Guidance and safety requirements for the creation and manipulation of engineered nanomaterials

Definition and Scope
This guidance is intended to assist Principle Investigators in the creation or manipulation of nanomaterials in undertaking risk assessments and developing control strategies that will ensure as fair as reasonably practicable that staff and students are not exposed to any unnecessary risk in relation to the use of nanomaterials.

Nanoparticles are usually defined as having one or more external dimensions in the order of 100nm or less i.e.: < 0.1 micrometre/micron. This guidance generally relates to controlling exposure at work to any potentially hazardous engineered particles in the nano or submicron range. To put this into context, a human hair is approximately 70,000 nm in diameter, a red blood cell is approximately 5,000 nm wide and simple organic molecules have sizes ranging from 0.5 to 5 nm.

Regulatory framework
The existing UK regulatory framework is seen as sufficiently covering the safe use and handling of manufactured nanomaterials. The applicable regulations are:

- The Control of Substances Hazardous to Health Regulations 2002
- The Dangerous Substances and Explosive Atmospheres Regulation 2002

Health Effects
It has been established for many years that exposure to particles causes health effects related to:

- **the dose -** i.e. the amount, duration and frequency of exposure
- **the toxicity -** for relatively insoluble particles, this appears to relate to the total surface area of the particles

Most of what is known about the health effects of particles relates to exposure by inhalation, and so in these cases it is the dose of particles reaching the lungs which is the key issue. The general mechanism understood to cause health effects in the lung is inflammation through a process known as oxidative stress. Inflammation due to oxidative stress can then lead to a number of diseases including asthma, cancer and COPD.

The risk from nanoparticles relate primarily to three main issues:

1. Because of their small size, nanoparticles can reach parts of biological systems which are normally not accessible by other larger particles. This includes:
    - The increased possibility of crossing cell boundaries, or
    - Of passing directly from the lungs into the bloodstream and so on to all of the organs in the body,
    - Through deposition in the nose, directly to the brain,
    - Through skin absorption or penetration

This process is known as translocation and in general, nanoparticles can translocate much more easily than other larger particles.

2. Because of their small size, nanoparticles have a relatively much higher surface area than the same mass of larger particles. If surface area is a driver for toxicity this clearly implies potentially increased toxic effects
3. A third issue is that the whole rationale for developing nanomaterials and nanoparticles is that they will have new and different properties than larger particles of the same material. If this is the case, it is certainly conceivable that these new properties could include increased toxicity.

It must be noted that there are currently no Workplace Exposure Limits specifically for nanoparticles. The information contained within the Material Safety Data Sheet [MSDS] for a substance in conventional micron size, cannot be regarded as relevant for the same substance in the nano range.

Comparisons between carbon nanotubes [CNTs] and asbestos

Asbestos has a fibrous nature with high aspect ratio (the ratio of length to diameter). Exposure to asbestos by inhalation causes disease because the particles can enter into the alveolar region of the lung. Macrophages (a type of cell) in the lung which act to clear particles by ingesting them and transporting them out of the lung, cannot take up the fibres because of their physical dimensions. Asbestos fibres are also highly durable and do not dissolve in the lung lining fluids. Hence they remain in the lung for a long period of time, causing inflammation and ultimately disease. Some forms of carbon nanotubes are likely to have similar morphology (shape) to asbestos making it difficult for macrophages to absorb them and will be highly durable and so may also persist in the lungs giving rise to similar concerns.

To date few studies have been published on the human effects of novel nanoparticles, though one study of particular note is Song et al [Eur Resp J, 2009; 43; 559-567]. There is an increasing body of evidence from animal studies that nanoparticles could be harmful in humans and therefore for this guidance document requires researchers to **adopt a precautionary approach** – i.e. Human exposure to nanoparticles generated through work activity must be eliminated or reduced to the lowest reasonable practicable level possible within current technology.

Fire and explosion properties of nanopowders

There is currently little available information on the explosion risks of these materials. The Health and Safety Executive therefore commissioned a research project to investigate the potential fire and explosion hazards associated with nanopowders. Generally, the explosibility of nanopowders were found to be broadly similar to conventional micron-scale powders. However, the minimum ignition energies of some nanopowders were found to be lower than the equivalent material at micron-scale. It was demonstrated that with increasing relative humidity the resistivity of most nanopowders decreases. There was also a tendency for nanopowders to have higher resistivity values than conventional micron-scale powders. All the powders produced electrostatic charge. Generally, the charge developed by nanopowders was comparable with the micron-scale powders. The full research report can be found at: http://www.hse.gov.uk/research/rrpdf/rr782.pdf

Risk management strategy

As with any procedure involving the use of hazardous substances the most important requirement is to undertake a risk assessment and identify the control measures that must be employed. For nanomaterials the primary concern will be the health effects due to inhalation, skin contact or ingestion. However consideration must also be given to the fire and explosion risk and control measures that may be required under DESEAR. In carrying out the risk assessment and identifying the appropriate risk control strategies the following hierarchy of controls must be applied:

- Consider first if there is any way of avoiding manipulation of nanomaterials, particularly in powder form.
- Consider the form which the nanomaterial is in and any manipulations within the process which will generate free nano powders or aerosols of solutions containing nano materials.
- If no other approach can be found any such manipulations should be undertaken in a ducted fume cupboard or other suitable local exhaust ventilation [LEV]. The risk assessment must determine whether it should be fitted with a HEPA filter on the extract taking into consideration the nature and quantity of nanomaterial used. Ductless recirculating HPA filtered cabinets and microbiological safety cabinets [MSCs] can be used for small quantities [1mg] subject to rigorous maintenance and performance checks to ensure they are effective at all times. Consideration must also be given to the safe removal of the HEPA filter should this be required. More details guidance on use of LEV and fume cupboards can be found in Appendix 1, page 8.
- In the case where the nanomaterial is in solution avoid aerosol production and where this is not possible, contain the process in a HEPA filtered fume cupboard/MSC.
- Seek to minimise the quantities of nanomaterials handled, the frequency and duration of use and the number of people potentially exposed.
- Employ handling methods that reduce the chance of the material becoming airborne- keep the material wet or damp.
- Employ suitable personal protective equipment:
    - Gloves - use single use Category 3 PPE gloves. Two layers of glove material are recommended as nanomaterials can diffuse into the skin across the skin barrier.
    - Respiratory protective equipment may be appropriate for powders, however this should only be worn in addition to other control measures for dealing with emergencies/spills outside of the primary containment. Employees using tight fitting RPE must be fully trained in its correct use and have had face fit testing. The RPE must have an assigned protection factor [APF] of 40 or higher.
    - Protective clothing should be such as polyethylene textiles [e.g. Tyvek] which does not retain dust or allow it to penetrate.
- All workers required to work with nanomaterials must be trained and competent in good working practices and in the use of any LEV and PPE. This must be recorded.

The project summary from Appendix 2, page 9 should be used to assist in the risk assessment process.

Labelling, cleaning up, waste disposal, transport, emergencies
Containers which are known to contain engineered nanomaterials must be clearly labelled to show that contents contain particles of nanoscale size.

Use wet wiping techniques for cleaning work areas and avoid use of vacuum cleaners unless they are HEPA filtered and are designed to minimise the risk of ignition of an combustible nanomaterials.

Waste nanomaterials, contaminated wet wipes, HEPA filters and protective clothing/gloves should be double bagged and incinerated as hazardous waste. No free nanomaterials should enter any non-hazardous waste stream or be disposed of via the drains.

Risk assessment must define suitable procedures for dealing with process equipment that needs to be cleaned for re-use to ensure that other workers involved in this are aware of the procedure and not put at risk.

Nanomaterials being transported between labs and buildings must be appropriately enclosed, double contained and labelled.

Emergency procedures and equipment must be in place to deal with spills, accidents and emergencies.

Health surveillance and recording exposure
Health surveillance is only appropriate in circumstances where:

- There is a disease associated with the substance in use (e.g. asthma, dermatitis, cancers)
- It is possible to detect the disease or adverse change [i.e. a biological effect] and reduce the risk of further harm
- The conditions in the workplace make it likely that the disease will appear

There is currently no research data to suggest any biological effect that could be monitored and, providing the control measures detailed above are adopted and adhered to, individuals' exposure will be effectively zero. Therefore health surveillance is not considered appropriate or necessary. Additionally, as there is no known safe level of exposure, there is little value in recording every time a material in nano form is handled/dispensed; however Schools/Departments must ensure that there is a recording system in place that enables individuals who have been involved in such work to be identified. This can best be achieved by ensuring that a list of authorised users is appended to the risk assessment for the procedure in which the nanomaterial is used [See Appendix 3].

The procedural risk assessment must include the following information:

- Title of project/procedure
- The full chemical name of the nanomaterial
- Quantity normally used in the procedure
- The form [powder or powder in solution]
- Name of responsible scientist/ PI
- A list of authorised users involved in the work including the date they started on the project and the date they finished

These records must be kept for 40 years. A suggested pro-forma for the record sheet to be appended to the risk assessment is included at Appendix 2.

Accident/incident recording
Where an incident occurs, that results in the potential or actual exposure of any individual to nanomaterial, even if there is no apparent health effect, it must be recorded on the University Accident/Incident reporting system. The Safety Office must be immediately informed as such an occurrence may be reportable to the HSE.

A copy of the incident report will be forwarded to Occupational Health who will review the circumstances of the exposure and ensure an appropriate entry is made on the individual's health record, and if deemed necessary invite the individual to attend for an appointment.

The above records must be kept for 40 years and be available for inspection.

Maintenance and monitoring of control measures

Fume cupboards/LEV
It is critical that LEV achieves and maintains adequate control of exposure at all times. The system requires regular maintenance, periodic monitoring to ensure controls are working and thorough examination and testing by a competent person at periods not greater than 14 months and more frequently if the assessment indicates a higher risk.

In addition you should establish a suitable frequency of regular in-house testing, training local users in how to undertake these checks. Records must be kept of daily, weekly and monthly checks, in addition to the checks undertaken by the competent person.

Environmental monitoring
It should be noted that nanoscale particles are widely occurring in work places from sources such as combustion, vehicle emissions and infiltration of outside air. Monitoring for airborne nanoparticles is an area under development and there is currently no consensus on what is the best method. As information becomes available this guidance will be updated.

Appendix 1

Additional information on Local Exhaust Ventilation [LEV]

Conventional ducted fume cupboards [FCs] and microbiological safety cabinets [MSCs]
Conventional ducted fume cupboards and microbiological safety cabinets may be used for handling nanomaterials.

It is important that a fume cupboard complies with BS EN 14175-4:2003 and on-site containment tests should be carried out to ensure effective containment. Where CNTs are used an additional robustness test must be carried out on the fume cupboard. The test only needs to be done once to make sure the fume cupboard contains under the condition described in the standard. The fume cupboard exhaust should be HEPA filtered, before venting to a safe place outside.

Microbiological safety cabinets conforming to BS N 12469:2000 of all classes can be used. The Class II and III microbiological safety cabinets, unlike the Class I type, provide protection for both the user and the material in the cabinet's working environment. All these cabinets exhaust air through a HEPA filter.

Ductless, recirculating fume cupboards and recirculating microbiological safet cabinets
These types of unit rely on effective filtration. They draw laboratory air over the work, through a dust filter, a carbon filter (and/or a HEPA filter) and return the cleaned air to the laboratory. They are designed to reduce the airborne concentrations of certain aerosols or vapours to acceptable levels. They are **not** designed to handle toxic substances.

Recirculating fume cupboards should conform to BS 7989:2001.

Recirculating MSCs exhaust 30% of the air through the exhaust HEPA filter in the top of the cabinet back into the room, with 70% going into the cabinet via another HEPA filter.

Because of the uncertainty about the risk of exposure to nanomaterials, the precautionary, good practice approach is not to use recirculating fume cupboards or cabinets for work with nanomaterials in quantities exceeding 1mg or for any work with CNTs.1

Appendix 2

University of Nottingham project summary assessment for working with engineered nanomaterials

Appendix 2 is available as a separate Word document from the Safety Office Website.

Appendix 3

Authorised user record form

This form is for appending to risk assessment of nanomaterial work. Appendix 3 is available as a separate Word document from the Safety Office Website.