has been collected for health and environment safety information.

All UBC employees working with and/or handling nanomaterials should follow these guidelines. It describes methods to safely handle, use, store nanomaterials. Emergency procedures for dealing with accidental spills or nanoparticles exposure are also included. If you or your lab have not worked with this hazard before and you are considering a procedure that requires you to do so, we recommend contacting SRS for risk assessment/guidance.

2. GLOSSARY

- **Engineered nanoparticles:** material purposefully produced with at least one dimension in the 1 – 100 nanometer range (as stated by the American Society for Testing and Materials' (ASTM) Committee on Nanotechnology). These materials have unique properties (such as size) that may result in an increased toxicity.
- **Ultra-fine particles:** Also referred to as nanometer-diameter particles that are not intentionally produced (< 100 nm size), such as naturally airborne particles or incidental products of processes involving combustion (e.g.: carbon black, smoke, welding fumes).
- **Engineered nanomaterial:** Intentionally manufactured material, containing particles (unbound state, aggregate or agglomerate) and where, for ≥50% of the particles in the number size distribution, one or more external dimensions is in the size range 1-100 nm.
- **Nano-powder:** A mass of dry nanoparticles.
- **Nano-aerosol:** A collection of nanoparticles suspended in a gas.
- **Nanofiber:** A nano-object with two similar external dimensions in the nanoscale and the third dimension significantly larger. Nanofibers can be flexible or rigid. The two similar external dimensions differ in size by <3 times and the significantly larger external dimension differs from the other two by more than three times. The largest external dimension is not necessarily in the nanoscale. If the nanofiber has a length > 5 µm, a width less than 3 µm and a length to width ratio (aspect ratio) > 3:1, it is called a World Health Organization (WHO) nanofiber.

3. TRAINING REQUIRED

Only trained and qualified personnel may handle nanomaterials. This training includes, but is not limited to:

- Chemical Safety Course (Chemical Safety - Research Safety (ubc.ca))
- Site specific training to the departmental/lab standard operating procedures and/or protocols
- Details of the training must be documented and saved.

4. BACKGROUND

Nanoparticles can occur naturally (e.g., volcanic eruptions, ocean spray, dust volatilization etc.), by accident (e.g., as side product from a reaction) or can be purposefully engineered. Engineered nanoparticles can be carbon-based, metal-based, polymer-based, lipid-based, composites or nanoemulsions and have numerous applications.

Table 1 Types of Engineered Nanoparticles and their Applications

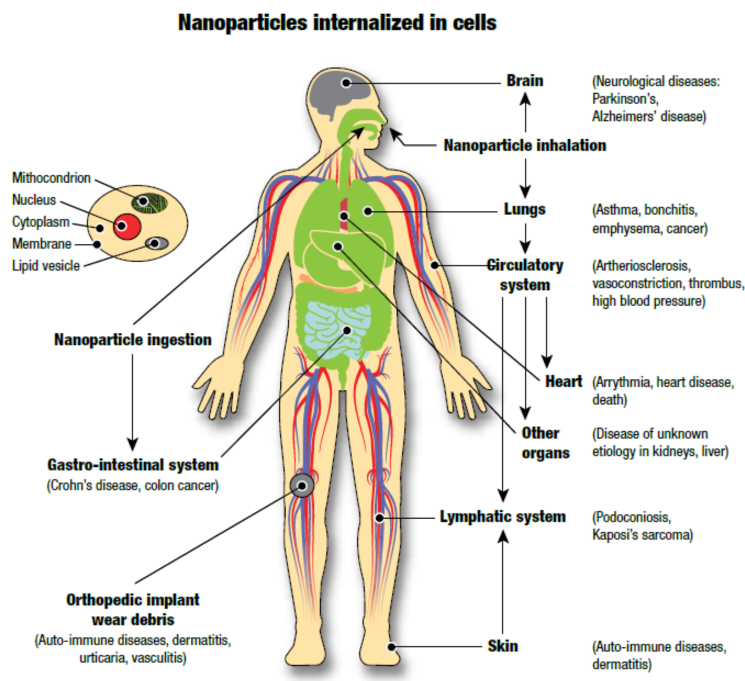
Engineered Nanoparticles	Applications
Carbon-based Nanoparticles	
Carbon Nanotubes and their Derivatives	Electronics, computers, plastics, catalysts, batteries, conductive coatings, supercapacitors, water purification systems, orthopedic implants, aircraft, sporting goods, car parts, concrete, ceramics, solar cells, textiles
Fullerenes	Removal of organometallic compounds, cancer treatment, cosmetics, magnetic resonance imaging, X-ray contrasting agent, anti-viral therapy
Metal-based: Metal Oxides, Zero-Valence Metal (Iron, Gold and Silver) and Quantum Dots	
Titanium dioxide	Sunscreen lotions, cosmetics, skin care products, solar cells, food colorant, clothing, sporting goods, paints, cement, windows, electronic coatings, and bioremediation.
Zinc Oxide	Skin care products, bottle coatings, gas purification, and contaminant sensors
Cerium Oxide	Combustion catalyst in diesel fuels, solar cells, oxygen pumps, coatings, electronics, glass/ceramics, and ophthalmic lenses.
Iron	Biosensors in combination with magnetic resonance imaging (MRI), targeted drug and gene delivery, and magnetic fluid hyperthermia
Gold	Tumor therapy, flexible conducting inks or films, catalyst, cosmetics, pregnancy tests, anti-microbial coatings
Silver	Biosensors, electronic devices, textiles, wound dressings, antimicrobial coatings, deodorants, air filters, paint, biomedical devices, appliances, food storage and food additives/supplements.
Quantum Dots	Semi-conductors, medical imaging, targeted therapeutics, solar cells, photovoltaic cells, security links, telecommunications.
Polymer-based Nanoparticles	
Dendrimers	Drug delivery, tumor treatment, manufacture of macrocapsules, nanolatex, coloured glasses, chemical sensors, and modified electrodes.
Lipid-based Nanoparticles	
Liposomes	Drug delivery systems.
Nanoemulsions	
Nanoemulsions	Vaccines and anti-cancer agents.

5. HAZARD

5.1. Health effects and routes of entry

The four possible routes of entry for hazardous chemical substances are inhalation, ingestion, injection, and dermal absorption (including eyes). Of these pathways, inhalation is the most common route of exposure for engineered nanoparticles, and indeed of most workplace hazards.

Figure 1 Exposure pathways and major diseases associated with nanoparticle exposure



A secondary route of entry is dermal absorption, whereby nanoparticles penetrate through unprotected skin and eyes. Accidental ingestion can also occur if the hands become contaminated with the chemical substance, usually caused by poor personal hygiene. Lastly, accidental injection of nanoparticles can occur if sharp objects are common in the workplace handling this contaminant.

Once nanoparticles enter the body, they disseminate systemically via the cardiovascular system.

Nanoparticle exposure is associated with a host of adverse pulmonary, immunological, cardiovascular, neurological, and carcinogenic effects (Figure 1).

Inhalation Exposure

Of the possible routes of entry, inhalation is the most significant pathway by which an employee is exposed to nanoparticles. Factors that influence the toxicity of *nanofibres* include composition, length, diameter, shape, and persistence. In experiments involving rat and mice models, studies have shown that single- and multi-walled carbon nanotubes (SWCNT and MWCNT) induce pulmonary inflammation and fibrosis. Researchers noted elevated rates of the following illnesses among nanoparticle-exposed individuals:

- Pulmonary fibrosis
- Pulmonary edema
- Chronic obstructive pulmonary disease (COPD)
- Lung cancer

There is still a lot of research needed to understand the mechanism by which nanoparticle inhalation causes the above-mentioned health effect. Most epidemiological studies to date were done with carbon black and titanium dioxide.

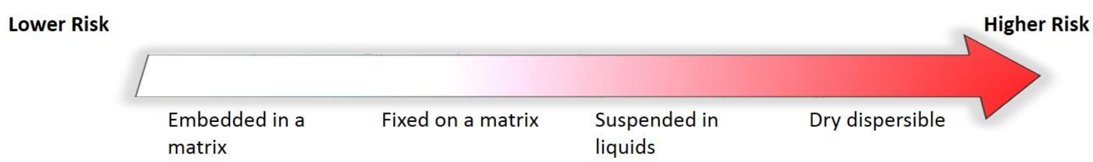
Dermal and Eye Exposure

Skin absorption is another significant route of entry in addition to inhalation. Skin is the first line of defense in the innate immune system and consists of three layers: epidermis, dermis, and subcutaneous. Literature shows that due to their small size, engineered nanoparticles can readily penetrate through skin and mucosal barriers. However, size is not the only determinant for skin penetration. For instance, a study on titanium dioxide nanoparticles (engineered for sunscreen manufacturing) found that particulates suspended in an oil-based solution penetrate deeper and faster into the skin than those immersed in an aqueous solution.

Compromised skin barriers, including abrasions and lesions, cause further concern for skin uptake of nanoparticles. Hair follicles also facilitate shunting of surface nanoparticles into the subcutaneous layers of the skin, which presents concern for hairier parts of the body such as the forearms.

The surface of the eyes, albeit small relative to the surface of the skin, presents a unique route of entry for nanoparticles. In a rabbit experiment, researchers demonstrated that titanium dioxide nanoparticles applied to the ocular surface induced damage. Some concern has also been brought up with regards to neuronal exposure via ocular entry. Engineered nanoparticles have been shown to gain access to the central nervous system (brain and spinal cord) via retrograde translocation along neurons. Overall, efforts are still underway in characterizing the skin and eyes as routes of entry for nanoparticles. The health effects of such exposures are not well known, although they have been associated with dermatitis, sensitization, and irritation.

Figure 2 Exposure risk for nanomaterials. This figure assumes that no disruptive force (e.g. sonication, grinding, burning is applied to the matrix.



5.2. Physical hazards

Both carbon-containing and metal dusts can explode if they are aerosolized at a high enough concentration and if oxygen and an ignition source are present. Some nanoparticles are designed to generate heat through the progression of reaction at the nanoscale. Such materials may present a fire hazard that is unique to engineered nanoparticles. For example, nanoscale Al/MoO_3 particles can ignite more than 300 times faster than corresponding micrometer-scale material.

6. OCCUPATIONAL EXPOSURE LIMITS (OELs) and OCCUPATIONAL EXPOSURE BANDS (OEBs)

To protect the health of employees in the workplace, occupational exposure limits (OELs) to various hazardous chemical substances have been developed by industrial hygienists in conjunction with policy-makers. Threshold Limit Values (TLVs®) with a few exceptions, are *health-based values* that represent concentrations at which nearly all employees may be repeatedly exposed over a working lifetime without adverse health effects.

There are three types of exposure limits:

1. TLV-time weighted averages (TLV-TWA): OEL for a full 8-hour shift
2. TLV-short term exposure limit (TLV-STEL): OEL for a 15-min period in an 8-hour shift
3. TLV-ceiling limit (TLV-C): peak OEL at any given time over an 8-hour shift

A single hazardous substance may have more than one type of TLV®, but TLVs® have not been developed for all chemical contaminants. Engineered nanoparticles are one such example. Globally, there is a lack of occupational exposure limits *specific* to nanoparticles despite the need to control employee exposures to this hazardous substance. Heterogeneity in the composition of nanomaterials, unique chemical/physical properties of nanomaterials, and limited toxicological data all present challenges for OEL development. Without OELs, measured exposure concentrations can only be compared to guideline values. Recommended exposure limits (REL) and nano reference values (NRV) are two such examples.

Table 2 Occupational Exposure Limits Associated with Some Nanomaterials

Material	US NIOSH[(1)]	ANSES[(2)]
Titanium dioxide nanoscale	REL[(3)] 300 μg/m³	TWA 0.80 mg/m³ STEL 4.0 mg/m³
Silver (<100 nm)	REL 0.9 mg/m³ (TWA)	-
Carbon Nano Fibres	REL[(3)] 1.0 μg/m³	-

(1) NIOSH – National Institute for Occupational Safety and Health
(2) ANSES – French Agency for Food, Environmental and Occupational Health and Safety
(3) Concentration at which employees may be exposed over the working lifetime

NIOSH released a draft of Approaches to Developing Occupational Exposure Limits or Bands for Engineered Nanomaterials: User Guide and Technical Report on July 13, 2021. The draft report is intended to offer methods of assessing scientific data for developing occupational exposure limits or bands for engineered nanomaterials.

Currently, there are thousands of chemicals, including engineered nanomaterials, that do not have occupational exposure limits (OELs) established. Assigning OELs to every chemical or material that exists today would not be practical. It is also not cost-effective to assign OELs to research and development materials that may never be produced in a large quantity.

Although OELs may not exist, employees' exposures to these materials must be considered and appropriate protective measures must be implemented. Where OELs do not currently exist, chemicals can be placed into categories or Occupational Exposure Bands (OEBs) based upon actual or estimated health effects. Currently, there are five OEBs (A through E), with the lowest toxicity in Band A and the highest toxicity in Band E. The OEBs would then be used to target controls for protecting workers' health. The proposal includes the addition of Band F to address the safe use of engineered nanomaterials.

7. EXPOSURE CONTROLS

7.1. Engineering controls

The primary engineering control related to nanoparticle work is ventilation to prevent airborne exposures. Feasible ventilation controls must be used to minimize potential exposure to airborne nanoparticles. Other controls (administrative and PPE) are not a substitute for engineering controls.

- In general, labs that handle non-encapsulated nanomaterials outside of fully-enclosed systems must have non-recirculating general ventilation systems. Lab pressurization must be negative to the hallway. Lab doors must be kept closed at all times to maintain negative pressurization. This is typical of the design for most laboratory type spaces.

- Activities that are likely to release nanomaterials (e.g., opening sample tubes, needle aspiration of liquids containing nanomaterials, weighing of dry nanomaterials, cleaning of reaction chambers, etc.) should be performed in a glove box, glove bag, fume hood, biosafety cabinet, or other exhausted enclosure. When enclosure in a ventilated device is not feasible, an articulating fume extractor positioned close to the work zone and with sufficient capture velocity may be an acceptable alternative.
- Exhaust gases generated by furnaces, reactors, and similar equipment used to manufacturer or process nanoparticles should be captured and directed outside of the building (local ventilation control).

Engineering controls are generally not required for nanomaterials that are encapsulated in a solid, nanocomposite, and surface coated material unless cutting or grinding is conducted.

7.2. Administrative controls

Conduct a Risk Assessment before starting work with nanomaterials (Nanomaterials: Questions to Ask), this will allow you to classify the work into one of the three risk level categories (See table 3).

Table 3 Risk Level Categories for Work with Nanomaterials

Risk Level	Description	Mitigation
High Risk	**Handling of solid nanomaterials.** The potential for release is significant as nanomaterials can disperse in air to an extent that is similar to vapors. Examples: • Generating nanomaterials; • Weighing powdered nanomaterials; • Non-wetted cleaning of furnaces or reactors and; • Cleaning or removing filters used for nanomaterials.	Minimum: use a fume hood or A2 biosafety cabinet (only for powders or aqueous solutions). Use of a glove box recommended for materials with the highest possibility of exposure, the highest toxicity of the macro scale material or for a nanomaterial known to be highly toxic. Examples include, but are not limited to, carbon nanotubes or As, Be, Cd nanoparticles.
Moderate Risk	**Nanomaterials suspended in a liquid.** Examples of activities: Sonication, spraying, any other aerosol generation. **Physically bound nanomaterials such as composites or films.** Power grinding, sanding, cutting or drilling.	Use a fume hood or A2 biosafety cabinet.
Low Risk	**Nanomaterials suspended in a liquid.** Examples of activities: Pipetting small quantities, cleaning up a wet spill, and brushing out a coating. **Physically bound nanomaterials such as composites or films.**	Possible to be conducted on the benchtop with appropriate post activity wet cleanup if required. Use of a ventilated enclosure may simplify post activity cleanup.

Develop site-specific Safe Work Procedures (SWP) to describe in detail how the procedure should be done safely. Depending on the chemical/physical properties of the nanomaterials and the activity performed, separate SWP might need to be developed.

When working with nanomaterials consider these guidelines:

- Do not work alone in the lab
- Purchase only enough material needed to complete an experiment and, if possible, purchase nanoparticles in solution or suspension
- Consult the SDS of the nanomaterial before using it
- Minimize potentially contaminated areas by confining operations to designated areas of the smallest feasible size
- Keep work areas clean and uncluttered. Dry sweeping or air hoses are prohibited for use when cleaning work areas potentially contaminated with nanomaterials. HEPA vacuums or wet-methods are acceptable, although wet methods are preferred. Clean work areas at the end of each work shift. If using a HEPA vacuum, change the filter within a ventilated enclosure to prevent exposure to nanomaterials. Clean work areas when likely to be contaminated and at the end of each work shift.

7.3. Personal protective equipment (PPE)

Nanomaterials are hazardous chemicals and their handling has to be done while wearing UBC mandatory PPE (safety glasses, and long-sleeved lab coat in addition to fully enclosed liquid resistant shoes and long loose fitted pants).

For many nanoparticles handling tasks, good-quality, disposable, single-use polymer gloves (e.g., of neoprene, nitrile, latex, or other chemical-resistant material) should be adequate. As in other chemical exposure situations, gloves should be selected for their effectiveness against the characteristics of the nanoparticles and other materials being handled, also considering other performance requirements (e.g., mechanical or heat challenges). If suspended in liquids, consider the resistance of the glove to both the nanoparticle and the liquid. Safety data sheets (SDSs) may provide useful guidance.

Glove thickness also contributes to effectiveness. Particle penetration is more likely when gloves are subjected to repeated mechanical deformation and when particles are present in colloidal solutions. Gloves should be changed out regularly. A precautionary approach includes double-gloving, especially when using thinner gloves or when handling materials of high concern. Gauntlet-type or extended sleeve gloves can protect wrists from exposure via a gap between the lab coat sleeve and glove.

If engineering controls are not adequate or are not available, and a potential aerosol exposure exists, respiratory protection is required. When working with nanomaterials, one of the following types of respirators must be worn:

- Filtering face piece (N-95 or greater)
- Elastomeric half- or full-face piece with N-100, R-100, or P-100 filters;
- Powered air-purifying respirator with N-100, R-100, or P-100 filters.

Contact SRS for guidance regarding the most suited type of respirator and to arrange for fit testing (mandatory and valid for 1 year).

8. EMERGENCY PROCEDURES

8.1. Spills

Strategies used to mitigate and cleanup a nanomaterial spill are similar to those employed for releases of chemicals and biological agents. Primary considerations include preventing exposures and minimizing the impacted area. As with any spill/release, evacuation of the area and notification of response authorities is appropriate if the situation is an imminent hazard.

Wet cleaning methods are preferred to HEPA vacuum methods. For solid/powder nanomaterials, dampen the surface of the spill with a compatible liquid (soap/water, cleaning oil, etc.). Take care to dampen gently to avoid the production of aerosols. Wet wipe the affected area with a disposable cloth/wipe. Repeat cleaning of the area several times using fresh cleaning solutions and wipes. Seal used wipes in a bag to prevent aerosolizing of the nanomaterials upon drying. Dispose of used wipers as hazardous waste.

Use the same strategy for liquid materials, except use a disposable wiper to first absorb the liquid. Appropriate PPE must be worn when cleaning up a spill. Do not use energetic cleaning methods such as dry sweeping or compressed air.

8.2. Personal exposure

Nanoparticles and nanomaterials toxicity are often found to be chemical specific. Refer to the SDS of the material and always consider the exposure to the solvent/matrix the nanomaterial is dissolved/suspended in.

If skin is exposed, the affected area must be washed with soap/mild detergent and rinsed with water for at least 15 minutes. In case of eye contact, immediately rinse eyes for at least 15 minutes.

Both spills and/or personal exposures must be reported via the UBC Centralized Accident/Incident Reporting System (CAIRS).

9. WASTE HANDLING

Any waste containing nanoparticles or nanomaterials should be disposed of as hazardous waste following SRS hazardous waste guideline. This includes pure nanomaterials in solid form, solutions of nanoparticles and contaminated objects.

Never dispose of nanoparticles or nanomaterials in the regular garbage or down the drain.

10. DOCUMENT INFORMATION

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