Interim Guidelines on the Safe Use of Engineered Nanomaterials

1. Introduction

Nanotechnology is the manipulation of matter on a near-atomic scale to produce new structures, materials, and devices. The technology is finding applications in an increasing number of areas, ranging from medical and pharmaceutical, through optoelectronic, electronic, data processing, cosmetic, material science to energy storage. As the applications of nanotechnology flourish in society, research activities involving nanotechnology have also increased rapidly in the past decade. It is estimated that US$9.8 billion was invested in nanotechnology research in 2009 and the figure is expected to rise annually.

Research and application of nanotechnology often involves the use of engineered nanomaterials (or nanoparticles) which are materials deliberately produced with at least one dimension between 1 and 100 nanometers. Nanomaterials often exhibit unique physical and chemical properties which may be very different from those of their corresponding bulk materials. These unique characteristics however, may have some undesirable effects on human health. Characteristics such as particle size, shape, surface area, charge, solubility, oxidant generation potential, and degree of agglomeration may play a role in inducing toxicity that is normally not observable with larger particles.

The University of Hong Kong, like many other world class research institutions, is also engaged in many nanotechnology research projects. It is the purpose of this guidance document to provide relevant researchers with the background information on nanotoxicology and the safe approaches they need to take to minimise the risk they may be exposed to in the course of their research.

2. Toxicity of Nanomaterials

Engineered nanomaterials have already found their way into many daily applications e.g. titanium oxide in photochemical air cleaning, zinc oxide in cosmetics and sunscreen products, copper oxide and silver in antimicrobial systems, and iron oxide in magnetic resonance imaging. While consumers may be exposed to nanomaterials through the use of these products, workers are also exposed to them in the manufacturing processes. In parallel with the research in nanotechnology, scientists are also researching into the potential toxic effects of engineered nanomaterials. "Nanotoxicology" is now a fast developing discipline worldwide. A few common types of nanomaterials, in particular, have been subject to many nanotoxicological studies in the past decade. These include studies in cell culture, animals and humans. Toxicological data is now accumulating and provides some evidence on the toxicity of nanomaterials at all levels of study. The four major types of nanomaterials most studied are: -

(1) Carbon nanotubes

These are allotropes of carbon with a cylindrical nanostructure. The structures are similar to that of graphite, but rolled into a cylindrical shape with extremely large length-to-diameter ratios. They can be singled-wall or multi-walled.

(2) Spherical fullerenes

These consist of repeating hexagonal and pentagonal rings of carbon atoms organised into a sphere. A common example is the C60 buckyball.

(3) Quantum dots

These are nanoparticles of semiconducting materials, metals or metal oxides. Because of their ultra-small sizes, they exhibit energy bands close to those of individual atoms and have tunable absorption and emission spectra over the visible range.

(4) Other nanoparticles

The common ones are carbon black, titanium dioxide, zinc oxide, iron oxide, platinum and silver.

In general, animal studies and in-vitro studies have provided evidence to indicate that nanomaterials can exhibit a higher toxicity than their corresponding bulk materials. For examples, carbon nanotubes, particularly multi-walled, are likely to be fibrogenic and carcinogenic to the lung. Nano titanium oxide can cause pulmonary inflammatory response on inhalation. Possible toxicological mechanisms suggested by scientists include surface activity in generating reactive oxidative species, insolubility in body fluids, penetration of biological membranes, persistence in the body, crossing of the blood-brain-barrier and direct migration in nerve fibres.

Some studies in workers exposed to aerosols of nanoscale particles have reported adverse lung effects. These observed health effects in humans are, however, uncertain.

3. Potential Health, Safety and Environmental Concerns in the Research Environment

Personnel engaged in research on nanotechnology may be exposed to engineered nanomaterials to different extents. Nanotechnology research such as nanolithography may not involve the handling of engineered nanomaterials, while others such as biomedical and composite material research may involve the direct handling of freely dispersed nanomaterials at various stages of the project. It is when engineered nanomaterials are handled without protective measures that research personnel may be at risk. The following processes are likely to result in exposure of research personnel to nanoparticles either by inhaling the particles into the respiratory system or absorbing the materials through the skin: -

- Weighing, dispensing, pouring and mixing of nanomaterials at an open bench.
- Cleaning and maintenance of equipment contaminated with nanomaterials.
- Working with nanomaterials in liquid media where a high energy output is involved like sonication or spraying liquids and handling without wearing gloves.
- Machining materials containing nanoparticles (e.g. sawing, polishing, grinding)
- Cleaning up spills and waste materials.

The improper disposal of waste nanomaterials into the general waste streams may also cause environmental hazards, though the effects on the flora and fauna are largely unknown because of the complicated processes of conglomeration and agglomeration in the waste media.

4. Safe Nanotechnology – A Precautionary Approach

While the scientific evidence on the toxicity of nanomaterials is accumulating, toxicologists and safety professionals are faced with the challenge of assessing the risk. Though the dose-response relationships for many chemical materials in the bulk form are known, similar relationships for their nano-counterparts are largely unknown. Conventional risk assessment for bulk materials is mostly based on a dose (or exposure) expressed in mass concentration. The toxicity of nanomaterials is however more dependent on particle numbers or surface area. There is also a lack of instruments which can accurately measure exposure expressed in particle numbers or surface area. These limitations have made risk assessment of nanomaterial exposure rather difficult. With the current uncertainties and limitations on exposure assessment, it is commonly agreed that a prudent approach should be taken. Precautionary measures should always be taken to minimise as far as reasonably practicable all exposure to engineered nanomaterials wherever the risk involved is uncertain. This approach should apply to both occupational risk and environmental risk.

5. Precautionary Measures

Based on the principle of prudence, outlined above, the following precautionary measures should be applied when designing and conducting research or teaching that involves engineered nanomaterials.

5.1 Safety Information

A proper Material Safety Data Sheet (MSDS) for each nanomaterial should be made available by the principal investigator (PI) in the laboratory where it is used.

5.2 Facilities Planning

The PI should review the facilities available in the laboratory where the nanomaterials are to be used. The purpose is to determine, before a project commences, what safety facilities are available or need to be acquired to control the risk. The PI should look into the ventilation system (in terms of both general and local exhaust, etc.) as well as the suitability of work surfaces ensuring they can be cleaned easily. Ideally, the laboratory should have a slight negative pressure relative to the corridor so that airborne nanoparticles, if any, will not spread to the outside. Some form of local exhaust ventilation with a filtration mechanism for nanoparticles should be available (see "Ventilation Control"). Work surfaces where nanomaterials are handled should be smooth, impermeable and free of joints and cracks for easy cleaning. A sink is needed for washing hands before leaving the worksite. If there is potential for spatters or spills of nanomaterials, an emergency shower and an eye wash are essential. It is also advisable to segregate the work area for handling nanomaterials, from the rest of the laboratory, so that other laboratory personnel not involved in nano-research are not exposed.

5.3 Safety Training and Instructions

The PI should provide general safety training and specific safety instructions to all those who handle the nanomaterials. For nanomaterials with known high toxicity, a Standard Operating

Procedure (SOP) should be developed and implemented.

5.4 Ventilation Control

It has been established that High Efficiency Particulate Air (HEPA) filters are effective in filtering out ultra-fine particles down to 2.5nm without suffering thermal rebound. So local exhaust ventilation equipped with a HEPA filter plus some form of enclosure is effective in controlling exposure to airborne nanoparticles. The HEPA-filtered exhaust air should be discharged to outside the facility as far as possible.

The use of the following is therefore suggested:

- A Class 1 or Class 2 Biological Safety Cabinet (BSC) is recommended for weighing, dispensing, applying, spraying or any form of handling of nanomaterials if no volatile or toxic chemical is to be used with the nanomaterials

- A fume cupboard equipped with HEPA filtration and ducted to the roof level of the building is recommended if volatile or toxic chemicals are used together with the nanomaterials

- Other forms of local exhaust ventilation equipped with a HEPA filter if the configuration of the experimental set up makes the use of a BSC or fume cupboard not feasible

- A glove box, if strict environmental control is needed and no volatile chemical is used. Glove boxes should be maintained at negative pressure so leaks are into the box rather than out of the box.

When one of the above is used to control nanomaterial exposure, it is advisable that the biological safety cabinet or fume cupboard has its internal surfaces decontaminated by wet-wiping after each use. It is also a good practice to dedicate a safety cabinet or fume cupboard exclusively for the use of nanomaterials if possible.

5.5 Personal Protective Equipment (PPE)

Whenever the risk of direct contact with nanomaterials or splashes cannot be avoided, it is essential that chemical resistant gloves and other relevant PPE such as laboratory coats, goggles and face shields are worn. The PPE should also be able to offer protection against any chemical matrix in which the nanoparticles are dispersed. Ventilation control should be the primary means of controlling exposure through inhalation. However, when ventilation control is not possible, the wearing of an appropriate respirator such as a half-face elastomeric respirator fitted with a HEPA filter may help to reduce the exposure to some extent.

5.6 Waste Disposal

Nanomaterials (including replaced HEPA filter which is contaminated with nanomaterials) should not be disposed of into the general waste streams. They should be treated as chemical waste. The Safety Office should be consulted on the specific procedures for chemical waste disposal.

5.7 Good Laboratory Practices

As with other chemical hazards, laboratory personnel handling nanomaterials should practice good personal hygiene at all times. Spilt nanomaterials or contaminated surfaces should be cleaned up using an industrial vacuum cleaner fitted with a HEPA filter or by wet-wiping. All procedures for handling nanomaterials should be designed to minimise aerosol formation.

5.8 Accidental Spills

When nanomaterials have been spilt, it is important that nearby personnel are alerted so that exposure to airborne nanoparticles is minimized. Depending on the amount and the type of material spilt, the room may have to be evacuated pending clean-up. Windows and doors should be kept closed. Clean-up should be done by either wet-wiping or vacuuming with an HEPA-fitted vacuum cleaner. Personnel doing the clean-up should put on the appropriate PPE as outlined in Section 5.5. All contaminated materials should then be treated as chemical waste.

6. Other Potential Hazards

Apart from the health risk that is directly attributable to the ultra small sizes of nanoparticles, nanotechnology research may also generate other hazards which are not unique to nanotechnology. For example, hydrothermal processes have become increasingly common in the synthesis of nanomaterials. The process typically involves the heating of aqueous chemical mixtures in an enclosed metal vessel, well above the boiling point of water, under self-generated pressure for a prolonged period of time. Hydrothermal vessels with safety devices (such as a pressure relief valve or a rupture disc, etc.) should be used instead of those without safety devices. They should be purchased from reputable manufacturers with clear certification/specification on the maximum working pressure and temperature. The use of hydrothermal vessels without such certification/specification poses an unknown risk to the users, and is not acceptable. A Standard Operating Procedure (SOP) for the hydrothermal process should also be established and observed.

Airborne nanoparticles in high concentrations may constitute a fire/explosion hazard because of their high surface area-to-volume ratio. Nanoscale materials can ignite up to 300 times faster than their corresponding micrometre-scale materials. It is therefore important to prevent the generation of high concentrations of nano-aerosols close to ignition sources such as spark producing equipment or a naked flame.

Some research has also suggested that nanoscale materials, because of their increased catalytic properties, may initiate chemical reactions that would otherwise not be anticipated. So, even chemically inert nanomaterials should not be mixed with chemicals unless it has been shown to be safe.

Use of various organic solvents may also be involved in the synthesis and application of nanomaterials. The solvents can be toxic or flammable, and may therefore pose a hazard to the users besides the nanotoxicity of the materials dissolved in them. In such cases, the usual safety precautions for using organic solvents should be observed, e.g. handling of organic solvents in fume cupboards and wearing chemical-resistant gloves.

7. Further Advice and Information

More comprehensive information on safe nanotechnology is available from the following documents:

1. BSI standards (2018) *PD ISO/TR 12885: 2018 Nanotechnologies – Health and safety practices in occupational settings.* British

Standards Institution.

2. European Commission (2014) *Working Safely with Manufactured Nanomaterials: Guidance for workers.* Employment, Social Affairs & Inclusion, European Commission.

3. European Commission (2013) *Guidance on the protection of the health and safety of workers from the potential risks related to nanomaterials at work. Guidance for employers and health and safety practitioners.* Employment, Social Affairs & Inclusion, European Commission.

4. HSE (2004) *Nanoparticles: An occupational hygiene review.* HSE Books. UK.

5. HSE (2013) *Using nanomaterials at work including carbon nanotubes (CNTs) and other biopersistent high aspect ratio nanomaterials (HARNs)* HSG272. Health and Safety Executive, UK.

6. HSE (2013) *The use of Nanomaterials in UK Universities: an overview of occupational health and safety.* Health and Safety Executive report, UK.

7. NIOSH (2012) *General Safe Practices for working with Engineered Nanomaterials in Research Laboratories.* Department of Health and Human Services, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health, DHHS (NIOSH) Publication No. 2012-147.

8. NIOSH (2016) *Building a safe program to protect the nanotechnology workface: A guide for small to medium-sized enterprises.* Cincinnati, OH: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health, DHHS (NIOSH) Publication No. 2016-102.

9. NIOSH (2018) *Workplace design solutions: protecting workers during the handling of nanomaterials.* Cincinnati, OH: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health, DHHS (NIOSH) Publication No. 2018-121.

10. Safe Work Australia (2009) *Engineered Nanomaterials: Evidence on the effectiveness of workplace controls to prevent exposure.* Safe Work Australia.

11. Safe Work Australia (2015) *Engineered Nanomaterials: An update on the Toxicology and Work Health Hazards.* Safe Work Australia.

12. UKNSPG (2016) *Working Safely with Nanomaterials in Research & development.* The UK NanoSafety Partnership Group.

13. World Health Organization (2017) *WHO Guidelines on protecting workers from potential risks of manufactured nanomaterials.* World Health Organization.

You may also visit the following websites for the latest information:

- US NIOSH Nanotechnology Topic Page
  http://www.cdc.gov/niosh/topics/nanotech/default.html
- UK HSE Nanotechnology Page
  http://www.hse.gov.uk/nanotechnology/