Nanomaterials Safety Guidelines

The study of nanoparticles and uncovering their potential to be incorporated in technology has evolved rapidly in the last two decades. Many of these nanoparticles are being added in merchandises such as wrinkle and stain resistant fabrics, sunscreen, glare-resistance eye glasses, medical uses and much more. Although this evolution of nanotechnology is vastly improving our current materials, the hazardous properties of these nanoparticles and their implication within workplace safety is long overdue and is now started to be investigated.

Concordia University Environmental Health & Safety (EHS) has developed this following document to provide guidelines concerning the work with nanoparticles within its laboratory facilities. These guidelines provide information about the properties of commonly used nanoparticles/nanomaterials, their health and safety hazards and ways to protect oneself from potential laboratory exposures. Emergency procedures for dealing with accidental spills or nanoparticles exposure are also included.

WARNING: *Since nanotechnology is an emerging field, many of 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 [a "precaution principle" as stated by the European Trade Union Confederation (ETUC)] until adequate amount of data on the hazards of these nanomaterials has been collected for health and environment safety information.*

1) Definitions

Nanoparticles can occur naturally in nature (e.g. volcanic eruptions, ocean spray, dust volatilization and etc.), occur by accident (e.g. as side product from a reaction) or can be purposefully engineered.

a) Engineered nanoparticles

They are defined as 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 are investigated since they have unique properties compared to their bulk and atomic counterparts. These novel properties in engineered nanoparticles are widely used and consumer's products containing engineered nanomaterials are quickly rising. However, with these unique properties and characteristics (such as size), it is possible that these materials have an increased toxicity compared to their counterparts (the bulk and atomic scale) (Fig. 1).

Figure 1: Size comparison of nanoparticles

(Picture obtained from https://www.niehs.nih.gov/health/topics/agents/sya-nano/)

b) Ultra-fine particles

Often referred as nanometer-diameter particles that are not intentionally produced (less than 100 nm size), such as naturally airborne particles or incidental products of processes involving combustion (e.g.: carbon black, smoke, welding fumes).

c) Engineered nanomaterial

Intentionally manufactured material, containing particles (unbound state, aggregate or agglomerate) and where, for 50% or more of the particles in the number size distribution, one or more external dimensions is in the size range 1-100 nm.

d) Nanopowder

A mass of dry nanoparticles.

e) Nanoaerosol

A collection of nanoparticles suspended in a gas.

f) Nanofibre

A nano-object with two similar external dimensions in the nanoscale and the third dimension significantly larger (Fig. 2). A nanofibre can be flexible or rigid. The two similar external dimensions are considered to differ in size by less than three times and the significantly larger external dimension is considered to differ from the other two by more than three times. The largest external dimension is not necessarily in the nanoscale. If the nanofibre has a length greater than 5 µm, a width less than 3 µm and a length to width ratio (aspect ratio) greater than 3:1, it is called a World Health Organization (WHO) nanofibre.

g) Nanoplatelet

A nanoparticle having a "platelet" morphology (a minute flattened body) that presents only one dimension in the nanoscale (meaning they have a very thin but wide aspect ratio) (Fig. 2).

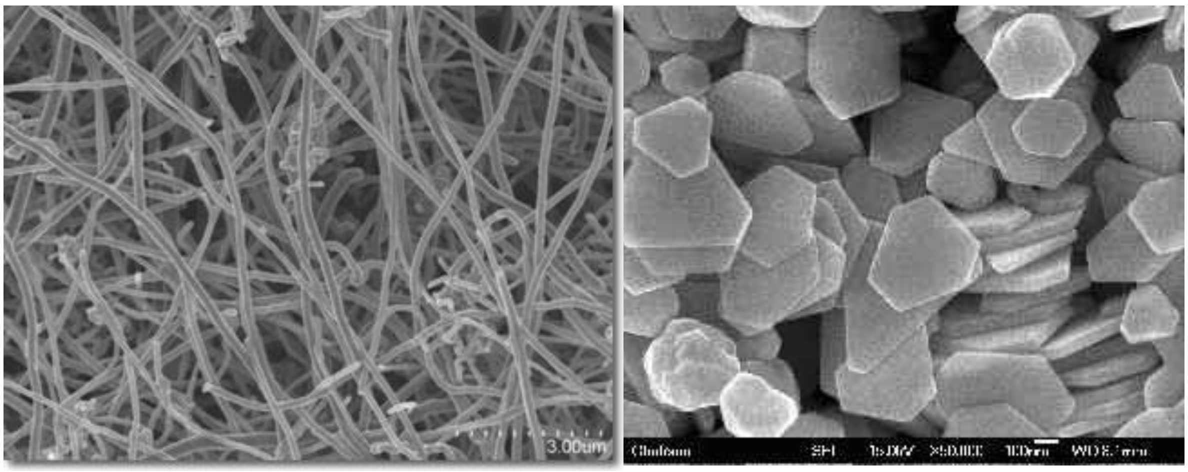


Figure 2: Carbon nanofibers (left) and silver nanoplatelets (right)

h) High Aspect Ratio Nanoparticles (HARNs)

Particles with one or two dimensions in the nanoscale that are much smaller than the others. Nanofibres and nanoplatelets are considered as HARNs.

i) Agglomerate

A group of nanoparticles held together by relatively weak forces (van der Waals, electrostatic or surface tension) (Fig. 3)

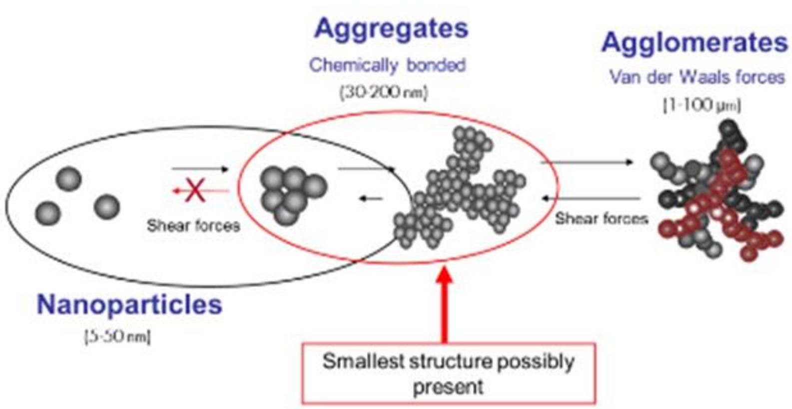


Figure 3: Nanoparticle aggregates and agglomerates

(Picture obtained from http://www.teknoscienze.com/Articles/HPC-Today-Nanotechnology-and-Sun-Care-A-Risk-Review.aspx)

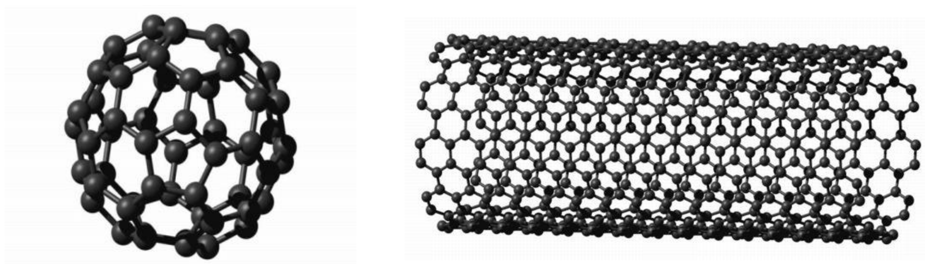
j) Aggregate

A heterogeneous particle in which the various components are held together by relatively strong forces not easily broken apart (Fig. 3).

2) Types of Engineered Nanoparticles

a) Carbon-Based Particles

- These are nanoparticles that are commonly composed of carbon. Their shapes may be in the form of spheres, ellipsoids as well as tubes. The spheres are known as fullerenes and the tubes are known as carbon nanotubes (Fig. 4).



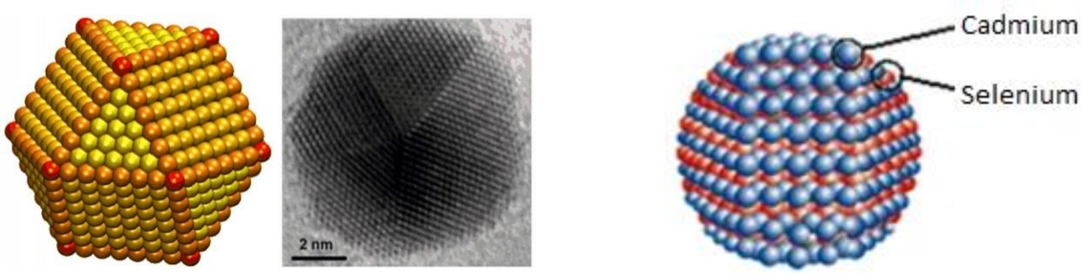
Fullerene ***Carbon Nanotubes***

Figure 4: Carbon-based engineered nanoparticles

(Picture obtained from - http://www.physics.ox.ac.uk/nanotech/research/nanotubes/index.html)

b) Metal-Based Particles

- These nanoparticles include metal oxides (e.g. TiO_2, ZnO, CeO_2), quantum dots (semi-conductor devices with chemical composition of CdSe or ZnS) and zero-valence metals (e.g. zero-valence Fe, colloidal silver and gold). They consist of closely packed metals with particulate sizes of a few nanometers to a 100 nm in diameter. These particles also have size sensitive optical properties (Fig. 5).



Metal Based Nanoparticle (Gold) ***Quantum Dot (CdSe)***

Figure 5: Metal-based engineered nanoparticles

(Picture obtained from (Gold) - http://news.brown.edu/pressreleases/2013/10/nanogold (Quantum Dot) - http://portal.uni-freiburg.de/ak-labahn/forschung/fluoreszenz)

c) Dendrimers

- These nanoparticles are synthesized polymers with many side branches. Different functional groups are on the surface of these dendrimers and are used for different function for applications. In addition, they have cavities in the inside that can host other types of molecules (Fig. 6).

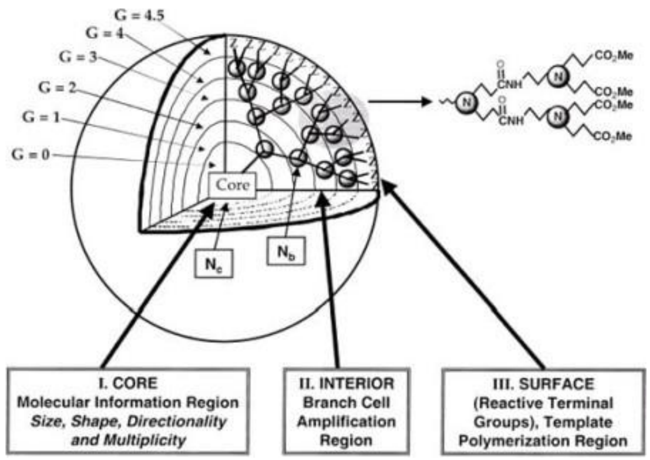


Figure 6: Dendrimer engineered nanoparticles

(Picture obtained from - http://www.pharmainfo.net/reviews/dendrimer-overview)

d) Composites

- These are nanoparticles combined with other nano or bulk materials. Some examples include using nanoparticles in a wide variety of merchandises to improve their current properties. Nanoclays are another example in particular (including mineral silicates, montmorillonite, bentonite, kaolinite, hectorite and hallosite) (Fig. 7).

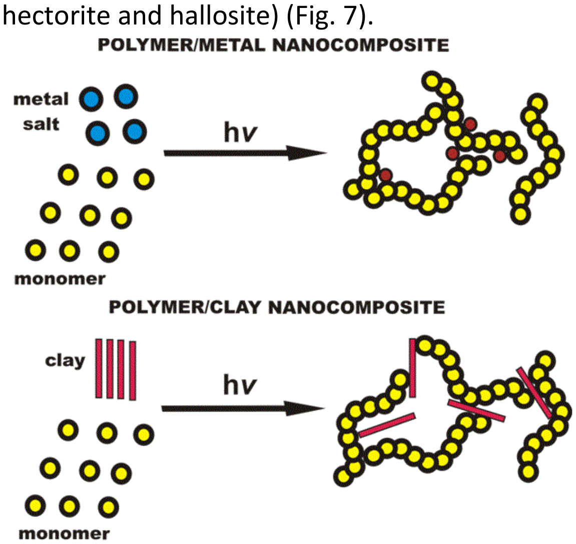


Figure 7: Nanocomposite materials

(Picture obtained from – http://web.itu.edu.tr/~yusuf/index-1.htm)

3) Properties

a) Names

- 1-dimensional nanomaterials (they are extended in the other two dimensions) are known as layers.
  → e.g. – Thin film or surface coatings
- 2-dimensional nanomaterials (they are extended in one dimension only) are known as wires.
  → e.g. – Nanowires or carbon nanotubes
- 3-dimensional nanomaterials (all three dimensions are in the nanoscale) are known as nanoprecipitates.
  → e.g. – Nanoparticles or quantum dots

Table 1: CAS Number of Common Nanoparticles

Nanoparticles	CAS #
Carbon Nanotubes	308068-56-6
Fullerenes	99685-96-8
TiO_2	13463-67-7*
ZnO	1314-13-2*
CeO_2	1306-38-3*
Quantum Dots (CdSe)	1306-24-7
Quantum Dots (CdS)	1306-23-6
Quantum Dots (CdTe)	106627-54-7
Zero Valent Iron	7439-89-6
Silver Nanoparticles	7440-22-4*
Gold Nanoparticle	7440-57-5*

*Note - * There is no exact CAS # for these nanoparticles, rather it is for their bulk material*

Table 2: Common uses of Nanoparticles

Engineered Nanoparticles	***Applications***
Carbonaceous Compounds	
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 Oxides	
TiO_2	Sunscreen lotions, cosmetics, skin care products, solar cells, food colorant, clothing, sporting goods, paints, cement, windows, electronic coatings, bioremediation
ZnO	Skin care products, bottle coatings, gas purification, contaminant sensors

CeO_2	Combustion catalyst in diesel fuels, solar cells, oxygen pumps, coatings, electronics, glass/ceramics, ophthalmic lenses
Semi-Conductor Devices	
Quantum dots	Medical imaging, targeted therapeutics, solar cells, photovoltaic cells, security links, telecommunications
Zero-Valence Metals	
Zero-valent iron	Remediation of water, sediments and soils to remove nitrates, detoxification of organochlorine pesticides and polychlorinated biphenyls
Nanoparticulate silver	Textiles (e.g., socks, shirts, pants), disinfectant sprays, deodorants, laundry soaps, wound dressings, air filters, toothpaste, baby products (milk bottles, teethers), cosmetics, medical instruments, hardware (computer, mobile phones), food storage containers, cooking utensils, food additive/supplements, appliances (hair dryers, vacuum cleaners, washing machines, refrigerators), coatings/paints
Colloidal elemental gold	Tumor therapy, flexible conducting inks or films, catalyst, cosmetics, pregnancy tests, anti-microbial coatings
Polymers	
Dendrimers	Drug delivery, tumor treatment, manufacture of macrocapsules, nanolatex, coloured glasses, chemical sensors, modified electrodes

b) Additional Physical Properties

Relative surface area and quantum effects are two important properties observed in nanoparticles compared to those in the bulk and atomic scale. These factors have the tendency to change/enhance reactivity, strength, optical and electrical properties of the nanoparticles compared to their bulk counterpart.

1) Relative Surface Area

The decrease of material size increases the number of surface atoms (or molecules) compared to the rest of the material (meaning atoms [or molecules] inside of the material) (Fig. 8). For example, a nanoparticle with a size of 30 nm will have 5% of its atoms on the surface, 10 nm will have 20% of its atoms on the surface and a 3 nm particle will have 50% of its atoms on the surface. Therefore, smaller particles have a larger surface area per units of mass compared to their bulk material. This means that an increase of efficiency can be observed with the nanoparticle compared to their bulk counterpart when using the same mass.

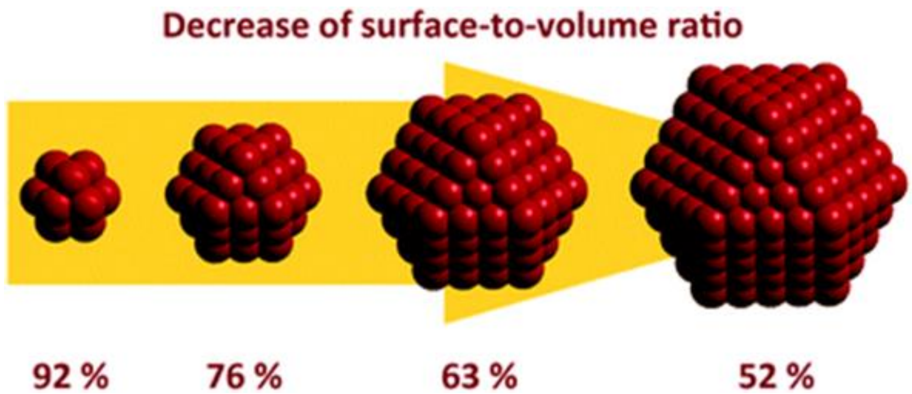


Figure 8: Surface-to-volume ratio of nanoparticles
(Picture obtained from: Bäumer et al., Phys. Chem. Chem. Phys., 2011, 13, 19270-19284)

2) Quantum Effects

When reducing the size of materials to the nanoscale, quantum effects begin to dominate (Fig. 9). These effects can change or enhance strength, optical and electrical properties. An example of this is the reduced defects on the surface for the nanoparticle which increases the strength of the nano-crystalline structure. Another example is the band gap change of bulk semiconductor relative to a quantum dot where fluorescence can be observed and controlled by the size of the quantum dot.

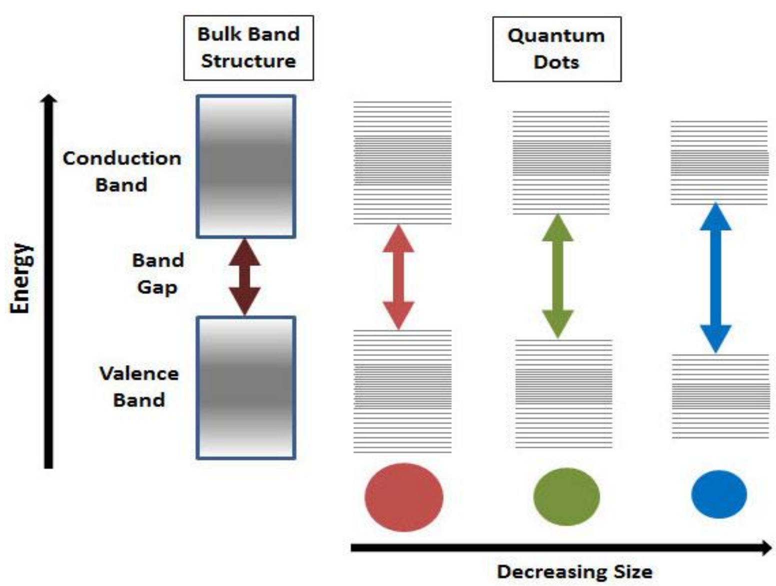


Figure 9: Quantum effects of size reduction of nanoparticles
(Picture obtained from - http://www.sigmaaldrich.com/materials-science/nanomaterials/quantum-dots.html)

4) Potential Hazards

Due to the differential changes in size and quantum effect properties of nanoparticles, the information available is limited concerning their potential threat on human health or on the environment. However, this does not negate the responsibility of protecting oneself from nanoparticles. When working with unknown materials, precautions must be taken in order to establish possible threats by examining potential dangerous scenarios and preventing them from happening. This includes toxicity issues, chemical dangers, fires, explosions, dusts inhalation, electrostatic, size, shape and concentration. Some examples include:

- Change of property based on size - it has been observed that >80 nm size aluminum nanoparticle dust is very inert compared to its smaller size counterpart (< 80 nm), which is very reactive and explosive.
- Chemical toxicity – quantum dots are generally made with toxic ions [Cd^{2+} or Hg^{2+}] and the quantum dots can dissociate into their ion state in the body or environment.

a) Legislation

There is currently no nanomaterial/nanoparticle-specific occupational health safety legislation in Quebec or Canada. In Quebec, the Part 1 of the *Regulation Respecting Occupational Health and Safety* provides permissible exposure limits for many chemicals of the same composition than nanoparticles. However, it does not take into consideration the particle size or the possibility of a different toxicity according to the granulometry of the specific chemical.

Health Canada and Environment Canada are currently studying a possible distinct legislation concerning the manufacturing, import and export of nanomaterials, including their use and their environmental management. The only current obligation for manufacturers or importers is to provide restricted information to Environment Canada or Health Canada.

The CSA group has developed standards concerning safe practices with nanomaterials and nanotechnologies; these standards are based on the consolidated results of science, technology and experience, aimed at the promotion of optimum community benefits.

- ***CSA Z12885-12 -*** Nanotechnologies - Exposure control program for engineered nanomaterials in occupational settings
- ***CAN/CSA-ISO/TR 13121:13 -*** Nanotechnologies - Nanomaterial risk evaluation
- ***CSA Z12901-15*** - Nanotechnologies - Occupational risk management applied to engineered nanomaterials - Part 2: Use of the control banding approach
- ***CSA Z13329-15*** - Nanomaterials - Preparation of safety data sheets (SDSs)

Other countries (USA and EU) are now considering nanomaterials as new chemical substances. Since 2008, the EPA requires certain nanomaterials (fullerenes, quantum dots, carbon nanotubes) to go through its New Chemical Review process. However, no official occupational exposure limit values (OELs) specific to nanomaterials have been set in the USA or in the EU level.

For certain nanomaterials, industry, research organisms and agencies have suggested either specific OELs (Table 3). Some companies and research institutes have also proposed an OEL for singlewall and/or multiwall carbon nanotubes (SWCNT & MWCNTs) (Bayer, Nanocyl and NIOSH). A threshold value for

Carbon Nanotubes has also been set in Switzerland in 2011 by the Swiss National Accident Insurance Fund at 0.01 fibres/mL. In any event, as a minimum, it is necessary to ensure compliance with any existing generic threshold limit values, such as general dust limit-values for alveolar and respirable dust fractions, irrespective of the sources contributing to these fractions. However, for most nanoparticles, no in-depth quantitative toxicological data are available for the determination of clear OELs.

Table 3: Suggested OELs

Product	Proposed Limit	Organism
Carbon nanotubes (SWCNT and MWCNT)	1 µg/m^3	NIOSH
Fibrous nanomaterials	0.1 fibre/mL	Safe Work Australia
TiO_2 (10-100 nm)	0.3 mg/m^3	NIOSH
TiO_2 (21 nm)	1.2 mg/m^3	AIST
Fullerenes	0.8 mg/m^3	AIST
Insoluble nanomaterials (<100 nm)	20,000 part/mL	Dutch Social Partners
Soluble nanomaterials	0.5 X TLV*	Dutch Social Partners

**TLV: threshold limit value*

b) Health Hazards

The risk of exposure strongly depends on the state of the nanoparticle. The potential risks for health are usually limited when working with nanomaterials incorporated in a solid matrix, if this one is not grinded, cut or physically transformed. When handling nanoparticles in solution (slurry), risks are usually associated with the nanoaerosol formation arising from mixing, stirring or sonication. The biggest exposure risks are coming when dry (louse) nanoparticles powder are being handled. Nanoparticles are known to travel great distances in air because of their increased mobility.

In preventing exposure, there are three main routes that nanoparticles can enter the human body:

- inhalation into the pulmonary system;
- absorption through the dermal system;
- ingestion through the gastrointestinal system.

It must be highlighted that inhalation exposure is of the greatest concern with regard to the effects of particulate nanomaterials on occupational health, and special attention is being given to studying impacts on the respiratory system and the cardio-vascular system. Dermal exposure is also of importance. However, healthy skin has a better barrier function when compared to the respiratory tract although this barrier function could be limited by skin lesions, strong mechanical strain or small nanoparticles (<5 to 10 nm). Exposure by ingestion is of lower concern within the workplace; following good personal hygiene and basic safety practice rules (such as washing hands with soap and water before breaks and at the end of the workday, not wearing personal protective clothing outside of work areas and not taking them home for cleaning) should avoid any oral uptake.

Due to the size effects, smaller particles may diffuse faster in air than their larger counterparts and can get further down the respiratory tract. In addition, it is hard to remove nanoparticles from the body as they are known to cross mucus membranes. Many potential health effects (Fig. 10) include:

- inflammation of airway (bronchitis, asthma, emphysema);
- lung cancer;
- neurodegenerative diseases (Parkinson's and Alzheimer's disease);
- cardiovascular effects and heart disease;
- liver cancer;
- Crohn's disease and colon cancer.

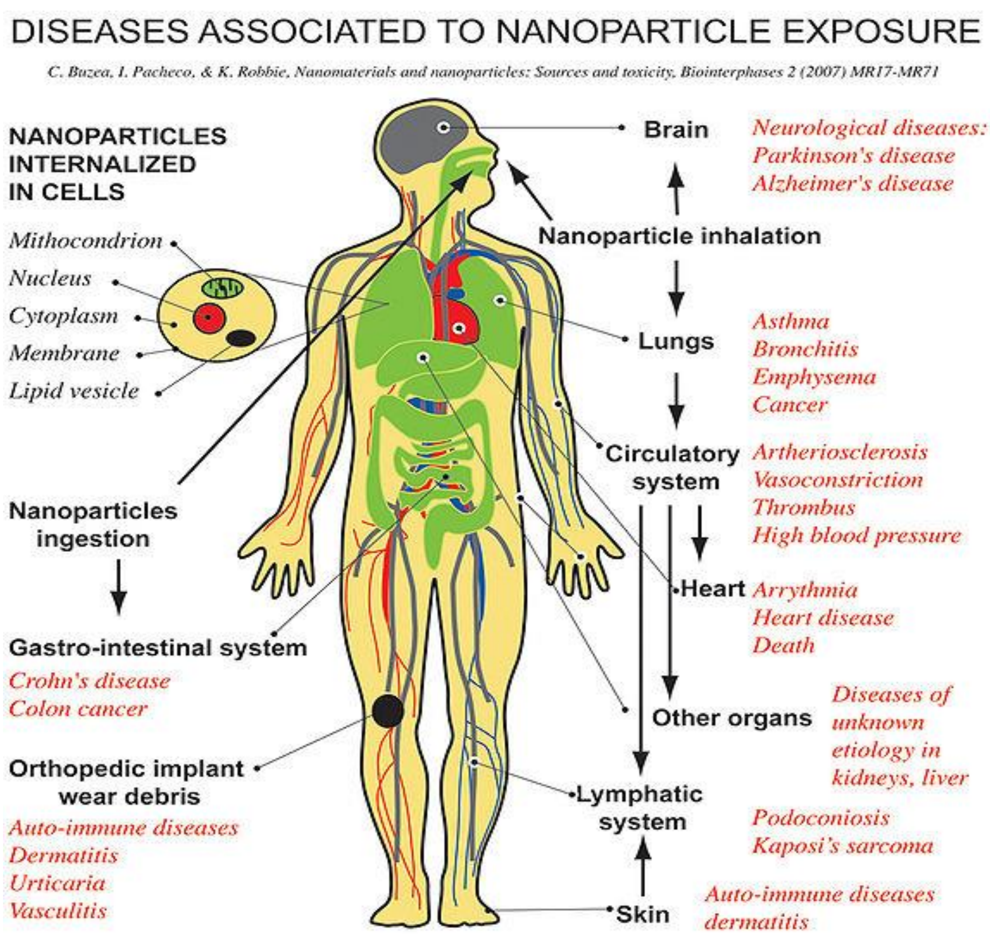


Figure 10: Diseases associated to nanoparticle exposure

Although, presently, it is still uncertain which parameters represent the best predictive value for toxicity, there is growing evidence that for nanomaterials a high aspect ratio (HARNs) and poor water solubility might lead to negative effects on human health.

In order to overcome the lack of specific data about the bio persistence of nanoparticles, water solubility is often used as a proxy for bio persistence. In terms of solubility only, poorly soluble or insoluble nanoparticles are considered of concern; soluble nanoparticles (with a water solubility above 100 mg/L) are considered of no concern. However, in some cases, a material may show a poor solubility in water but a good solubility in biological media as, for example, cobalt which is insoluble in water but soluble in serum.

A categorisation rating for the level of concern relating to the possible health hazard effects of nanoparticles based on the shape and persistence/water solubility characteristics is proposed in Table 4.

Table 4: Concern Categorisation

Concern Category	Characteristics of nanoparticles	Examples
High	Poorly soluble or insoluble (water solubility <100 mg/L)	some carbon nanotubes
Medium - High	Poorly soluble or insoluble (water solubility <100 mg/L) nanoparticles with specific toxicity and poorly soluble or insoluble HARNs	nano-silver gold nanoparticles zinc oxide nanoparticles
Medium - Low	Poorly soluble or insoluble nanoparticles with no specific toxicity	carbon black titanium dioxide
Low	Soluble nanoparticles	sodium chloride nanoparticles lipid nanoparticles flour nanoparticles amorphous silica

1) Inhalation

Nanoparticles suspended in the air represent the greatest risk of exposure since they can breakdown to breathable-sized particles. Once nanoparticles are in the lungs, they can translocate to other organs or cells, providing an entryway to the body with the possibility of bio accumulation. The wall thickness on the capillaries and alveolar are approximately 0.5 µm thick, which allows airborne particles in the micro- and nano-scale to be easily inhaled into the body. Exposure can be separated into three categories: more than 2.5 µm, less than 2.5 µm and less than 100 nm. (Fig. 11)

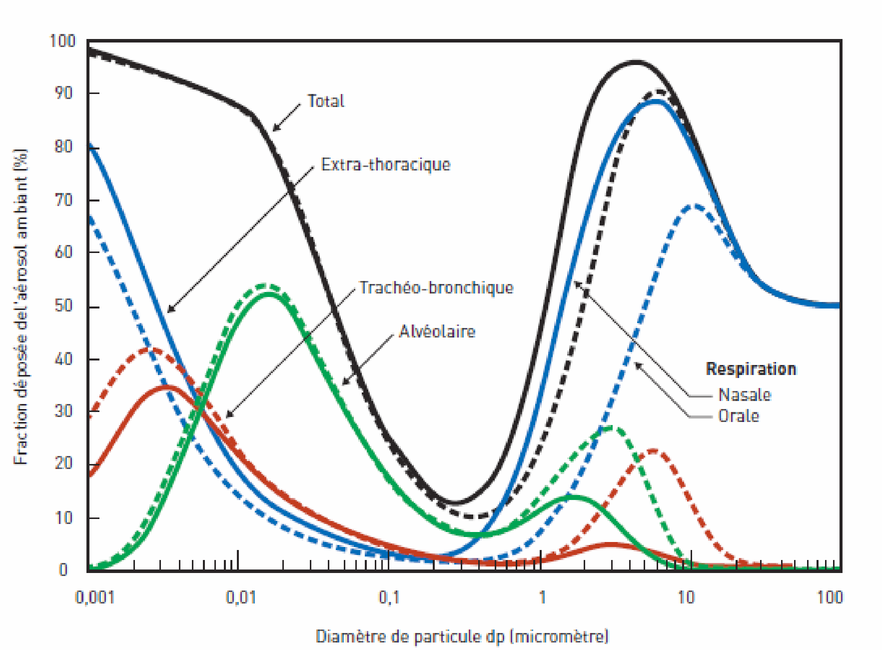


Figure 11: Distribution of particles in airways

(Picture obtained from - O. Witschger et al. INRS ND 2227, 2005)

- Micro-particles above 2.5 µm tend to settle in the upper airway and are released by mucociliary escalator or in the mucous lining of the bronchi and pushed out by the upper airway by coughing, sneezing, being blown out or swallowed.
- Micro-particles less than 2.5 µm penetrate deeper into the alveolar region and are only removed via an alveolar macrophage.
- Nano-particles less than 100 nm start to behave more like gas rather than a solid particulate. They begin to diffuse in the body by the pulmonary system. They have the ability to penetrate the lung and enter the bloodstream.
- When particles enter the blood stream, it allows them to be engulfed by cells and accumulate in organs like the heart, spleen, kidney, bone marrow, and liver. In addition some of these materials can also damage DNA and cause cancer (Fig. 12).

Particular care is suggested when considering the risks that may be posed by nanoparticles possessing certain physical aspect characteristics. In particular, some HARNs demonstrated similarities in their physical characteristics to materials known to be hazardous, such as asbestos or some man-made mineral fibres. Studies suggested that HARNs may be retained in the pleural cavity for long periods of time if they show the additional characteristics:

- thinner than 3 µm;
- longer than 10-20 µm;
- bio persistent;
- do not dissolve/break into shorter fibres.

As for nanofibres, concerns have been raised over nanoplatelets and their aerodynamic behaviour which might result in them penetrating deep within the lung.

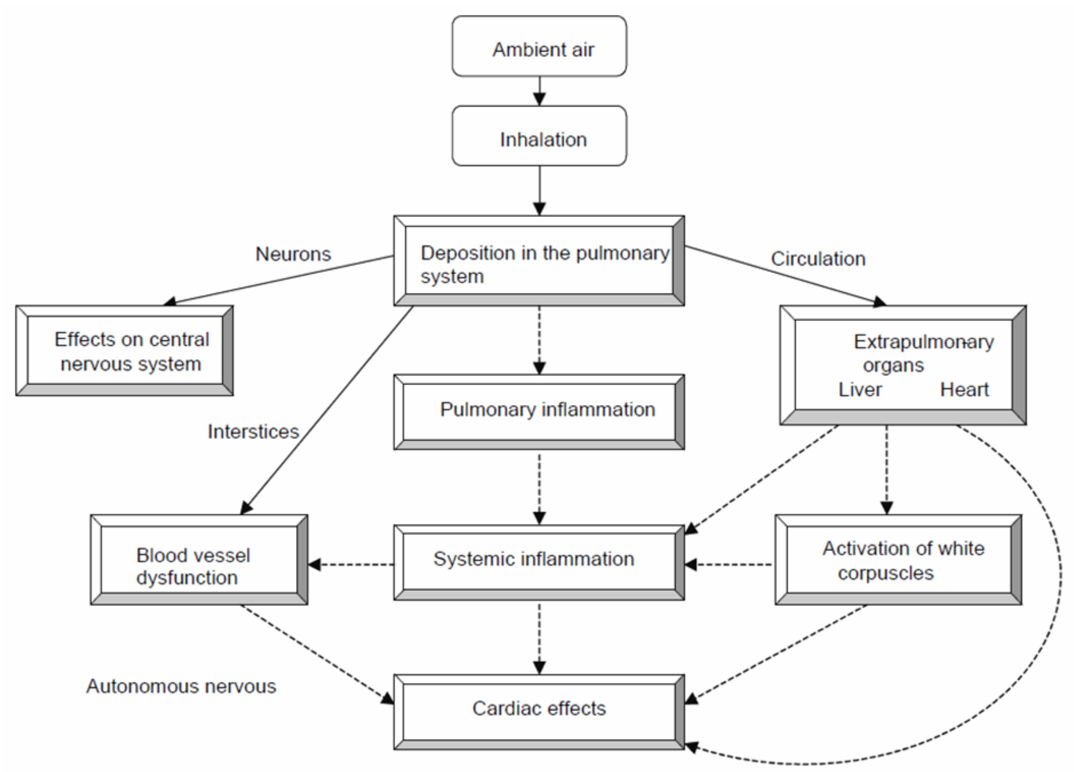


Figure 12: Possible health effects of nanoparticles
(Image from Oberdörster G., 2005)

2) Dermal Exposure

Local skin irritation is one of the primary effects observed upon nanoparticles exposure. Certain metals, such as nickel, are also known to cause dermatitis. The three layers of skin (epidermis, dermis and subcutaneous) make it difficult for ionic molecules to penetrate through. In addition, larger micro-particles cannot penetrate through the skin as well. However, nanoparticles can pass through the skin due to their smaller sizes (Fig. 13). They may pass through pores and hair follicles and go deep under the skin. Even if direct penetration of the skin has been reported for smaller particles (Table 5), most studies showed that nanoparticles can penetrate deeper skin layers only under unfavorable conditions (e.g. injured or stressed skin). Damaged skin (such as sun burns, eczema, acne and opened wounds) can accelerate the uptake of nanomaterials. Nanoparticles can also be absorbed to the bloodstream and bioaccumulate into organs. They can be very toxic to tissues by increasing oxidative stress and inflammation of cytokine production resulting to cell death.

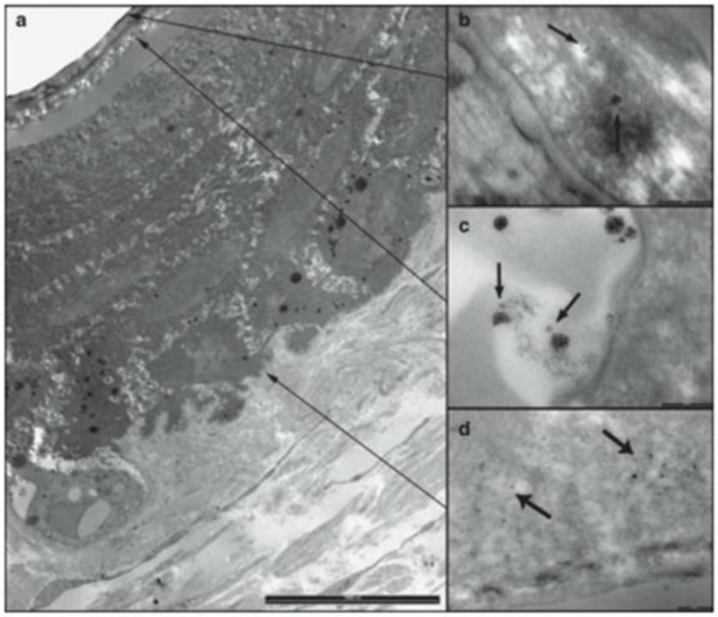


Figure 6. (a) TEM micrograph of AuNPs-treated skin sample (Barr = 10 μm). (b, c, d) Some details of the stratum corneum (b, c.), and of the dermis (d) Black arrows show gold nanoparticles in the tissue. (Barr = 200 nm).

Figure 13: Penetration of gold nanoparticles through intact human skin

(Image from F.L. Filon et *al.*, Nanotox. Online, 2011, pp.1-9)

Table 5: Skin penetration of nanoparticles

Size	Skin penetration / permeation
> 45 nm	Unlikely to have skin penetration
21 – 45 nm	Penetration / permeation through damaged skin
4 – 20 nm	Possible penetration / permeation mostly through hair follicles
< 4 nm	Skin penetration / permeation reported

3) Ingestion

Nanoparticles can be inadvertently consumed orally and passes through the gastrointestinal track. An increase of absorption in the bloodstream is observed due to the increased surface area compared to the skin. In addition, smaller nanoparticles are easily absorbed compared to their larger counterpart. In general, only the smaller nanoparticles are absorbed this way but the extent of absorption levels are unknown. Ingestion usually occurs via a hand-to-mouth transfer of unwashed materials/hands or contaminated food and drinks. The adverse effects of ingested nanoparticles are still no completely understood. However, the materials have been observed to accumulate in the liver, spleen, kidney and may cause permanent liver damage.

c) Fire and explosion 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. Accidental explosions have been reported involving metal nanopowders that have resulted in deaths of workers.

Because the surface-to-volume ratio increases as a particle becomes smaller, nanoparticles may be more prone to explosion than an equivalent mass concentration of larger particles. Dust explosions can occur where any powdered combustible material is present in an enclosed atmosphere or, in general, in high enough concentrations of dispersed combustible particles in atmosphere or other suitable gaseous medium such as molecular oxygen. Bench-scale research should present a low risk of explosion compared to work in pilot plants or full-scale manufacturing facilities. Nonetheless, researchers should avoid creating concentrated aerosols of combustible nanoparticles.

Decreasing the particle size of combustible materials can increase combustion potential and combustion rate, leading to the possibility of relatively inert materials becoming highly reactive in the nanometer size range. Some nanoparticles are designed to generate heat through the progression of reactions at the nanoscale. Such materials may present a fire hazard that is unique to engineered nanoparticles. One example is aluminum powder; particles bigger than 80 nm are known to be inert when exposed to air / oxygen. On the opposite, particles less than 80 nm are known to be very reactive and can cause explosion. Another example is nanoscale Al/MoO_3 particles that can ignite more than 300 times faster than corresponding micrometer-scale material.

d) Environmental hazards

There are limited publications on the effects of engineered nanoparticles on animals and plants in the environment. To date only few quantitative analytical techniques for measuring nanoparticles in natural systems are available, which results in a serious lack of information about their occurrence in the environment.

The main concern will be if any of the nanoparticles entering the environment are toxic or could become toxic to living species in the environment. For example, there is the possibility of nanoparticles being toxic to microorganisms in the soil and groundwater. Following on from this would be possible hazards from the nanoparticles or from consuming the microorganisms affected by the nanoparticles for fish, insects or mammals. There is also a risk to plants from nanoparticles which again could have a follow-on effect on the food chain. For example the deposition of atmospheric particles on crops could provide another route for toxic or reactive nanoparticles into the food chain (Fig. 14).

Release of nanoparticles may come from point sources such as production facilities, landfills, or wastewater treatment plants or from nonpoint sources such as wear from materials containing NP. Accidental release during production or transport is also possible. In addition to the unintentional release there are also nanoparticles released intentionally into the environment.

A number of studies have examined the uptake and effects of nanoparticles at a cellular level to evaluate their impact on humans; it can reasonably be assumed that the conclusions of these studies may be extrapolated to other species, but more research is needed to confirm this assumption. As a fact, a consistent body of evidence shows that nanosized particles are taken up by a wide variety of mammalian cell types and are able to cross the cell membrane and become internalized. Results from eco-toxicological studies show that certain nanoparticles have effects on organisms under environmental conditions, though mostly at elevated concentrations. However, persistent insoluble nanoparticles may cause problems in the environment that are much greater than those revealed by human health assessments.

5) Risk Assessment and Safety Precautions for Nanomaterial Uses

The risk of toxicity can be determined using this formula:

$$\boldsymbol{Risk\ for\ health\ effects = Toxicity\ of\ material\ X\ Exposure\ to\ the\ material}$$

Exposure is defined as the chance of release for a specific material. Since engineered nanoparticles are relatively new, they are to be considered toxic and the potential of an exposure must be investigated to minimize the risk.

Routine workplace activities and other foreseeable events (e.g. accidental spills or other equipment failure scenarios) which may potentially result in the release of nanoparticles and subsequent exposure of workers should be defined. A list of lab activities which can present a potential risk of exposure could consist of:

- material reception, unpacking, delivery or shipment;
- laboratory operations(e.g. weighing);
- cleaning and maintenance;
- storage and packaging;
- waste management;
- possible emergency situations (e.g. spill).

a) Risk Assessment and SOPs

Risk assessment is defined as the systematic process of evaluating the potential risk of an activity or a project. It is important to take a good health/safety approach when working with engineered nanoparticles. This can be done by following these 4 elemental steps:

i. *Identifying the hazard*
ii. *Assessing the risk*
iii. *Preventing or controlling the risk*
iv. *Evaluating the effectiveness of the control measures*

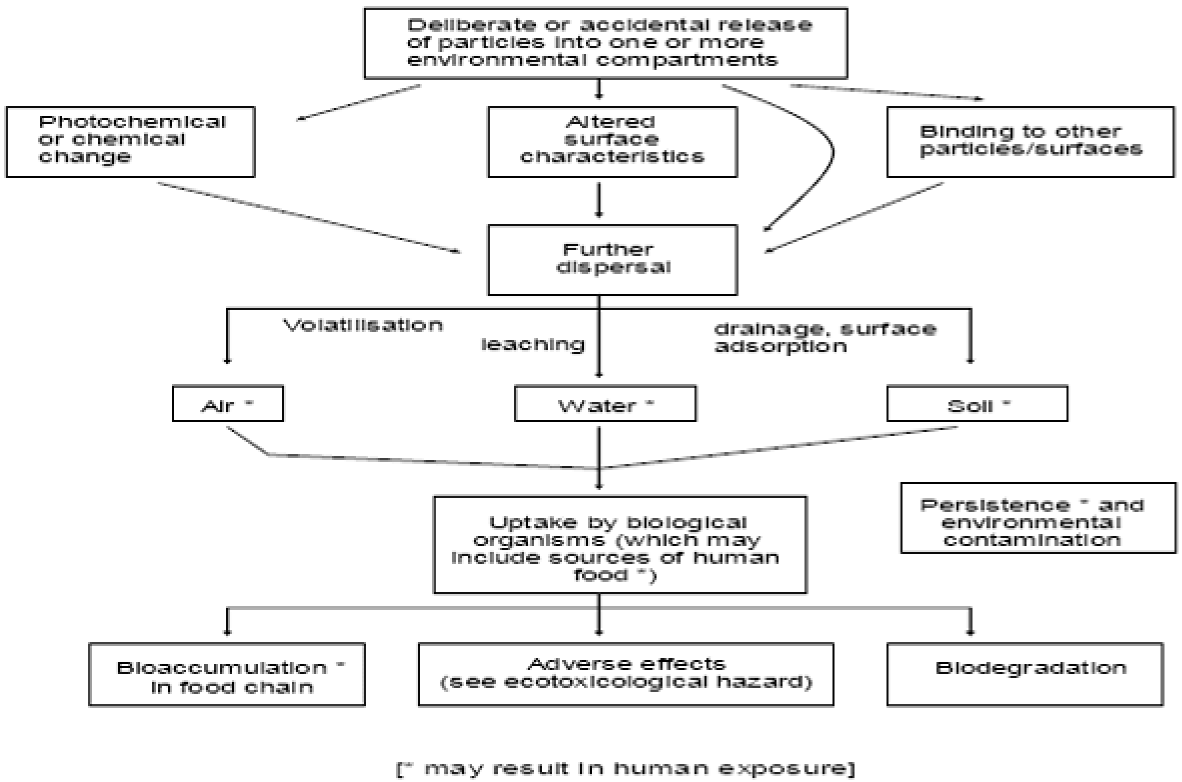


Figure 14: Fate of Nanoparticles in the environment

(Image from: "The appropriateness of existing methodologies to assess the potential risks associated with engineered and adventitious products of nanotechnologies", European Commission Health & Consumer Protection Directorate-General, March 2006)

Risk assessment should be conducted based on the type of nanoparticles being used (e.g. a suspended solution vs. a dry powder). When conducting an assessment, one should always refer to the MSDS/SDS (Material Safety Data Sheet or Safety Data Sheet) of the material being used. Currently, specific information on the physicochemical characteristics of nanoparticles is not always reported in MSDS/SDS. Moreover, toxicological and ecotoxicological data specific to nanoparticles may be lacking; the level of toxicological data for most nanoparticles is considered to be within a *minimal to suggestive* range (Fig. 15). However, if the macro form of a substance is classified as a carcinogen, mutagen or reproductive toxin, as a sensitizer or for another significant toxicity, then it should be assumed that the nanoform will also show these properties, unless proven otherwise.

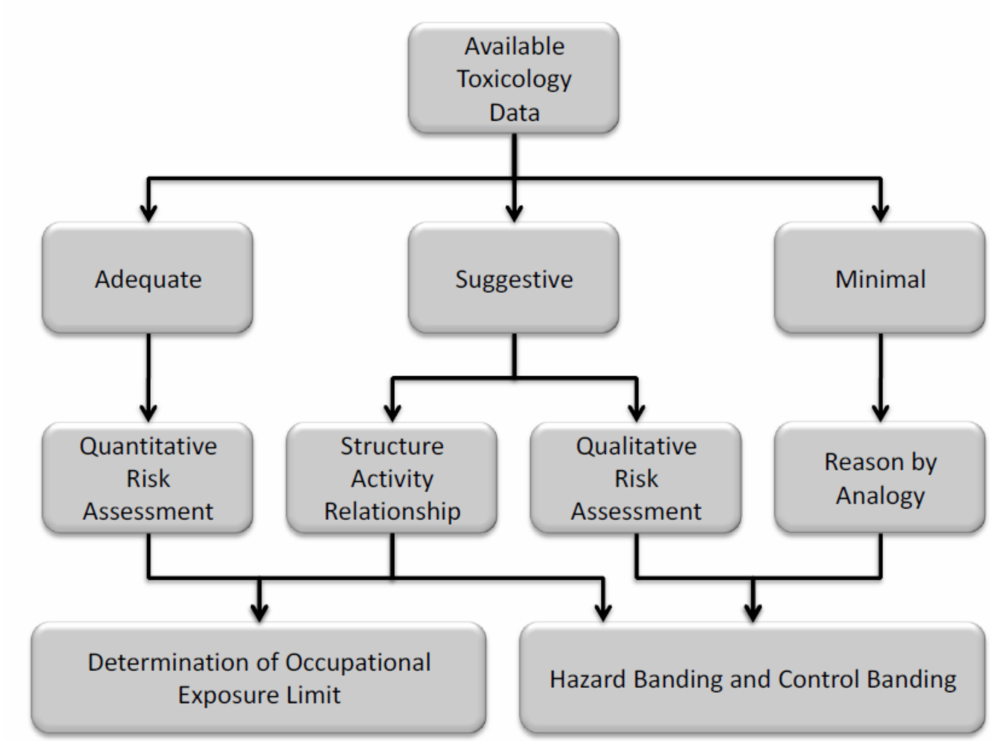


Figure 15: Example of the risk assessment according to level of toxicological data available.
(obtained from *Working Safely with Nanomaterials in Research & Development*, The UK NanoSafety Partnership Group)

Hazard/control banding approach is considered as a more practical solution in the absence of OEL data for nanoparticles. Risk assessment tools, such as control banding are available from different organism web sites. Control banding is a qualitative strategy for assessing and managing hazards associated with chemical exposures in the workplace (Fig. 16). The concept is used to manage exposures to potentially hazardous materials through the application recommended control approaches. Such tools may help in assessing the level of risks associated with nanoparticles work.

Laboratories intending to commence projects involving nanoparticles are asked to contact EHS and request a hazard assessment for their location. EHS will require that labs preparing to work with nanoparticles prepare and submit SOPs for approval before beginning to handle the material.

Exposure Duration	Bound Materials	Potential Release	Free / Unbound
Hazard Group A (Known to be inert)			
Short	1	1	2
Medium	1	1	2
Long	1	2	2
Hazard Group B (Understand reactivity/function)			
Short	1	2	2
Medium	1	2	3
Long	1	3	3
Hazard Group C (Unknown Properties)			
Short	2	2	3
Medium	2	3	4
Long	2	4	4

- Band 1: Use good industrial hygiene practice and general ventilation.
- Band 2: Use an engineering control, typically local exhaust ventilation.
- Band 3: Enclose the process.
- Band 4: Seek expert advice.

Figure 16: Example of control banding tool
(obtained from The GoodNanoGuide www.goodnanoguide.org)

b) Controlling exposure

As for any potentially hazardous materials, there are several methods to use in controlling a nanoparticles exposure.

1) Elimination or substitution

This method consists of eliminating or substituting the toxic components being used. However, this method is not always feasible since the material of study may be toxic. This approach can be tackled by changing some aspects of process, such as:

- using a liquid suspension instead of a free powder
- using of less toxic solvents

2) Engineering controls

This method consists of using an exhaust or containment system to protect oneself from an exposure risk. Using this method strongly depends on the system that is being utilized (Fig. 17).

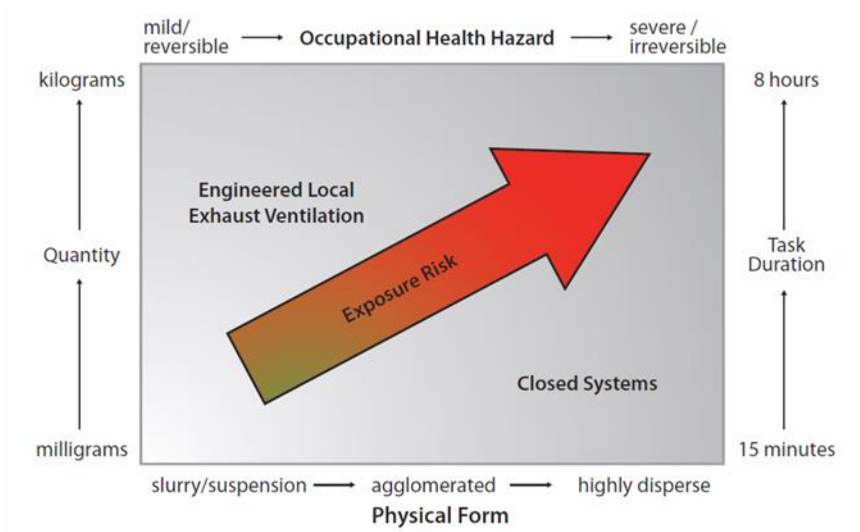


Figure 17: Engineering controls vs exposure risk to nanoparticles

Chemical fume hoods are common in laboratories and used to protect lab users against dangerous fumes and vapors. When different types of fume hoods (constant air volume (CAV) and variable air volume (VAV)) were tested in different studies for the handling of powders consisting of nano-sized particles, results showed that significant amount of airborne nanoparticles can be released from the fume hood into the laboratory environment, including the researcher's breathing zone. Many variables were found to affect the extent of particle release. This lead to these generalized safety recommendations concerning the handlings of nanoparticles using chemical fume hoods:

- Fume hoods should be operated with a face velocity between 0.4 and 0.6 m/s (80–120 ft/min): average face velocities of less than 60 ft/min were not adequate to prevent the escape of nanoparticles;
- Sash heights should remain as low as possible when manipulating nanomaterials, within this velocity range;
- VAV hoods provide better operator protection than conventional (CAV) fume hoods when handling dry nanomaterials. VAV hoods are designed to maintain the hood face velocity in desired range regardless sash height.
- Efforts should be made to reduce/eliminate room air currents in the vicinity of the hood;
- Nanoparticle operations inside fume hoods should be performed using the smallest possible quantity of nanoparticles and the least energetic handling methods.

However, Concordia University general exhaust ventilation (including fume hoods) is not equipped with any scrubbing system able to filter nanoparticles before their release in the environment. It is therefore recommended to work with an exhaust system equipped with HEPA (High Efficiency Particulate Air;

99.97% efficiency for 300 nm particles) or ULPA (Ultra Low Penetration Air; 99.999% efficiency of 120 nm particles) filters.

Examples of exhaust systems equipped with HEPA or ULPA filtering devices that can be used with nanoparticles (Fig. 18) are:

- Nano-safety cabinet (Labconco);
- Biological safety cabinet;
- Table-top HEPA filtration unit.

Figure 18: Engineering controls: nano-safety cabinet (Labconco); biosafety cabinet and table-top HEPA filtration unit

An alternative engineering control is to use a glove box or an enclosed system (Fig. 19). The primary advantage of using a glovebox is the protection it affords; when used properly to manipulate nanoparticle powders. The disadvantages of using a glovebox relate to the extra time required to move materials and equipment in and out of the enclosure, the difficulty of manipulating nanomaterials when wearing gloves, and the need to periodically clean the enclosure. The two most likely sources of exposure when using a glovebox are the transfer of materials into and out of the box and the cleaning of the box following its use.

If a positive pressure using an inert atmosphere (e.g. nitrogen or argon) needs to be maintained in the enclosed system, one has to make sure that any exhaust getting out of the enclosure must be connected to a HEPA or ULPA unit in order to avoid any potential leak of nanoparticles.

Figure 19: Examples of enclosed systems

3) Safe laboratory work practices

Those practices include:

- awareness or safety training for students, staff, employees or anyone involved working with nanoparticles;
- development and application of standard operating procedures (SOPs) when working with specific nanoparticles;
- work area restriction for non-users or unauthorized personnel;
- no eating or drinking in the work laboratory;
- good sanitary practices, such as frequent hand washing;
- clear work-zone delimitation (e.g. signs or marking tape) within the laboratory area specific for nanoparticles/nanomaterial work: high-circulating areas, such as areas close to doors or hallways should be avoided.

In addition, clean room mats or tacky mats can be used to reduce the spreading of nanoparticles. These mats help trap impurities for locations that require stringent dust and dirt control. The tacky surface removes particles from shoes avoiding therefore spreading of nanoparticles in nanoparticles-free areas. Other tolls such as anti-static devices can also be used when handling dry powders (Fig. 20) to avoid spreading of air born particles.

4) Personal Protective Equipment (PPE)

Even though Personal protective equipment (PPE) should never be considered as the first line of defense against contaminants, nevertheless they must always be used in order to minimise users' exposure to nanoparticles.

Figure 20: Example of tacky mats and laboratory anti-static devices

Basic nanoparticles PPE should include:

- **Hand protection**

Gloves must always be worn when handling dry nanoparticles or nanoparticles suspension in various solvents. Even though studies have demonstrated that most types of gloves (latex, nitrile, vinyl, etc.) offer a good barrier against most nanoparticles in the powder form, nitrile gloves proved to offer an increased protection when suspension in solvents are used.

Recently, the IRSST examined were certain models of disposable gloves made of nitrile, latex and neoprene. A test rig was designed to deform the gloves and simulate opening and closing of the hand in the way that workers do. In addition, a physiological solution mimicking sweat was put inside the gloves while the outside of the glove was placed in contact with a solution containing nanoparticles. It was found that, in certain cases, the integrity of the materials composing them was compromised to the point of allowing nanoparticles to pass through (Table 6).

Double gloving is highly recommended for extensive use and gloves with gauntlets (extended sleeves) reduce risks of skin exposure and therefore offer a better protection (Fig. 21). Disposable gloves should be changed routinely or at the first sign of contamination. Even if there are no apparent tears or scratches, the gloves should not be worn for more than two hours at a time and should never be used again once removed.

Table 6: Test results from mechanical deformations of gloves in the presence of nanoparticles

	Gold (5nm)	Gold (50nm)	Silver (50nm)
Nitrile (73 µm)	Not recommended	Fair	Bad
Nitrile (117 µm)	Fair	Fair	Fair
Nitrile (67 µm)	Bad	Bad	Fair
Latex (123 µm)	Fair	Fair	Fair
Neoprene (397 µm)	Fair	Fair	Fair

- **Eye protection**

Safety glasses are mandatory in all Concordia University laboratories and should therefore be the minimal eye protection to be worn when appropriate engineering controls (e.g. nano-cabinet or glove box) is being used.

However, safety goggles offer an increased eye protection compared to safety glasses and should be favored when:

  - appropriate engineering controls are deficient or not available;
  - a heavy use or large amounts of nanoparticles are being used;
  - a suspension of nanoparticles in solvents is being generated and splash or aerosol generation is possible.

Figure 21: Skin exposure due to improper glove use

- **Protective clothing**

It was demonstrated the nanoparticles could get through most of regular woven fabrics (e.g. cotton). Therefore, regular lab coats do not offer an appropriate protection from nanoparticles. Impervious disposable clothing, such as Tyvek® lab coats, sleeves and shoe covers should rather be used (Fig. 22).

Their fabrics are shown to be impermeable to nanoparticles. If a head scarf is worn by the lab user, a Tyvek® hood should be worn on top of it to avoid possible contamination of the cloth.

Figure 22: Examples of Tyvek® protecting-gear (images from Dupont company)

Protecting clothing should be stored and donned in a dedicated "buffer" area in lab area in order to avoid cross-contamination. Protection clothing should not be worn outside lab and non-disposable work clothes should not be taken home for cleaning; re-usable protective clothing should rather be laundered through department laundering services. Disposable protecting clothing (gloves and Tyvek® gear) should be disposed of as chemical waste.

- **Respiratory protection**

Respiratory protection should be worn when working with dry nano-powders and when appropriate engineering controls (e.g. nano-safety cabinet) are deficient or not available. Here are descriptions of different types of respirators or masks available on the market along with their intended use; it has to be noted that these respirators cannot be used in areas of low oxygen concentration (i.e. an oxygen deficient atmosphere).

- *Surgical masks*

  Those are loose-fitting and disposable masks preventing the release of contaminants from the user to the environment. They are not meant to protect against dust or nanoparticles and should therefore not be used in laboratories using nanoparticles.
- *Filtering Face-piece Respirators (FFRs)*

  Those are the most commonly used disposable respiratory masks and they protect user from dusts and aerosols according to their NIOSH certification:
  - N : not resistant to oil particles
  - R : somewhat resistant to oil particles (8 hours of continuous or intermittent use)

- P : strongly resistant to oil particles(oil proof)
- 95, 99 or 100 : protection rating (%) in NIOSH test

FFRs do not act as sieves but rather intercept nanoparticles using different types of filtering mechanisms; impaction, interception, diffusion and electrostatic attraction (when electret filter media is used). Once the particles are trapped within the FFRs filter media, they cannot be removed (not a reversible process).

Several tests performed by different institutes (e.g. NIOSH, OSHA, IRSST…) demonstrated that typical N95 masks met the NIOSH filtering standards (< 5% penetration for particles less than 100 nm) offering therefore an adequate protection against nanoparticles. However, their efficacy was greatly affected by humidity and breathing rate.

The main safety issue observed with the disposable FFRs resides in achieving proper seal around nose and mouth. Improper use or bad work practices by workers (e.g. putting de FFRs on top of the head) often results in a lose fit which allow nanoparticles to enter the mask (Fig. 23). Therefore, their use for work with nanoparticles is not recommended by EHS.

- *Half or full-face respirators*

Half or full-face respirators consist of a rubber (i.e. silicone) mask, worn over the nose and mouth and held in place by adjustable straps which go over and behind the user's head (Fig. 24). The respirators are fitted with two removable filter cartridges. These units are heavier than the disposable FFRs, but provide far better protection for the wearer, provided that they are fitted properly. Anyone requiring to wear a half or full-face respirator must previously get fit-tested by EHS. This can be done contacting EHS at ehs@concordia.ca.

Figure 23: N95 FFR with an improper use of mask: the white powder around the nostrils shows that this mask did not have a tight fit.

The respirators require periodic maintenance and cleaning. They are washable and reusable but should not be shared among users. They require filter cartridges adapted to risk.

Figure 24: Examples of half and full-face respirators

When working with nanoparticles in the absence of appropriate engineering controls, EHS recommends the use of a half-face respirator since it offers a better seal then disposable masks. The half-face respirator should be equipped with P100 filter cartridges which are comparable to HEPA filters. Studies demonstrate that they are good in protecting users from nanoparticles with sizes down to 2.5 nm.

6) Storage, Waste Handling, Waste Issues and Spills

a) Storage

Nanoparticles, nanomaterials and nanopowders must be stored in closed and sealed containers at all times, in a cool and well-ventilated area clearly identified (e.g. 'Nanomaterials storage area – 'POTENTIALLY TOXIC'). If possible, a lab cabinet restricted to nanomaterials storage only should be dedicated.
All containers with nanoparticles in should be clearly identified (e.g. Nanoscale Gold Nanoparticles). If the nanoparticles are received in plastic (Ziploc) bags from the supplier, the bag should be placed in a secondary hard sealable container. Nanoparticles and nanopowders should be stored away from acids, oxidizers and other metals.

b) Waste Handling

There are currently no specific regulation or guidelines for proper disposal of nanoparticles. It is therefore important to handle nanoparticles very cautiously since they are to be considered as toxic. Any waste containing nanoparticles or nanomaterials should never be disposed of in regular garbage and flushed down the drain. Nanoparticles should be disposed of following EHS chemical waste guidelines:

- any contaminated objects (paper, wipes, tips) should be disposed of as solid chemical waste;

- any contaminated disposable PPE (e.g. gloves, disposable lab coats) should be disposed of as solid chemical waste;
- pure nanomaterials/nanoparticles in the solid (including powder) form should also be disposed of as chemical waste;
- nanoparticles in solution can be disposed of as liquid chemical waste.

All waste containers should be properly labelled, mentioning that they contain nanoparticles and should be properly sealed once full and ready to be picked up. For any concerns about nanomaterials waste, please contact EHS at hazardouswaste@concordia.ca.

c) Spills

The potential for inhalation exposure during cleanup will be influenced by the likelihood of nanoparticles becoming airborne, with powder form presenting a greater inhalation potential than the solution forms.

Small nanoparticle spills that occur on non-porous surfaces (e.g. linoleum, stainless steel, hardwood flooring) can be cleaned by trained lab personnel. However, if the spill occurs on a porous surface or item (e.g. rug or mat), it might become difficult to fully decontaminate this surface and therefore the item should be discarded along with other nanomaterial waste.

1) In the event of a small spill

If lab users are within their comfort zone or have been trained for spill response, they can clean up the spill using the following techniques:

- Any solid nanoparticles should be cleaned up using wet wiping.
- Dry sweeping or air hoses should not be used to clean work areas. If dry vacuuming is to be used, only a vacuum cleaner equipped with a HEPA is to be used.
- Absorbent wipes for liquid suspensions.

NIOSH recommends the following equipment included in a nanomaterial spill kit to be readily available in or near each laboratory working with such materials. A nanomaterial spill kit for a laboratory environment may contain the following:

- Barricade tape
- Nitrile gloves
- Elastomeric respirator with appropriate filters
- Adsorbent material
- Wipes
- Sealable plastic bags
- Walk-off mat (e.g., Tacki-Mat®)
- Spray bottle with deionized water or other appropriate liquid

Procedure:

1. Clean-up the spill immediately after it has occurred.
2. Prevent the spread of the spilled nanomaterials. DO NOT allow people to walk through spill area.
3. Wear PPE (like disposable gloves and shoe covers or place double plastic bags over your shoes) during the clean up.
4. Place the collected nanoparticles into a clearly labelled and sealed chemical waste container.
5. Contact EHS (hazardouswaste@concordia.ca) for waste pick-up.

2) In the event of a large spill

Large spills or spills of highly toxic or dangerously reactive materials should not be handled by lab users. In the event of any large spills, lab users should readily contact Security at extension 3717.

Procedure:

1. Advise and warn co-worker
2. Help contaminated or injured persons.
3. Evacuate the spill area and do not touch the hazardous material
4. Keep others from entering contaminated area.
5. Notify Security at extension **3717 or 514-848-3717** and provide them with the following information:
   - Location of spill;
   - Name of hazardous material;
   - Quantity involved;
   - Related health hazards and precautions to be taken.
6. Provide Material Safety Data Sheet or Safety Data Sheet (MSDS/SDS) or appropriate documentation.

Lab users need to remain available to the Emergency Response Team or Security in order to provide assistance. An Injury/near-miss report must be filled up in the event of any types of spill. Injury/near miss reports can be found on the EHS website in the injury report section.

7) Emergency Procedures

Nanoparticles and nanomaterials toxicity are often found to be chemical-specific. The effects of exposure to nanoparticles may therefore vary depending on the type of materials being used (e.g. nanoclays, carbon nanotubes or metals). One must therefore always refer to the MSDS/SDS of the chemical being used. Here are some general guidelines in the event of exposure.

a) Skin Contact

1. Remove any contaminated clothing immediately.
2. Wash affected area with soap or mild detergent and large amounts of water until no evidence of the nanomaterial remains (15-20min).

3. Refer to MSDS/SDS of material.
4. Contact Security ext. **3717** to get medical attention.
5. Any contaminated clothing should be washed before reuse.

b) Eye Contact

1. Immediately rinse eyes and inner surface of eyelid with water for 15 minutes by forcibly holding the eye open.
2. Refer to MSDS/SDS of material.
3. Contact Security ext. **3717** to get medical attention.

c) Inhalation

1. Remove from exposure and move affected person to fresh air immediately.
2. Refer to MSDS/SDS of material.
3. Contact Security ext. **3717** to get medical attention.
4. If breathing is difficult, give oxygen.
5. If breathing has ceased, apply artificial respiration using oxygen and a suitable mechanical device such as a bag and a mask; never give direct mouth-to-mouth resuscitation to avoid any potential contamination.

d) Ingestion

1. Rinse inside of mouth with water.
2. Do not induce vomiting.
3. Refer to MSDS/SDS of material.
4. Never give anything by mouth to an unconscious person.
5. Contact Security ext. **3717** to get medical attention.

All nanomaterial incidents must be reported to your Supervisor and to EHS. An Injury/near-miss report must be filled up for any incident involving nanomaterials/nanoparticles spill or exposure. Injury/near miss reports can be found on the EHS website in the injury report section.

If you have any concerns about the use of nanoparticles or nanomaterials at Concordia University, please contact EHS at **ehs@concordia.ca**

Last revision: April 2017

References:

- National Institute of Environmental Health and Safety
    - http://www.niehs.nih.gov/health/topics/agents/sya-nano/
- CAUT Health and SafetyFact Sheet

- http://www.caut.ca/docs/default-source/health-safety-fact-sheets/animal-hazards.pdf?sfvrsn=8
- Florida State University – Laboratory Safety
    - http://www.safety.fsu.edu/lab-nano.html
- University of Dayton – Environmental Health and Safety/Risk Management – Nanotechnology Safety
    - http://campus.udayton.edu/~UDCampusPlanning/EHSRM/index.php?option=com_content&view=article&id=18&Itemid=205
- The National Institute for Occupational Safety and Health, division nanotechnology
    - https://www.cdc.gov/niosh/topics/nanotech/default.html
- National Collaborating Center for Environmental Health - Nanotechnology: A Review of Exposure, Health Risks and Recent Regulatory Developments
    - http://www.ncceh.ca/sites/default/files/Nanotechnology_Review_Aug_2011.pdf
- Scientific Committee on Emerging and Newly Identified Health Risks - Risk Assessment of Products of Nanotechnologies
    - http://ec.europa.eu/health/ph_risk/committees/04_scenihr/docs/scenihr_o_023.pdf
- European Commission - Guidance on the protection of the health and safety of workers from the potential risks related to nanomaterials at work
    - https://osha.europa.eu/en/news/eu-safe-use-of-nanomaterials-commission-publishes-guidance-for-employers-and-workers
- Safe Work Australia – Safety Hazards of Engineered Nanomaterials Information Sheet
    - http://www.safeworkaustralia.gov.au/sites/SWA/about/Publications/Documents/762/Safety-hazards-engineered-nanomaterials.pdf
- IRSST - Development of a Procedure to Measure the Effectiveness of N95 Respirator Filters against Nanoparticles, R-754
- IRSST - Development of a Method of Measuring Nanoparticle Penetration through Protective Glove Materials under Conditions Simulating Workplace Use, R-785
- IRSST – Nanomatériaux; Guide de bonnes pratiques favorisant la gestion des risques en milieu de travail, 2e édition, R-840
- IRSST - Mesure de l'efficacité des gants de protection contre les nanoparticules dans des conditions simulant leur utilisation en milieu de travail, R-933
- Working Safely with Nanomaterials in Research & Development, The UK NanoSafety Partnership Group, 2012
- Francesca Larese Filona et al., Occupational dermal exposure to nanoparticles and nano-enabled products: Part I—Factors affecting skin absorption, International Journal of Hygiene and Environmental Health, 2016
- S.-J. Tsai et al., Airborne nanoparticle exposures associated with the manual handling of nanoalumina and nanosilver in fume hoods, J. Nanopart. Res., 2009.
- K.H. Dunn et al., Evaluation of leakage from fume hoods using tracer gas, tracer nanoparticles and nanopowder handling test technologies, J. Occup. Environ. Hyg., 2014.

Books:

- Adverse Effects of Engineered Nanomaterials: Exposure, Toxicology, and Impact on Human Health
    - http://books.google.ca/books/about/Adverse_Effects_of_Engineered_Nanomateri.html?id=rC7mkNykKR4C&redir_esc=y
- Nanotechnology Safety
    - http://books.google.ca/books/about/Nanotechnology_Safety.html?id=WmenH4XSX9AC&redir_esc=y

- Adverse Effects of Engineered Nanomaterials: Exposure, Toxicology, and Impact on Human Health
    - http://books.google.ca/books/about/Adverse_Effects_of_Engineered_Nanomateri.html?id=rC7mkNykKR4C&redir_esc=y

Additional Reference:

- Good Nano Guide (NIOSH)
- International Council on Nanotechnology (ICON)
- NIOSH Safety and Health Topic: Nanotechnology
- OSHA Safety and Health Topics: Nanotechnology
- Institut de Recherche Robert-Sauvé en Santé et Sécurité du Travail (IRSST)
- NaNoQuebec
- CSA Group