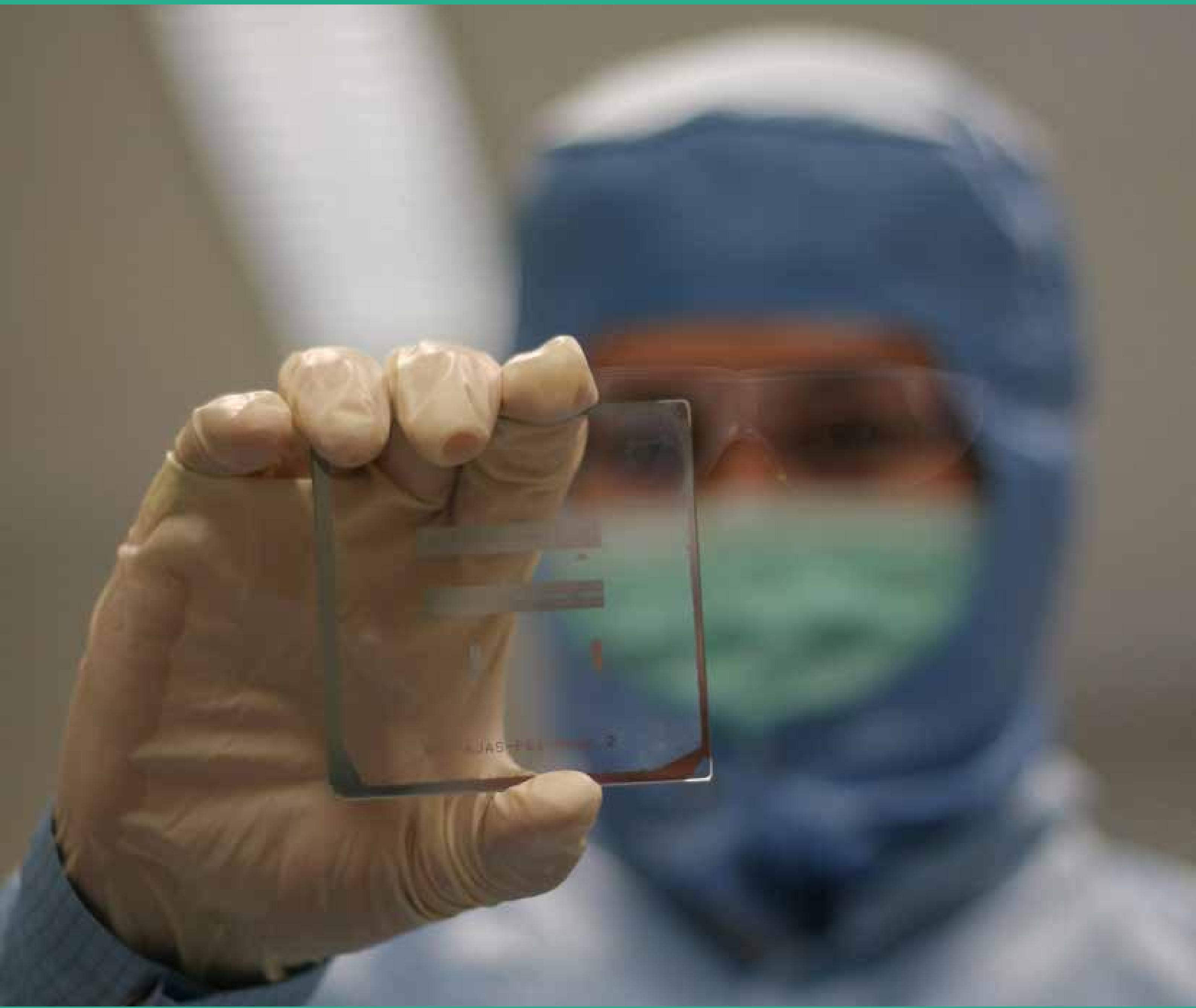
Guidelines and Best Practices for Safe Handling of Nanomaterials in Research Laboratories and Industries



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(with inputs from Nanoregulatory Task Force)

By

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About the Report

Realising the emerging importance of safe handling of Nanomaterials, the Nano Mission of Govt. of India constituted a Nanoregulatory Task Force consisting of eminent experts to bring out a comprehensive document on "**Guidelines and Best Practices for Safe Handling of Nanomaterials in Research Laboratories and Industries**".

Under the able guidance of Nano Mission and Nanoregulatory Task Force, CKMNT has brought out this comprehensive document based on published reports by regulatory bodies like ISO, OECD, NIOSH, OSHA and other reports available in public domain.

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1. Introduction

Engineered nanomaterials, as for example, nanospheres, nanotubes, nanowires and nanosheets, possess a unique combination of physical, chemical, biological, mechanical, electrical and thermal properties. This makes them promising candidates for a variety of structural and functional applications. However, due to their extremely small dimensions, large surface area and high reactivity, they have the potential ability to penetrate living cells quite readily. As a result, their unique nano-features may also make them potentially hazardous for human health and environmental safety. Therefore, intense research activity is being undertaken in various R&D institutions, universities and industries across the world to evaluate their toxicity and critical exposure levels. Currently, evidence regarding the toxic effects of nanomaterials on humans in the scientific and technical literature is insufficient and consequently their risk remains unknown.

Under the umbrella of the Government of India's Nano Mission, as well as by virtue of substantial research funding from other sources, a large number of researchers from national laboratories, universities and industries are pursuing R&D work on various projects involving ceramic nanoparticles, carbon nanotubes, nanowires, nanostructured alloys etc. There is every likelihood that persons associated with these projects, as well as their colleagues, could be inadvertently exposed to the various nanomaterials being investigated in their laboratories, which may cause health related problems if proper precautions are not taken in handling them. Nanomaterials-related safety has been a growing concern among the research community and the regulatory agencies in India. In view of this, the Nano Mission has decided to formulate a regulatory framework to address the issues of Environment, Health and Safety (EH&S) impact and risk from nanomaterials and nano-related products. Recently, a task force has been set up under the chairmanship of Dr. Baldev Raj, former director, Indira Gandhi Center for Atomic Research (IGCAR) to lay a roadmap to regulatory framework for nanotechnology in India. Based on the recommendations of the above task force, the Centre for Knowledge Management of Nanoscience and Technology (CKMNT), partially funded by the nano mission and the International Advanced Research Centre for Powder Metallurgy & New Materials (ARCI), has taken up a new initiative to prepare guidelines for scientists and technocrats working in R&D laboratories to implement best practices for safe handling of nanomaterials at their work places. The following guidelines address the exposure risks and prudent control measures to be followed while working with nanomaterials to reduce risks. It is recommended that the researchers planning to work with nanomaterials must implement a combination of engineering controls, work practices, and personal protective equipment to minimize potential exposure to themselves and others. It is hoped that this document would serve as an interim reference until a comprehensive regulatory framework that covers the potential risks and safe handling procedures of nanomaterials is formulated. This will ensure that nanomaterials are produced, handled and used in a safe and sustainable way that is essential to exploit their societal benefits. Over the years, regulators and industry have put in place systematic processes for identifying, managing and reducing potential environmental, safety and health risks of chemicals across their entire life cycle. As nanomaterials are chemical substances, this approach also applies to them. The EU's comprehensive regulatory framework, including REACH, can be implemented and where necessary adapted to effectively regulate nanomaterials.

Looking beyond the potential technical risks associated with nanomaterials, there is actually only scarce information available about the impact of nanomaterials on non-human species, on ecosystems or the global environment. Even within established questions of toxicology, still the fact is unclear about how different nanoparticles exactly interact within the human body or with the environment, which means that more data is needed.

With a view of providing basic guidelines to the researchers on safe handling of nanomaterials, CKMNT has compiled this document based on published reports by regulatory bodies like ISO, OECD, NIOSH, OSHA available with public domain and experience, of Indian experts.

2. Identifying hazards

The identification of hazards is the first step in determining risk and exposure. This step involves identifying chemicals or nanomaterials, and their associated processes that pose toxic, physical (e.g. high levels of noise, high pressures and vacuum, strong electromagnetic flux, etc.) and physicochemical hazards.

When assessing the risks associated with nanomaterials, special care should be taken to identify the specific effect of surface chemistry, shape, size and morphology on toxicity caused to various organs. The following primary hazard categories may be considered when assessing risk associated with nanomaterials.

Surface charge

- The most interesting physicochemical feature of nanoparticle relating to cytotoxicity is the surface charge, with toxicity increasing in the following way:
  neutral < anionic < cationic.
  [Ref: Angeles Villanueva et al., "The influence of surface functionalization on the enhanced internalization of magnetic nanoparticles in cancer cells", Nanotechnology 20 (2009) 115103]

Surface chemistry

- Surface chemistry of nanoparticles may have a role in the generation of free radicals, which influences the overall surface reactivity and toxicity of ingested particles.

Particle shape

- Studies have clearly established that exposure to fibrous particles like asbestos increases the risk of fibrosis and cancer. Similarly, the tubular structure of carbon nanotubes is believed to cause inflammation and lesions in lungs.

Particle size

- Nanoparticles have a greater chance of depositing in the lungs than micro-sized particles, and therefore have the potential to cause damage by acting directly at the site of deposition by translocating to other organs or by being absorbed through the blood. Nanoparticles can penetrate the membrane barriers resulting in significant damages. For example, silver nanoparticles with size < 9 nm can penetrate the nuclear membrane of certain human cells nucleus and cause significant DNA damage or mutation.

Solubility

- Poorly soluble inhaled nanoparticles can cause oxidative stress, leading to inflammation, fibrosis, or cancer. Studies have shown significantly higher toxicity of nano metals when compared to nano ceramics, which has been attributed to higher dissolution rate in water.

Toxic hazards

- Nanomaterials provided with the guidelines for exposure, such as threshold limit values (TLV) or permissible exposure limits (PEL) helps in determining proper safety precautions, including control measures and safety apparel.
- Materials with TLV or PEL less than 50 ppm should be handled with utmost care preferably under fume hood.
- High vapor pressure indicate potential hazard. However, low vapor pressure of even 5-10 mm Hg with low TLV (less than 10) can be highly hazardous.
- When TLV or PEL values are not available for a substance, the chemical must be used inside the fume hood.
- Whenever the chemicals have high vapor pressure, it must be used only under a fume hood. The Material Safety Data Sheet (MSDS) or container label identifies or describes the substance as toxic.

Fire Hazard

Flammability of a chemical is determined by its flash point.

- Any chemical with a flash point below 200°F (93°C) should be considered as a fire hazard.
- When used in quantities in excess of 100 mL, fire hazard procedures should be followed.
- When stored in quantities in excess of 500 mL, the restrictions on containers listed in table: 1 should be observed.

Table 1: PERMISSIBLE range of containers according to National Fire Protection Association (NFPA) 45 guidelines (2011)

	Flammable Liquids			**Combustible Liquids**	
Container Type	IA	IB	IC	II	IIIA
Glass	500 mL (1 pt)	1L (1 qt)	4L (1 gal)	4L (1 gal)	20 L (5 gal)
Metal (Other than DOT drums approved plastic)	4L (1 gal)	20 L (5 gal)	20 L (5 gal)	20 L (5 gal)	20 L (5 gal)
Safety cans	10 L (2.6 gal)	20 L (5 gal)	20 L (5 gal)	20 L (5 gal)	20 L (5 gal)
Metal container (DOT specification)	4L (1 gal)	20 L (5 gal)	20 L (5 gal)	227 L (60 gal)	227 L (60 gal)
Polyethylene (DOT specification 34, UN1H1, or as authorized by DOT special permit)	4L (1 gal)	20 L (5 gal)	20 L (5 gal)	227 L (60 gal)	227 L (60 gal)
Pressurized liquid dispensing containers	20 L (5 gal)	227 L (60 gal)	227 L (60 gal)	227 L (60 gal)	227 L (60 gal)

Note: The above table is based on 6.2.3 of NFPA 30, (Flammable and Combustible liquid code), except for allowable quantities of flammable liquids in metal (DOT specification) drums and pressurized liquids and dispensing containers.

Definitions of the various classes of flammable and combustible liquids.

- *Flammable Liquid*. A liquid having a flash point below 100^{o}F (38.7ºC) and having a vapor pressure not exceeding 40 lbs/in^2 (2.72 atm.) absolute at 100^{o}F (38.7ºC) is designated a Class I liquid by NFPA
- *Combustible Liquid*. A liquid having a flash point at or above 100^{o}F (38.7ºC)
- Class IA - Liquids having flash points below 73^{o}F (23^{o}C) and boiling point below 100^{o}F (38.7^{o}C).
- Class IB - Liquids having flash point below 73^{o}F (23^{o}C) and boiling point above 100^{o}F (38.7^{o}C).
- Class IC - Liquids having flash point at or above 73^{o}F (23^{o}C) but below 100^{o}F (38.7^{o}C).
- Class II - Liquids having flash points at or above 100^{o}F (37.8^{o}C) and boiling point below 140^{o}F (60^{o}C).
- Class IIIA- Liquids having flash points at or above 140^{o}F (60^{o}C) and boiling point below 200^{o}F (93.4^{o}C).

- To pose a fire risk, nanopowders need to be present in layers containing many grams, even kilograms of material. At present, such quantities will be present only in storage. Any fire assessment therefore needs to address nanomaterials in storage conditions.

Explosion hazard

The flammability and explosivity of nanomaterials can be determined by calculating the minimum ignition energy (MIE) and the minimum exposable dust concentration (MEC) also known as lower explosion limit (LEL). To assess the impact of effects and the explosion severity, parameters like the maximum pressure of explosion and maximum rate of pressure rise (K_{st}) need to be considered. Table: 2 shows the severity of explosion based on rate of pressure rise, K_{st}.

Table 2: Classification according to the maximum rate of pressure

Dust explosion class	**K_{st} (bar m/s)**	**Characteristics**
St 0	0	no explosion
St 1	>0 - <200	weak explosion
St 2	>200 - <300	strong explosion
St 3	>300	very strong explosion

Correlation of K_{st} -Value with Maximum Pressure Rise per Unit Time (dp/dt) max.:
$(dp/dt)_{max} * V^{(1/3)} = K_{st}$, (V: Volume of the vessel)

In case of nanopowders having large surface area, the particles can be easily charged electro statically thereby increasing the risk of ignition. The small size of nanoparticles makes them to remain in the air for longer time, creating potentially explosive dust clouds. Aggregated nanoparticles with size in the range of microns may pose threat to explosion or fire risk by ignition or even spontaneous combustion. As for example, the explosion sensibilities and severities of carbon black and carbon nanotubes were found to be of the same order, and their explosion class was assessed as St 1. The aluminium powders having much lower MIE pose much higher flammability hazard and hence the severity of the explosion was classified as strong or very strong (St 2 or St 3) based on the particle size.

3. Pathways and common tasks that could result in exposure

The primary routes to exposure for nanoparticles are inhalation, dermal absorption and ingestion. The state of the nanoparticles or nanomaterials decides the exposure potential. For example, nanoparticles in powdered form present a large inhalation hazard potential when compared to nanoparticles in suspension. Table: 3 summarize the exposure pathways and suggested prevention methods.

Table 3: Exposure pathways and safety measures

Type of Exposure	Pathway	Safety measures
Dermal	Nanoparticles can migrate through skin and circulate in the body while handling nanoparticle suspensions or dry powders. Skin absorption is much less likely for solid bound or matrixed nanomaterials.	Wear gloves and lab coat while handling the nanoparticles.
Ingestion	Ingestion can occur if good hygiene practices are not followed. Nanoparticles might be absorbed and transported within the body by the circulatory system.	Eating and drinking are not allowed in laboratories. Spills of nanoparticles should be quickly and properly cleaned-up.
Inhalation	Respiratory absorption through the mucosal lining of the trachea, bronchioles or the alveoli of the lung.	Nanoparticles are to be handled in a form that is not easily airborne, such as in solution or on a substrate. Use of respiratory air filters N100 or N95 is recommended.
Injection	Exposure by accidental injection (skin puncture), when working with animals or needles.	Wear gloves and lab coats, and apply the standard practices for working with sharp objects.
Ocular	Exposure to airborne nanoparticles placed near the eye, accidentally splashed onto the eye or transferred from hands during rubbing of eyes.	Wear safety glasses, goggles, full facepiece respirator (Recommended when there is exposure to solvent or hot material). Note: Do not wear contact lenses at work place

4. Exposure Control Strategies

a. Engineering controls

Exposure to nanoparticles should be controlled by applying protection measures appropriate to the activity. Engineering control techniques include:

- Source enclosure (i.e., isolating the generation source).
- Exhaust ventilation system with high-efficiency particulate air (HEPA) filters for capturing airborne nanoparticles.
- Routine monitoring of the ventilation systems and proper maintenance of the records for its effective use.
- Use glove bags, glove boxes, fume hoods, or other containment or exhausted enclosures when there is a potential for aerosolization, such as: handling powders; creating nanoparticles in gas phase; pouring or mixing liquid media which involves a high degree of agitation. (DO NOT use horizontal laminar flow hoods (clean benches), as these devices direct the air flow towards the worker.).
- Use fume hoods or other local exhaust devices to exhaust tube furnaces and or chemical reaction vessels.
- Air lock and sealed containers are to be used for collecting nanomaterials from reactors.
- Use of distillation system for evaporating solvent from a colloidal dispersion within an explosion-proof enclosure.
- Remote control set up for nanomaterial production equipment.

b. Administrative (procedural) controls

Administrative means of control comprise of a supplementary approach when other methods have not achieved the expected control levels, and these control strategies include:

(i) Training

When handling nanomaterials, effective training and instruction for the workers is critical to ensure health and safety. A number of issues should be considered while training the personnel working with nanomaterials as listed below.

- Safe handling of nanomaterials and standard operating procedures (SOP)
- Hazards and toxicity
- Personal protective equipments(PPE)
- Engineering controls and equipment maintenance
- Emergency procedures
- Waste handling
- Definition of nanoparticles
- Environmental release/shipping/customer protection
- Exposure monitoring
- Applicable regulation
- Labeling and handling of nanomaterials waste

(ii) Housekeeping

Good housekeeping practices in laboratories where nanomaterials are handled can minimize the risk of exposure.

- Clean all working surfaces potentially contaminated with nanoparticles (i.e., benches, glassware, apparatus, exhaust hoods, support equipment) at the end of each day using industrial vacuum cleaner equipped with HEPA filters.
- The HEPA vacuums should be labeled "For use with nanoparticles only" and must be used only for this purpose.
- Do not dry sweep or use compressed air.
- Dispose of used cleaning materials in accordance with the hazardous-waste procedures.

(iii) Work practices

- Whenever possible, handle nanomaterials in solutions or attached to substrates to minimize airborne release.
- Consult the material safety data sheet (MSDS), if available or other appropriate references prior to using a chemical or nanomaterial.
- While working with nanomaterials in liquids
    - Avoid spreading of the liquid by working in a spill container.
    - Wear gloves that are suited for the liquid being handled.
    - Avoid the dispersion of liquid droplets in the lab air.
    - Directly clean up spills, before evaporation or further spreading occurs.
- While working with nanomaterials in gas phase reactors
    - Work in a closed reaction vessel, preferably around atmospheric or lower than atmospheric pressure.
    - Make sensitive leak checks between runs.
    - When working with systems under positive pressure obey the standard safety rules for pressurized vessels and put the vessel into an enclosed safety vessel.
    - For small positive pressure set-ups a closed fume hood is sufficient.
    - Mount a HEPA filter (e.g. Emflon PFR filter from pall, > 3 nm) on the exhaust side of the process before leading into the fume hood and the outside air.
- While working with nanomaterial powders
    - Handle free nanomaterial powder exclusively in a closed fume-hood or an enclosed vessel (glove box).
    - If handling outside a closed environment cannot be avoided, wear class P3 (Filters at least 99.95% of airborne particles) certified respiratory filters.
    - For characterization purposes such as XRD analysis, use a drop of oil to contain the powder and preventing it from becoming airborne.
    - Clean all parts that have been in contact with nanoparticles and spills after using appropriate protection.

(iv) Medical surveillance

The use of health surveillance program is an indicator of whether exposure is occurring, rather than in determining that levels of exposure are safe.

- Several potential disease conditions such as chronic immune responses of inflammation, allergy, respiratory disorders, gastrointestinal related disorders, neurological disorders, several types of cancers resulting from oxidative damage to DNA and tissue damages are emerging with the increased use of nanomaterials.

- It is recommended to have a regular health monitoring program and periodical medical surveillance of pulmonary, renal, liver and hematopoietic functions.
- The regular health monitoring helps in the early detection of any health effects which would considerably reduce the likelihood of long term harm.
- It is recommended that a basic worker health monitoring program is established. Such a program should include at a minimum
- Identifying staff exposed to engineered nanoparticles of unknown health effects.
- Conducting workplace characterization and worker exposure assessments
- Providing workers with baseline medical evaluations and including them in a non-specific routine health monitoring program.

(v) Record keeping

In order to establish and maintain safe and healthy workplaces, effective record keeping is required. Records of the following areas need to be maintained:

- Induction and training programs
- Risk assessments
- Servicing and testing of equipment
- Workplace monitoring
- Health surveillance (to be kept confidential)
- Work related injuries and illnesses
- Work place engineering control maintenance, daily checks and examinations
- Disposal records

vi) Workplace monitoring

Reported studies have proved that the work place monitoring is important because it can significantly help the research group or organizations to describe the nanomaterial risk. The work place monitoring includes

- Monitoring the particle concentrations at the working place using different types of particle counters, condensation particle counters, scanning mobility particle sizers or other means of particle collections, such as witness plates and particle size analysis by electron microscopy.

(vii) Storage

- Storing nanoparticles might involve special protection to safeguard the products and to ensure workplace health and safety.
- Storage containers of nanoparticles should accommodate different granulometric characteristics and reactivity of particles.
- In order to avoid oxidation or explosion in case of certain metal nanoparticles, they are often needed to be protected from exposure in air and stored under inert gas/liquid bath.

c. Personal Protective Equipments (PPE)

Nanoparticle exposure is often due to the wearing of inadequate PPE. Typical protective clothing's should include:

- Closed-toed shoes made of a low permeability material.
- Long pants without cuff.
- Long sleeved shirt.
- Nitrile gloves with extended sleeves. (Note: Advisable to use two pairs of gloves, as in case of carcinogenic material, to exercise abundant caution).
- Chemical splash goggles, safety glasses and full-face shields are recommended for eye-protection when there is potential for exposure to nanomaterials.
- Respiratory air filters (N100 recommended or N95).
- Full facepiece respirators offer eye protection in addition to respiratory protection.

d. Waste disposal

- Milligram range nanomaterials residues can be poured in sealed containers appropriately labeled and disposed off following the standard procedure in the hazard area proclaimed by the respective authority.
- Quantities of nanomaterials (powders, colloids) exceeding the milligram range should be treated as hazardous chemical waste, if the particle solubility in water is very small (inorganic materials like metals, metal oxides etc.).
- If the solubility is higher, the rules according to the toxicity class of the macroscopic material apply.
- Do not put engineered nanomaterials waste in the regular trash or dump it down the drain.
- All nanomaterials waste, as defined above, should be collected in labeled, enclosed hazardous waste containers with secure caps or covers. The label should include a description of the waste and prominently the words "*contains nanomaterials*".
- Collect paper, wipes, PPE and other items with loose contamination in a plastic bag or other sealable container and store it in a fume hood until it is full, then double-bag it, label it, securely tie or seal it, and dispose of it following appropriate procedures.
- Nanomaterial hazardous waste containers shall be collected and disposed of as hazardous waste following the standard procedures.

5. Best practices to be followed while handling nanoparticles

a. Locating emergency equipment

- Know the location and proper use of emergency equipment, such as safety showers, fire extinguishers, and fire alarms.

b. Hygiene

- Do not consume or store food and beverages, or apply cosmetics where chemicals or nanomaterials are used or stored since this practice increases the likelihood of exposure by ingestion.
- Do not use mouth suction for pipetting or siphoning.
- Wash hands frequently to minimize potential chemical or nanoparticle exposure through ingestion and dermal contact.

- Remove gloves when leaving the laboratory, so as not to contaminate doorknobs, or when handling common use objects such as phones, multiuser computers, etc.

c. Labeling and signage

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

d. Cleaning procedures and spills

- Specifically watch out for exposure during cleaning operations.
- Wear gloves and work in a fume hood if the equipment allows this. Clean the fume hood afterwards.
- If needed, monitor the lab air nanomaterial concentrations during clean-up.
- Wear respiration protection when working outside a fume hood or in an open fume hood and consider overall protection.
- All contaminated material must be disposed of as chemical waste.
- Materials and surfaces can be cleaned by following techniques:
    - Wiped with a wet cloth (use water or solvent) where possible, rinsing off the cloth with water or disposing it off.
    - Vacuum cleaned, where the exhaust of the vacuum cleaner is equipped with a HEPA filter and is not equipped with a pressure relief valve that bypasses this HEPA filter if blocked. Monitor the exhaust of the vacuum cleaner during operation. A malfunctioning filter can increase the exposure by dispersing the nanomaterial in the air.
    - HEPA-filtered vacuum cleaners with combination of wet wiping are more suitable for most nanomaterial clean-up.
    - Energetic cleaning methods such as dry cleaning or use of compressed air should be prohibited.
    - Collect spill cleanup materials in a tightly closed container.
    - Manage spill cleanup debris as hazardous waste.

- Make Nanoparticle spill kit containing the following items readily available to respond to spills.
    - Barricade tape
    - Latex or nitrile gloves
    - Disposable N100 (best rated filter by the CDC and WHO and is recommended for ultimate protection, have a minimum filter efficiency of 99.97% of particulate matter of average particle size less than 0.3 micron.) respirators
    - Adsorbent material
    - Wipes
    - Sealable plastic bags

  - Walk-off mat
- Small spills can be cleaned as described above.

6. Best practices and adequate approaches regarding making and handling of nanopowders and use of products relating to food and healthcare

Nanotechnologies offer a variety of possibilities for application in various areas of food technology that include packaging, processing, quality and shelf-life, ingredients and additives. Nanotechnology could also revolutionize healthcare in three major areas namely, diagnosis, prevention and treatment. Eventually, nanotechnology will be able to deal with medical issues such as repair of damaged organs, diagnosis and treatment of cancer, creation of artificial materials for diagnosis or delivery of new and better drugs, creation of artificial tissues, etc. However, there are a number of concerns regarding the safety, environmental, ethical, policy and regulatory issues. The main safety concern arises from the lack of knowledge among common people about the potential effects and impacts of nano-sized materials on human health and the environment. The difficulty in characterizing various nanomaterials used in food, their detection and measurement in food and biological systems, limited information on toxicology, toxico- kinetics, and lack of optimal test methods make the risk assessment and management of nanotechnologies more difficult. A precautionary approach with detailed life cycle assessment and strong binding procedures with respect to stakeholder involvement for various players should be adapted while formulating best practices that will support a sustainable growth of nanotechnology in food sector while regulating the potential risk to humans and environment.

The possible hazards of nanomaterials on human health and environment are now a well established issue. Humans are exposed to nanomaterials via oral route through the residues present in cultivated crops, meat and milk produced for consumption. Further, oral exposure is most significant in food processing technology and functional foods. Nanomaterial exposure from food packaging is mainly dermal, arising from handling such materials. Studies using engineered nanoparticles (ENPs) in isolated cell experiments showed DNA damage. Short-term ENP exposure in animals has also produced dose-dependent inflammatory responses and pulmonary fibrosis. Hence there is an urgent need to establish the long-term safety of engineered nanoparticles (ENPs) in humans.

It is clear that even though nanotechnology is being increasingly explored in various food technologies and healthcare, at the same time, more and more studies are revealing the various toxic effects of nanomaterials on humans and environment. Hence it is mandated to have a stringent quality control of the nanotechnology enabled products, regulatory compliance and provide health and safety reassurance to the consumer. Following are few recommendations that may be implemented to reduce risks associated with nanomaterials while their handling and manufacturing as well as in the finished products.

<u>During manufacturing and handling of nanomaterials:</u>

1. Nanomaterials must be stored and transported in sealed shatter-resistant containers. Containers must be labeled with nanomaterial name (or composition) and approximate particle size, along with any known hazard warnings.
2. Weighing and measuring of dry powders where aerosolization and release of nanomaterials are possible should be conducted in defined and closed areas (see Table 4).
3. Various processing steps such as dispersing, mixing, spraying, machining, gas phase processing have the potential to generate nanoparticles with a high concentration. There is a significant chance of inhalation, dermal and ingestion exposures during these steps. Hence

all nanomaterial generators must have sufficient operating controls (see Table 4) to prevent employee exposure to nanomaterials during operating and maintenance procedures. Personal protective equipment should be used to minimize dermal and eye exposure.

4. Employing a closed facility to process nanomaterials will considerably reduce the occupational exposure during the production and processing stages. Particular care should be taken to avoid disturbance of the closed facilities and cleaning up of residues should be carried out in wet conditions or with a liquid medium to avoid dust dispersion and thus exposure through inhalation.
5. During working steps which cannot be performed in closed facility (e.g. filling, milling, packaging, sampling), various organizational measures such as efficient extractor systems should be used.
6. Working areas with potential nanoparticle emissions should be monitored by workplace or exposure measurement. A suitable method for technical monitoring of working areas is by total dust measurement.
7. Corporate responsibility is very important in the development of nanotechnology products. Various players in industry and business should take initiatives to specifically evaluate the effects of nanoproducts production and consumption with regard to health, environment and society.
8. Removal of waste and by-products generated at the production facility should be carried out with minimum exposure to humans and the environment.

Table 4: Details of enclosure and isolation controls while working with nanopowders

Control in place	Details
Air lock and sealed containers for collecting nanomaterials from the reactor.	The reactors have to be operated under vacuum and collections need to be done in an air lock sealed container. The air lock allowed for any residual particulate matter to be removed by vacuum before removing the sealed container from the reactor.
Synthesis of nanomaterials in an enclosed environment.	Synthesis of nanomaterials has to be done under fume hood.
Clean rooms with positive pressure differentials.	The clean rooms should have positive pressure differentials that could be exhausted with intermediate spaces of lower pressure between labs and offices.
Portable peristaltic pumps to transfer liquid to waste containers.	To prevent potential spills and reduce aerosolization of the material, peristaltic pumps, can be used as they work on positive displacement and are less prone to producing aerosols than conventional high pressure pumps.
Use of distillation system for evaporating solvent from a colloidal dispersion within an explosion-proof enclosure.	This enclosure need to be designed with concern for the potential of these nanomaterials to be explosive.
Using an in-line disperser device, which would open a bag of fine particulate feed stock and transfer the material to the chemical reactor.	Use of in-line disperser device is advisable within a HEPA filtered enclosure, which would allow for an exposure and emission-free process.
Remote control set up for the nanomaterial production equipment.	Nanomaterial production setup needs to be operated in an isolated environment within a well ventilated enclosure. Only certain trained and respirator-

	equipped individuals need to be allowed access to the room for cleaning or maintenance.
Use of safety alarms for nanomaterial production.	Safety alarms within the closed system need to be installed which prevents the potential release of nanomaterials due to a malfunction or accident.

7. Safety Practices

a. Transporting

- Use sealed, double-contained container when transporting nanomaterials inside or outside the building.

b. Buddy system

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

c. Explosion safety

- Due to their large surface-to-volume ratio and enhanced reactivity of a strongly curved solid surface, all oxidizable nanomaterials in the powder state must be considered as potentially pyrophoric when put in contact with air. Thus, explosive behavior is possible.
- Assess the risk of an incident in a process where a large un-oxidized sample is momentarily exposed to air. In a process that produces nanomaterial from the gas phase, the particles tend to become cleaner and cleaner while the process runs, e.g. less oxidized.
- Little is known about nano pyrophoricity, so it is recommended to test the pyrophoricity by bringing a small quantity of material in contact with air before producing or handling quantities on the level of one gram or more.
- Be certain that the test is not performed on partially oxidized particles.
- Anti-static shoes and mats should be used in areas where potentially explosive nanomaterials are handled. The shoes reduce the build-up of static charge, which could potentially ignite the materials.
- A distillation system for evaporating solvent from a colloidal dispersion being housed within an explosion-proof enclosure. This enclosure was designed with concern for the potential for these particular nanomaterials to be explosive.

d. Access control

- Determine the extent of area reasonably expected to have been affected, and demarcate it with barricade tape or use another reliable means of restricting entry into the area.
- Assess the extent of the spill. Significant spills are defined as those of more than a few grams of nanoparticles.
- Smaller spills can be cleaned up by trained personnel from the lab using the procedure described under section 6d (Cleaning procedures and spills).

e. Dry materials

- Position a walk-off mat (e.g., Tacki-Mat) where clean-up personnel will exit the access controlled area.
- Do not dry sweep spilled accumulations of dry nanomaterials. Small quantities of dry materials (i.e., gram quantities) can be cleaned up with wet wipes. Dispose of the wipes as hazardous waste, as described above. Significant spills should be vacuum cleaned. Use only HEPA-filtered vacuum cleaners to clean up nanoparticles.
- Ensure that the functioning of the HEPA filters is properly tested as frequently as the manufacturer's recommends. HEPA vacuums for nanomaterials should be dedicated and labeled "For Use with Nanomaterials Only". Used HEPA filters must be appropriately characterized, collected, and disposed of as hazardous or potentially hazardous waste based on the material involved.

8. Product stewardship

Various types of guidance information are provided by the organization/manufacturers supplying nanomaterials to customers. Different types of guidance information provided by the suppliers are listed below. MSDS is the most common form of guidance among these and should be kept at a easily accessible central location

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- Material safety data sheet (MSDS)
- Product information sheet
- Technical instructions
- Personal interaction
- Accompanying letter
- Technical data sheets
- Specification sheets
- Certificates of analysis
- Operation manuals

References

General

- Nanotechnologies — Health and safety practices in occupational settings relevant to nanotechnologies, ISO/TR 12885:2008(E), First edition 2008-10-01.
- Angeles Villanueva et al., "The influence of surface functionalization on the enhanced internalization of magnetic nanoparticles in cancer cells", Nanotechnology 20 (2009) 115103.
- Alok Dhawan, Rishi Shanker,Mukal Das, C. Kailash Gupta, "Guidance for safe handling of nanomaterials" J. Biomed. Nanotechnol, 7 (2011), 218-224.
- Robert A Yokel, Robert Macphail, "Engineered nanomaterials: exposures, hazards and risk prevention", J. Occupational Medicine and Toxicology, 6(7) (2011).
- Marilyn F.Hallock, PamGreenley, Lou DiBerardinis, Dan Kallin, "Potential risks of nanomaterials and how to safely handle material of uncertain toxicity", J. Chemical Health and Safety, 16 (2009), 16-23.
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- Nanotechnologies -- Health and safety practices in occupational settings relevant to nanotechnologies, http://www.nen.nl/web/Normshop/Norm/NPRISOTR-128852008-en.htm.
- Joseph A Conti, Keith K. "Health and Safety practices in the Nanomaterials work place results from an international survey", Environ. Sci. Technol. 2008, DOI: 10.1021/CS702158q and references therein.
- Gh. Amoabeding et al., "Guidelines for safe handling, use and disposal of nanoparticles", J. Physics: Conference Series, 170 (2009) 012037, DOI:10.1088/1742-6596/170/012037 and references therein.
- Volmat Richeter, et al., "of fine powders, hardmetals, hazards and health risks", Metal powder report 62 (2007) 12-14.
- R. Dobashi, "Risk of dust explosions of combustible nanomaterials", Nanosafe 2008: Int. Conf. on safe production and use of nanomaterials, J. Physics: Conference Series 170 (2009) 012029.

Websites for Additional Information on guidelines

- Nanotechnologies-Health and safety practices in occupational settings relevant to nanotechnologies(ISO/TR 12885:2008)
  http://www.iso.org/iso/catalogue_detail?csnumber=52093
- Safety of manufactured nanomaterials
  www.oecd.org/env/nanosafety
- NIOSH workplace safety & health topics
  www.cdc.gov/niosh/topics/nanotech
- Approaches to safe nanotechnology- Managing the health and safety concerns associated with engineered nanomaterials
  http://www.cdc.gov/niosh/docs/2009-125/
- Health effects and workplace assessments and controls
  http://www.osha.gov/dsg/nanotechnology/nanotechnology.html
- Good workplace practices for handling nanomaterials
  http://goodnanoguide.org/tiki-index.php?page=HomePage

- Environmental ,health and safety issues
  http://www.nano.gov
- Fire and explosion properties of nanopowders: A research report-prepared by the health and safety laboratory for the health and safety executive http://www.hse.gov.uk/research/rrpdf/rr782.pdf.
- Explosion hazards associated with nanopowders-A literature review, health and safety laboratory, HSL/2004/12.
  http://www.hse.gov.uk/research/hsl_pdf/2004/hsl04-12.pdf
- Work place exposure to nanoparticle-A report on European risk observatory, European agency for safety and health at work (2009).
  http://osha.europa.eu/en/publications/literature_reviews/workplace_exposure_to_nanoparticles
- Identification of potential health and safety issues associated with MacDiarmid institute funded nanomaterial research in university laboratories-Report prepared for the MacDiarmid Institute (2009).
  http://www.chem.canterbury.ac.nz/research/pubs2009.shtml
- Nanotechnology and life cycle assessment
  http://www.nanoker-society.org/index.aspx?ID_Page=158&ID=417&ID_Plantilla=301&TIPO=asyContenido
- Key guidance for managing the potential risks of nanotechnology
  http://www.safenano.org/KnowledgeBase/Guidance.aspx
- Flammable and combustible liquids code: NFPA 30
  http://www.nfpa.org/aboutthecodes/AboutTheCodes.asp?DocNum=30
- Standard on fire protection for laboratories using chemicals: NFPA 45
  http://www.nfpa.org/aboutthecodes/aboutthecodes.asp?docnum=45

University materials/websites containing information about the safety guidelines

- DOE Nanoscale science researcher centers. Approach to nanomaterial ES&H (June 2007).
  www.sc.doe.gov/bes/DOE_NSRC_ Approach_to_Nanomaterial_ESH.pdf
- MIT. Potential risks of nanomaterials and how to safely handle materials of uncertain toxicity.
  http://web.mit.edu/environment/ehs/ topic/nanomaterial.html
- Texas A&M engineering. Interim guideline for working safely with nanotechnology.
  http://engineering.tamu.edu/safety/ guidelines/Nanotechnology/NANO_
- General principles and practices for working safely with engineered nanomaterials, Stanford university
  http://www.stanford.edu/dept/EHS/prod/researchlab/IH/nano/lab_safety_guidelines.html
- Nanosafety guidelines preventing exposure to nanomaterials at the faculty of applied sciences, Delft university
  https://intranet.tudelft.nl/.../pagina.jsp?...Guidelines_Nano_Safety...pdf
- University of Pittsburgh safety manual: EH&S guideline number 02-003 dated 04/04/2011, “Storage and handling of flammable and combustible liquids”, pp. 1-10 (2011).

Abbreviations

ARCI	International Advanced Research Centre for Powder Metallurgy & New Materials
CDC	Centre for Disease Control and Prevention
CKMNT	Center for Knowledge Management of Nanoscience and Technology
DOT	Department of Transportation
EH &S	Environment, Health & Safety
EPA	Environmental Protection Agency
HEPA	High-Efficiency Particulate Air
IGCAR	Indira Gandhi Center for Atomic Research
ISO	International Organization for Standardization
LCA	Life Cycle Assessment
MSDS	Material Safety Data Sheet
NIOSH	National Institute for Occupational Safety and Health
NFPA	National Fire Protection Association
OECD	Organization for Economic Co-operation & Development
OSHA	Occupational Safety and Health Administration
PEL	Permissible Exposure Limit
PPE	Personal Protective Equipments
REACH	Registration, Evaluation, Authorization and Restriction of Chemical Substances
SOP	Standard Operating Procedures
TLV	Threshold Limit Values
WHO	World Health Organization

Glossary

HEPA Filter	HEPA is an acronym for "high efficiency particulate air". Basically HEPA is a type of filter that can trap a large amount of very small particles that other vacuum cleaners would simply recirculate back into the air.
Nanomaterials	Can be subdivided into nanoparticles, nanofilms and nanocomposites. The focus of nanomaterials is a bottom up approach to structures and functional effects whereby the building blocks of materials are designed and assembled in controlled ways.
Nanometer	Nanometer (nm) is one billionth of a meter.
Nanoparticles	A particle having one or more dimensions of the order of 100nm or less.
Nanotube	It can be regarded as segments of graphene (individual graphite layer) sheets that have been rolled up to form seamless cylinders.
Nanowires	Semiconductor nanowires are one-dimensional structures, with unique electrical and optical properties, that are used as building blocks in nanoscale devices.
NIOSH	The National Institute for Occupational Safety and Health (or NIOSH) is the United States federal agency responsible for conducting research and making recommendations for the prevention of work-related injury and illness.
N95	A particulate respirator with least 95% efficiency. The "N" means it is not oil resistant.
N100	N100 is NIOSH's highest particulate filtration rating, encompassing and exceeding N95. The "N" indicates it is not oil resistant and "100" means it will filter at least 99.97% of airborne particles.
PEL	The permissible exposure limit (PEL), is the maximum amount or airborne concentration of a substance to which a worker may be legally exposed.
PPE	OSHA requires the use of personal protective equipment (PPE) to reduce employee exposure to hazards when engineering and administrative controls are not feasible or effective in reducing these exposures to acceptable levels.
REACH:	It is a European Community Regulation on chemicals and their safe use (EC 1907/2006). It deals with the Registration, Evaluation, Authorization and Restriction of Chemical substances.
TLV	A threshold limit value (TLV), reflects the level of exposure that the typical worker can experience without an unreasonable risk of disease or injury

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